This work is protected by copyright and other intellectual property rights and duplication or sale of all or part is not permitted, except that material may be duplicated by you for research, private study, criticism/review or educational purposes. Electronic or print copies are for your own personal, non-commercial use and shall not be passed to any other individual. No quotation may be published without proper acknowledgement. For any other use, or to quote extensively from the work, permission must be obtained from the copyright holder/s.

Assessment of fracture risk tools in care home residents

Felix Emwinghama Ihama

Thesis submitted for Doctor of Medicine
December 2019
Keele University

Abstract

Introduction

Fragility fractures are common in care home residents. National guidelines recommend risk assessment to allow initiation of prophylactic measures. Currently available risk assessment tools have been tested in community dwelling adults but not in care home residents. It is possible that one or more of the existing tools are also practicable in this population.

Aim

The aim of this project was to identify fracture risk assessment tools which are usable in care home residents and to determine which is the most suitable for use in this population.

Objectives

1. To conduct a systematic literature review of existing fragility fracture risk assessment tools and select those that can be used in care home residents.
2. To develop a composite questionnaire which can be used to test the identified fragility fracture risk assessment tools in a care home population. This will be done by using the covariates in each tool to design a questionnaire, the acceptability of which will be assessed by consultation visits to two care homes to aid its refinement.
3. To undertake an observational pilot study of the fragility fracture risk assessment in a cohort of care home residents
4. To design a Clinical Algorithm.

Methods

1. A literature search was performed by a combination of electronic and manual literature searches and studies of assessment tools potentially usable in a care home population were selected and assessed based on content and quality criteria. The search was updated on 12/08/2019
2. A questionnaire was designed based on information from the literature review and tested by a cross-sectional survey in two care homes in Staffordshire.
3. A cohort observational study was conducted using the above questionnaire in 18 care homes in Boston, Lincolnshire, England.

Results

1. In the systematic review, 33 fragility tools were identified and four were potentially practicable in care home residents. These were: FRAX, QFractureScores, Garvan nomogram and Body Mass Index (BMI). The updated search identified a fifth-measure micro ribonucleic acid (miRNA). However, this was not implemented.
2. A composite questionnaire and information leaflet were designed and refined following feedback gleaned from the consultation visits.
3. In the feasibility study 217 (35%) participants out of 618 residents in the 18 care homes were enrolled. Out of the 217 participants, 147 (68%) had mental capacity and only 70 (32%) did not. This was because there was difficulty in obtaining informed consent from the consultees in residents without mental capacity.
4. Low BMI and history of dementia were identified as the risk factors for falls, fractures and combined falls and fractures in the cohort. Charlson Commorbidity Index predicted mortality ($p= 0.034$) and a score of $\geq 36\%$ was identified as the threshold for identifying participants who would not benefit from treatment. These three variables were used to design a Clinical Algorithm.

The fragility tools were easy to use given that the average duration for assessment was between 1 and 2 minutes. BMI of 25kg/m² or less had the highest sensitivity of 74.5% for falls. The sensitivity and specificity of FRAX and Garvan nomogram were not calculated because neither tool predicted falls, fractures or combined falls and fractures. The odds ratios for the prediction of the outcomes were as follows: FRAX falls 1.003, SE 0.011 (p=0.813), fractures 1.027, SE 0.024 (p=0.267), combined falls and fractures 1.027, SE 0.024 (p=0.267); QFractureScores falls 1.007 SE 0.005 (p=.160), fractures 1.024, SE 0.011 (p=0.036), combined falls and fractures 1.024, SE 0.011 (p=0.036); Garvan nomogram fall, 1.010, SE 0.005 (p=0.054), fractures 1.021, SE 0.011 (p=0.0620, combined falls and fractures 1.021, SE 0.011 (p=0.062); BMI falls 0.952, SE 0.021 (p=0.015), fractures 0.868, SE 0.073 (p=0.024), combined falls and fractures 0.868, SE 0.073 (p=0.024). Of the 10 incident fractures, 40% occurred in the participants who had dementia.

Conclusions

The systematic literature review identified many fragility risk assessment tools, but only four were potentially practicable in a care home population. Recruitment to the observational study was restricted mainly to residents who possessed mental capacity, because it was difficult to obtain consultee consent in this setting.

Although the fragility tools were easy to use, generally they had poor screening performance for the prediction of falls. BMI of 25kg/m² had the highest sensitivity. BMI was the best predictor of falls, fractures and combined falls and fractures but the associations were weak. QFractureScores was a predictor of fractures and combined falls and fractures. Neither FRAX nor Garvan nomogram were predictors of these outcomes. Of the 10 incident fractures, 40% were observed in participants who had dementia despite the small representation of this group, thus dementia is a strong risk factor for fractures in this cohort.

A fully powered and representative study is unlikely to be feasible, if individual consent is required, as the majority of care home residents do not have mental capacity, and legal representative consent is difficult to obtain in this setting. The results of this thesis suggest that BMI and dementia are strong predictors of falls and fractures. An algorithm was then designed using these to guide selection of suitable residents for treatment.

List of Contents

Declaration x

Dedication xi

Acknowledgements xii

Copyright and Ownership rights xv

Abbreviations xvi

List of tables xx

List of figures xxii

List of appendices xxiii

Chapter 1: Introduction and Background Information 1

1.1 Introduction 1

1.2 Fragility fractures 6

1.3 Aims and objectives of this study 66

Chapter 2: Risk Assessment Tools to identify those useable for Care Home Residents: A Systematic Review 69

2.1 Abstract 69

2.2 Background 71

2.3 Methodology 73

2.4 Results 83

2.5 Discussion 128

2.6 Conclusion 153

Chapter 3: Consultation visits to two Care Homes to determine the acceptability of a fragility risk assessment questionnaire 157

3.1 Abstract 157

3.2 Background 158

3.3 Methodology 161

3.4 Results 165

3.5 Discussion 170

3.6 Conclusion 173

Chapter 4: Observational study of falls and fracture in a care home population **174**

4.1 Abstract 174

4.2 Background 177

4.3 Methodology 177

4.4 Results 199

4.5 Discussion 218

Chapter 5: Exploratory analyses of the data of the Observational study and Clinical Algorithm **230**

5.1 Abstract 230

5.2 Background 232

5.3 Methodology 232

5.4 Results 233

5.5 Discussion 253

Chapter 6: General Discussion and Conclusions **273**

6.1 Introduction 273

6.2. The systematic review 274

6.3. The Consultation visit 275

6.4 The Prospective Observational Study 276

6.5 Exploratory analysis 278

6.6 Implications of the findings 281

6.7 The need for research in Care Home residents and the challenges 287

6.8 Strengths and weaknesses of the study 290

6.9 Recommendations for future reference 290

6.10 Conclusions 291

6.11 Funding source and conflict of interest declaration 292

References 293

Appendices 343

Declaration

I hereby declare that no portion of this thesis has been submitted for another degree or qualification to another Institution. This research has been entirely self-funded and I have received no financial assistance to conduct it. The views expressed are from the results of the study.

Dedication

This thesis is deservedly dedicated with great respect to the memory of my late parents: Deaconess Deborah Imarenakhue Ihama and Chief Moses Idumwonyi Ihama, for their steadfast support and unwavering devotion. Sadly, they died in 1997 and 1998 respectively. In my eyes, they were the role models of good parenting. They taught me early in life that what is worth having is worth sweating for. This thesis underpins the principle they always believed: ‘engaging in activities that make the world a better place for others’.

Acknowledgements

The arduousness of writing this thesis has been more than compensated for by the privilege of meeting with many people from whom I have learnt much. These people have touched my life so profoundly as to defy categorisation or description. I have found working with them a totally positive experience as a researcher because they shared their wisdom, knowledge and truth and demonstrated infinite patience and commitment. The author is particularly indebted to the following:

The Almighty GOD, the first, last and always, the source of all knowledge, wisdom, truth, strength and life itself. To you, Lord, my creator, mentor, friend, partner be glory, honour and dominion now and forever, Amen.

Professor Christine Roffe, the chief supervisor. Christine was never too busy to organise meetings and share her vast wealth of experience in research. Words alone cannot do justice to her faultless supervisory skills, commitment and the stylistic advice generously provided when I started to write the thesis. She provided extremely helpful, detailed and constructive comments and demonstrated the virtues of patience, understanding, humility and kindness which are qualities individuals should aspire to acquire. Many thanks Christine.

Professor A D Pandyan, the co-supervisor. I wish to record my admiration for the constructive criticisms of the structure of the thesis and the expertise in data analysis of the relevant sections.

Dr Frank Lally, Keele University independent adviser. Frank organised several one to one sessions to ensure that the reports were up to the standard required for the Doctor of Medicine degree progression, peer review and IRAS application.

Dr John Belcher, Keele University (Statistician) for his advice on the number of participants needed for the observational study and Dr Yuhua Su, Dr Su Statistics, Hawaii, USA (Statistician) for the power calculation for future studies.

My modular teachers at Keele University for educating me on the basic tenets in research methodology.

The Librarians: Rachael Gick and Scott McGowan both of Keele University, for the invaluable support with RefWorks. Liz Carr and Joanna Criddle both of ULHT, for the punctiliousness in retrieving the desired articles and proof reading the manuscript.

Jane Thorn and Lucy Hampsted, Information Technology (IT) trainers (ULHT), Catherine Boreham (ULHT) my secretary and Osarodion Ihama my son, IT Consultant (Copenhagen, Demark) for assistance with some of the herculean job of word processing involved.

My family, for allowing me the space and time to undertake this research and particularly my wife Cherrida Ihama for her tolerance.

To Dr Patrick Osayande, my brother, Marian Ekebafe, my niece, Dr Lawrence Ekebafe, my brother in-law, Professor Nosakhare Eghafona and Sunny Agbontaen, my dear friends for their encouragement and prayers.

I would also wish to give formal acknowledgement to the International Osteoporosis Foundation (IOF), Oxford University Press, United Lincolnshire NHS Trust (ULHT) and Wikipedia for copyright permission for some of the materials used in this thesis.

Copyright and Ownership Rights

All rights reserved. No part of this thesis may be reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, recording, or by any information storage and retrieval systems without the prior written permission of the author who will describe the terms and conditions of such agreement.

Abbreviations

AP : Anand Pandyan

ADL: Activity of Daily Living

AUC: Areas Under Curve

BGS: British Geriatrics Society

BMD: Bone Mineral Density

BMI : Body Mass Index

BOA: British Orthopaedic Association

BPT: Best Practice Tariff

BTM: Bone Turnover Marker

CCI: Charlson Comorbidity Index

CDC: Centre for Disease Control and Prevention

CI: Confidence Interval

CKS: Clinical Knowledge Summaries (of NICE)

CQC: Care Quality Commission

CR: Christine Roffe

CRF: Clinical Risk Factor

CTF: Catch The Fracture

DALY: Disability-Adjusted Life Year

DEXA: Dual Energy X-ray Absorptiometry

DM: Diabetes Mellitus

DOES: Dubbo Osteoporosis Epidemiology Study

DOH: Department of Health

EMA: European Medicine Agency

EPIDOS: Epidemiology of Osteoporosis Study

FI: Felix Ihama

FFA: Falls and Fracture Alliance

FFN: Fragility Fracture Network

FLS: Fracture Liaison Service

FRAX: Fracture Risk Assessment Tool

GDP: Gross Domestic Product

GP: General Practitioner

HI: Hospital Inpatient

HR: Hazard Ratio

ICD: International Classification of Disease

IGCP: International Guidelines for Good Medical Practice

INDEC: Intituto Nacional de Estadistica y Censos

IOF: International Osteoporosis Foundation

IQR: Interquartile range

IRAS: Integrated Research Application System

MeSH: Medical Subject Headings

MOH: Ministry of Health

MUAC: Mid Upper Arm Circumference

NFPCG: National Falls Prevention Coordination Group

NHR: Nursing Home Resident

NHFD: National Hip Fracture Database

NHS: National Health Service

NHANES: National Health and Nutrition Examination Survey

NICE: National Institute for Health and Care Excellence

NIHR: National Institute for Health Research

NOF: National Osteoporosis Foundation

NOGG: National Osteoporosis Guideline Group

NOS: National Osteoporosis Society

OECD: Organisation for Economic Co-operation and Development

OFELY: Os des Femmes de Lyon (Prospective population-based study of the determinants of bone loss)

OG: Oral Glucocorticiod

OPCS: Office of Population Census and Surveys

OR: Odds ratio

PDF: Portable Document File

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis

PROFET: Prevention of falls in the Elderly Trial

PSSRU: Personal Social Services Research Unit

QUADAS: Quality Assessment of Diagnostic Accuracy Studies

QUALEFFO: Quality of Life questionnaire of the European Foundation for Osteoporosis

QALY: Quality Adjusted Life Year

QUS: Quantitative Ultrasound

RCP: Royal College of Physicians

R&D: Research and Development

RH: Residential Home

ROC: Receiver Operating Characteristic

RR: Relative Risk

SD: Standard Deviation

SE: Standard error

SHA: Strategic Health Authority

SIGN: Scottish Intercollegiate Guide Network

SOF: Study of Osteoporosis Fracture

TUGT: Timed Up & Go Test

UK: United Kingdom

ULHT: United Lincolnshire Hospitals NHS Trust

USA: United States of America

USD: United States Dollar

UVB: Ultraviolet light type B

WHI: Women Health Initiative

WHO: World Health Organisation

WMA: World Medical Association

List of Tables

1. Age-standardised hip fracture rates in some Scandinavian countries 10

2. Age-standardised hip fracture rates in some countries in Asia/Australasia 11

3. Age-standardised hip fracture rates in some countries in the Middle East 12

4. Age-standardised hip fracture rates in some countries in Africa 13

5. Age-standardised hip fracture rates in some countries in North and South America 14

6. Age-standardised hip fracture rates in some countries in Europe 15

7. Elderly and ‘old old` population in some countries 20

8. Population of persons age 60 years and over in some countries 22

9. Numbers of hip fractures in Pilgrim Hospital, Boston, Lincolnshire UK 34

10. Mortality of fracture neck of femur in Pilgrim Hospital 38

11. Cost of three common diseases in Pilgrim Hospital 42

12. The tools in the first part of the systematic literature review 85

13. Review articles of the systematic literature review 88

14. Summary of prospective data of meta-analysis of systematic literature review 91

15. Summary of case-control data of meta-analysis of systematic literature review 93

16. Demography of study population of Meta-analysis of BMI 95

17. Relative risk of fracture with and without BMD in meta-analysis 97

18. Demography of the participants of the original articles of the systematic literature review 100

19. Methodology of the original studies of the systematic literature review 104

20. Findings from the original studies of the systematic literature review 109

21. Scores of studies on QUADAS of the systematic literature review 114

22. Summary of the responses of the tools on QUADAS 115

23. Characteristics of the fragility risk assessment tools identified from the original articles of systematic literature review 119

24. Predictors in the fragility tools identified for care home residents 127

25. The composite questionnaire 167

26. Recruitment and mental capacity of residents in the 18 care homes 202

27. Baseline characteristics of the participants 205

28. Duration of fragility risk assessment of each tool 207

29. Telephone interview survey of 20 care home managers in Lincolnshire 208

30. Screening performance of the fragility tools 211

31. Summary of the screening performances of the tools 212

32. Mean scores of the participants on each of the four fragility tools in the pilot study 214

33. Odds ratios of binary logistic regression models 216

34. Falls and fractures in residents and participants 235

35. Falls in each of the 18 care homes 237

36. Fallers with and without fracture in each of the 18 care homes 240

37. Odds ratios of binary logistic regression models 242

38. Demography and clinical characteristics of the three subgroups 245

39. Anti-fracture efficacy of approved treatments for postmenopausal osteoporosis 285

List of Figures

1. Proportion of hospital admission (stroke, heart attack, breast cancer and osteoporotic fractures) 33

2. Flow diagram of the first part of the systematic literature review 84

3. Flow diagram of the second part of the systematic literature review 124

4. A map showing Lincolnshire 181

5. A map of Lincolnshire showing Boston 182

6. Flow diagram showing recruitment of the participants 201

7. Box plot of body mass index of the three subgroups of the participants 251

8. Algorithm for the prevention of fragility fractures in care home residents 284

.

List of Appendices

Appendix A: IRAS approval 343

Appendix B: IRAS approval for minor amendment 347

Appendix C: Research & Development approval 349

Appendix D: Letter of invitation to participants 351

Appendix E: Participant information sheet 352

Appendix F: Letter of invitation to consultee 358

Appendix G: Consultee information sheet 359

Appendix H: Consent form 365

Appendix I: Consultee form 367

Appendix J: Letter to General Practitioner 369

Appendix K: Research pathway 370

Appendix L: Template of screening log 373

Appendix M: Scoring system of the composite questionnaire 374

Appendix N: Definition of terms 379

Appendix O: The QUADAS 381

Appendix P: The order of selection of the care homes 382

Appendix Q: The Power calculation for future studies 383

Appendix R: Data extraction template 385

Appendix S: Pilgrim Hospital named best Hospital in the Country for Hip Fracture Management 386

Chapter 1 Introduction and background information

1.1 Introduction

Fragility fractures are common in older people. Globally in the year 2000, there were an estimated 9 million new fractures (Johnell, Kanis, 2006). 1 in 2 women over 50 years of age and 1 in 5 men will sustain a fracture (Van Staa et al., 2001, Kanis et al. on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis [ESCEO] and the Committee of Scientific Advisors of the International Osteoporosis Foundation [IOF], 2012). In the next two decades, almost half a billion people will reach retirement age and as this demographic shift ensues, fragility fractures will be expected to increase. Fragility fractures affect many bones in the body but the most frequently affected sites are the vertebrae, wrist and hips. The two determinants of fragility fractures are trauma and impaired bone strength, both of which are common in older people. Fragility fractures are associated with high morbidity, mortality and the cost associated with managing them is substantial (Johnell, Kanis, 2004). Both hip and spinal fractures are associated with a higher risk of death; twenty percent or more of those who suffer hip fractures die within 6 months after the fracture and the burden of care of fragility fractures is increasingly being felt in every continent (Johnell, Kanis, 2006).

With the anticipated exponential increase of the ageing population, many older persons will be admitted to care homes and fragility fractures will be expected to increase in this cohort. Consequently, a well-coordinated, systematic global approach at primary prevention through risk assessment is needed because once a fragility fracture has occurred secondary prevention

is less effective, thus the identification of high risk older people is a priority (Torgerson, Gosden & Reid, 1997).

With the advances in medical research, the scope for reducing fragility fractures has increased through collaborative initiatives such as contained in the Blue Book (The British Orthopaedic Association, 2007), which provided a summary of current knowledge and evicence based treatment recommendations and the National Hip Fracture Database (NHFD) (RCP, 2018), both pionnered in the United Kingdom. The NHFD provides a benchmarking care and allows units to also monitor their case-mix, outcomes and offer the opportunity to conduct large scale multi-centre research in hip fractures. More recent guidance for fragility fracture prevention has been published by NICE in 2016 (NICE 2016) and the NHS RightCare (Public Health England, National Osteoporosis Society, and the NHS RightCare) in 2017. These include recommendations for service organization, pharmaceutical treatments, and therapy interventions. The NHS RightCare Pathway recommends that Commissioners responsible for Falls and Fragility Fractures for their population should focus on the three priorities for optimisation:

- Falls prevention
- Detecting and managing Osteoporosis
- Optimal support after a fragility fracture

These objectives can be achieved by working across the system to ensure that schemes to deliver the higher value interventions are in place by :

- Targeted case-finding for osteoporosis, fraility and falls risk
- Strength and balance training for those at low to moderate risk of falls

- Multi-factorial intervention for those at higher risk of falls
- Fracture liaison service for those who have had a fragility fracture

The document recommend that Commissioners should use the Falls Prevention Consensus and Resource Pack especially the implementation checklist

Preventing falls requires a multifactorial approach, including targeted case finding, comprehensive assessment of risk factors and implementation of appropriate interventions (Close et al 2001). Pharmaceutical treatments for osteoporosis include medications which increase bone strength. These drugs offer protection against fractures due to minor trauma and include alendronate or risedronate as first line prevention of fragility fractures for the majority of cases. For patients who are intolerant of oral bisphosphonates or in whom they are contraindicated, intravenous bisphosphonates or denosumab provide the most appropriate alternatives, with raloxifene or hormone replacement therapy as additional options. But these are not useful in care home residents many of whom are very old. The high cost of teriparatide restricts its use to those at very high risk, particularly for vertebral fractures (NOGG 2017). These measures should be supplemeted with lifestyle and dietary measures. A daily calcium intake of between 700 and 1200 mg should be advised through dietary intake if possible, with use of supplements if necessary. The recommendations for calcium and vitamin D intake for different groups of people are detailed in NICE guidiance of 2016 and this is discussed in more details in chapter 6 of this thesis.. Regular weight bearing exercise should be advised, tailored according to needs and abilities of the individual patient (NOGG 2017).

The most effective healthcare solution to fracture prevention is the Fracture Liaison Service (FLS) (McLellan et al., 2003) which is designed to identify and assess patients presenting with new fractures. Between half and two thirds of patients with hip fractures would have had a prior fracture therefore secondary prevention is important because fracture begets fracture (Klotzbuecher et al., 2000, Kanis et al., 2004). The FLS is an integrated service which is usually delivered by a Nurse Specialist supported by a Lead Clinician in Osteoporosis in a `one stop` FLS clinic for appropriate patients. In addition to other routine tests, all patients who are aged 50 years and over presenting with a fragility fracture should undergo assessment of osteoporosis by axial bone densitometry. Appropriate patients are offered bone protection therapy as this has shown 50% reduction in fracture incidence during 3 years of treatment. The guidance for treatment is detailed in the National Institute for Care Excellence (NICE) Technology Appraisal document (NICE 2016) as well as new guidance issued by the National Osteoporosis Guideline Group (NOGG 2017); recommendations from the Scottish intercollegiate Guidelines Network (SIGN) guideline have been incorporated (SIGN 2015). Appropriate patients should be referred to the falls service.

Most fragility fractures result from minor trauma, often falls, but only a minority of these are complicated by fractures (Tinetti, Williams, 1997). To identify people who can potentially sustain fractures from falls, risk assessment is a key (The National Falls Prevention Coordination Group (NFPCG), 2017). Almost 40 years ago, the World Health Organization (WHO) commissioned a report on screening. The report published in 1968 was entitled “Principles and practice of screening for diseases” (Wilson, Jungner, 1968). The criteria presented in the report are still upheld today as classics (Hall, Stewart-Brown, 1998), the gold

standard of screening assessment (Linnane, Paul & Parry, 1999), having stood the test of time (Population cancer screening in Canada, 2002).

The practice of the report relies heavily on screening tools. With regards to falls and factures, there are currently no validated tools exclusively for care home residents. It is therefore important to conduct a study to identify the best fragility tool within the existing pool or to create a new tool for use in this cohort. There are inherent difficulties in conducting research in care homes and the aims of this research are to conduct a pilot study to determine the recruitment rate, identify if the existing scores for fracture risk have relevance for care home use in the frail elderly, is it easy to apply the tools and can a clinical algorithm be developed as most tools are there for 10 year prediction risk (not relevant in a care home population).

In chapter 1 of this thesis a discussion of the background information relating to the relevant aspects of fragility fractures will be presented. Chapter 2 (project 1) is the systematic literature review of fragility risk assessment tools. Chapter 3 (project 2) is a report of the consultation visit to two care homes to access the acceptability of the questionnaire designed from the results of the systematic review. Chapters 4 and 5 (project 3) are the reports of the observational study in care homes in Boston using the questionnaire from project 3 and finally, chapter 6 will present the highlights of each chapter and the clinical algorithms which were developed from the study. The methodology of each project will be presented in the corresponding chapters.

1.2 Fragility fractures

1.2.1 Definition of Fragility Fractures

A fragility fracture is defined as a fracture that occurs spontaneously or results from low energy trauma (low-level trauma) (Kanis et al., 2001)**.** The World Health Organisation (WHO) has quantified this as forces equivalent to a fall from a standing height or less (National Institute for Clinical Excellence (NICE), 2012b). In simple terms, fragility fractures occur because bones with reduced strength are subjected to critical forces which often arise from minor trauma (Pasco et al., 1999). Individuals susceptible to low energy trauma are also more likely to sustain fractures following heavy impact injuries. Although the above definition is generally accepted, there are views that fragility fractures should now be defined in terms of age and bone mineral density (BMD) (Stone et al., 2003, Seeley et al., 1991) because they are the two strongest risk factors.

If it is a fragility fracture, the argument is that it should be related to low BMD and or advancing age because age and bone mineral density (BMD) are the strongest known risk factors. Using these criteria for diagnosis has the merit of eliminating the ‘low energy trauma or standing height’ criteria, which are both subjective assessments. Some fractures such as skull, facial, ankle and digital fractures are not considered osteoporotic because they are neither related to the degree of trauma, BMD or age. Fragility fracture is used synonymously with osteoporotic fracture. *Osteo* means `bone` and *porosis* means `porous`.

1.2.2 The Incidence and Prevalence of Fragility Fractures

Fragility fractures show differences in their patterns of incidence by age, sex, ethnic group, geographical area and season, and many of these differences are unexplained (Kanis et al. 2012). Globally, fragility fractures occur every 3 seconds and a vertebral fracture every 22 seconds. This translates to about 25,000 fractures daily or 9 million annually (Zanchetta, 2012). Europe and the Americas accounted for 51% of the fragility fractures, while most of the remainder occurred in the Western Pacific region and South East Asia. Worldwide in 1990, there were about 1.65 million hip fractures; by 2050, it is estimated there will be 6.3 million with 50% predicted to occur in Asia and Latin America (Cooper, Campion & Melton, 1992). Osteoporotic fractures occur in about 0.5% of the population per annum in some countries such as the United States, European countries and Australia (Access Economics Pty Limited, 2001).

The Surgeon General`s report in the United States of America (USA) estimated 1.5 million fragility fractures occurred in people over 50 years old in 2004 and over 34 million are at risk because of the ageing population (US Department of Health and Human Services., 2004). Assuming there is a constant age-specific hip fracture risk and a projected increase of people aged 65 years and over, this will result a three-fold increase of hip fractures from 32 million in 1990 to 69 million by 2050. In 2010, there were 3.5 million new fractures comprising approximately 620,000 hip fractures, 520,000 vertebral fractures, 560,000 forearm fractures and 1,800,000 other fractures in Europe. This number will rise to 4.8 million by 2025, an increase of 28% if no treatment is given. In Europe, the Scandinavian countries currently have the highest prevalence of osteoporotic fractures, which is more than would be expected from

the demographic changes in age and sex ratio (Cooper, Campion & Melton, 1992). In the United Kingdom in 2010, there were approximately 536,000 new fragility fractures of which 70,000 were hip fractures; this is predicted to increase to 91,500 in 2015 and 101,000 in 2020 (British Orthopaedic Association, 2007).

An audit on fragility fractures in South America also showed increased incidence and prevalence of fragility fractures in both sexes in most countries (Zanchetta, 2012). The same trends were observed in many countries in Asia. For example in Japan, the incidence of hip fracture, which was one of the lowest in the world, has increased 1.6-fold in men and 1.5-fold in women between 1980 and 1998. (Mithal, 2013). Fracture data from the Middle East show a similar trajectory (Fuleihan et al 2011). There are scarce data on fragility fractures from many countries in Africa, other social conditions causing more burdens. Less than 3% of the population is over 65 years old and the life expectancy is 57 years. However the limited data available suggest the same pattern (Zebaze, Seeman, 2003).

The age-standardised hip fracture rates in some countries in different regions of the world, Scandinavia, Asia, Middle East, Africa, North & South America and Europe, are shown in tables 1 to 6**.** These tables are presented separately to highlight the global nature of the problem. These tables show that hip fracture rates are highest in European countries and epidemiological data show that hip fractures are most common after the age of 80 years. The life span in many developing countries is currently below this.

Table 1 shows a transient unexplainable decrease in some Scandinavian countries which have the highest incidence of fragility worldwide. Between 1983 and 1984 in Norway, the age-adjusted rates of hip fractures were 1293 and 561 in females and males respectively, but these decreased to 563 and 263 between 1994 and 2008 (Maggi et al., 1991). Similarly, between 1972 and 1981 in Sweden, the age adjusted rates for hip fractures were 622 and 291 in females and males respectively; by 1991, these had decreased to 539 and 247 respectively (Maggi et al., 1991, Kanis et al., 2012).

There is no clear reason why the incidences in Sweden and Norway declined over time, but it is in line with the development of several other health problems (Modig et al., 2013 Karampampa et al., 2014). Socioeconomic and clinical factors could have contributed to the change. In Sweden, the age-specific risk for a first and subsequent hospitalisation decreased (Karampampa et al., 2014) suggesting that the occurrence of chronic illnessness such as cardiovascular disease decreased (Modig et al., 2013, Marks 2010). These well recognised risk factors for hip fractures decreased over time; changes in life style factors among the elderly such as smoking cessation could also have contributed (Abrahamsen Vestergaard 2010). Also, the rising trends of body weight among the elderly, a protective factor for hip fracture (Abrahamsen, Vestergaard, 2010) could have played a part (Dey et al., 2001)

Table 1: Age-standardised hip fracture rates (per 100,000) in three Scandinavian countries

Country	**Source**	**Age-adjusted rates/100,000 in females (1972 – 2005)**	**Age-adjusted rates/100,000 in males (1972 - 2005)**
Norway	Finsen et al. 1987 Emaus et al. 2011	1293 (1983-84) 563 (1994-08)	551 (1983-84) 263 (1994-08)
Sweden	Hedlund et al. 1987 Kanis et al. 1991	622 (1972-81) 539 (1991-92)	291 (1972-81) 247 (1991-92)
Denmark	Frandsen et al. 1983 Abrahamson et al. 2010	620 (1973-79) 574 (2004-05)	203 (1973-79) 290 (2004-05)

Source: adapted from (Kanis et al., 2012)

Table 1 shows the age-standardised hip fracture rates in three Scandinavian countries. Between 1983 and 2008 in Norway, there was a decrease in hip fracture rates in both females and males. Between 1972 and 1991 in Sweden, there was a decrease in hip fracture rates in both females and males. Between 1973 and 2004 in Demark, there was a decrease in hip fracture rates in females but increase in males. These data show there was a consistent reduction in hip fracture rates in females and in males (except in Denmark) in these countries for over two decades.

Interpretation: The countries are located in the same geographical area and they may have had a common and effective strategy to address the problems of hip fractures. The Swedish and Norwegian cost estimates indicate that the medical care for osteoporotic fractures represent 1 to 2% of the total health expenditure (Christensen, Brixen & Kristiansen, 2003).

Table 2: Age-standardised hip fracture rates (per 100,000) in some countries in Asia/Australasia

Country	Source	Age-adjusted rates/100,000 in females(2007-2013	Age-adjusted rates/100,000 in males(2007-2013
Australia	Crisp et al. 2012	295	170
China	Xia et al. 2012	229	129
Japan	Orimo et al. 2007	180	50
Republic of Korea	Yoon et al. 2011	207	98
Singapore	Asia-Pacific Audit 2013	402	152
Thailand	Wongtriratanachai et al. 2013	368	136

Source: adapted from (Kanis et al., 2012) and the International Osteoporosis Foundation (IOF) Asia-Pacific Regional Audits 2009 & 2013

Table 2 shows the age-standardised hip fracture rates in some countries in Asia. The data show variation in the hip fracture rates; the hip fracture rate is highest in Singapore in females and lowest in Japan in both females and males. In both sexes, the rates are higher in Singapore and Thailand compared to the other countries.

Interpretation: The data suggest that compared to the other countries, hip fracture rate was lowest in Japan because of the good prevention programmes. These include prevention of falls and osteoporosis through education appropriate to each age group, guidance on maintenance of adequate weight, active intake of calcium, weight-bearing excercises, diet and treatment with pharmacological drugs (Orimo, et al 2012). The Ministry of Health, Labour and Welfare in Japan has performed osteoporosis screening since 1995 and the number of examinees was 295,434 in 2006. In 2009, Japan had a total of 10,369 DEXA machines (0.8/10000) which was high compared to other countries (MOH of Japan). In 2009, Singapore had a total of 14 DEXA machines with the scanner availability of 0.15/10,000 and Thailand a total of 50 DEXA machines with a scanner availability of 0.008/10,000 (Mithal, Lau, 2009). Also, the Japanese traditional lifestyle, nutritional habits, genetic differences in body build and more fracture-resistant bones have been suggested (Fujita, 1994).

Table 3: Age-standardised hip fracture rates (per 100,000) in some countries in the Middle East

Country	**Source**	**Age-adjusted rates/100,000 in females(1995-2013)**	**Age-adjusted rates/100,000 in males(1995-2013)**
Iran	Moayyeri et al 2006	165	127
Lebanon	Sibal et al 2011	164-188	88-107
Saudi Arabia	Al Nuaim et al 1995	135	77
Kuwait	Asia Pacific Audit 2013	295	200

Source: adapted from (Kanis et al., 2012) and the IOF Middle East & African Regional Audit 2011

Table 3 shows the age-standardised hip fracture rates in some countries in the Middle East. The data show variation: the hip fracture rate is highest in Kuwait, intermediate in Iran and Lebanon, and lowest in Saudi Arabia.

Interpretation: The variation in hip fracture rates could be due to: differences in the: healthcare delivery programmes, BMD due to vitamin D deficiency, physical activity, body build, alcohol intake and data collection methods. (Maaloufet al,2007). Solid epidemiological research on osteoporosis and related outcomes is scarce at best; access to densitometry and care is limited in many countries often only available in urban centres; reimbursement for diagnostic and therapeutics varies widely; the level of awareness of osteoporosis among primary healthcare professionals is estimated as poor to medium in many countries; education and lifestyle prevention programmes for the general public are generally lacking (Fuleihan, Adib 2011)**.**

Table 4: Age-standardised hip fracture rates (per 100,000) in two countries in Africa

Country	Source	Age-adjusted rates/100,000 in Females(1991-2011)	Age-adjusted rates/100,000 in Males(1991-2011)
Morocco	Middle East & Africa Regional Audit 2011	52.1	43.7
Nigeria	Adebajo et al 1991	2	2

Source: adapted from (Kanis et al., 2012) and the IOF Middle East & African Regional Audit 2011

Table 4 shows the age-standardised hip fracture rates in two countries in Africa. The data show variations; the hip fracture rate is low in Nigeria and higher in Morocco.

Interpretation: The same explanation for table 3 also holds. West Africa appears to be uniquely different with respect to osteoporosis. A study published in Nature reviewed hip fracture incidence worldwide and included a chart of age standardised osteoporosis rates. The Nigeria values were 2 hip fractures per 100,000 females whereas that of Norway was 532 (Cauley et al., 2014). A 2-year project conducted by Zebaze and colleagues (Zebaze et al., 2003) in the West African nation of Cameroon reported a low energy trauma rate for females over 35 years at 4.1 per 100,000.

This uniquely low rate did not cause any surprises in the medical community because it was theorized as far back as 1966 that Africans did not suffer from post menopausal osteoporosis because of short life expectancy, a more active life style than Westerners and lack of medical facilities to track and record osteoporosis (Adebajo 1989, Nordin, 1966). But these assumptions proved incorrect when osteoporosis rates were compared within regions of Africa that shared similar life expectancies and socio-economic conditions.

Genetic tests have shown that Africans have a more efficient process of calcium homeostasis compared to European ethnicities despite being low to non-diary consuming (Redmond et al., 2014), this more than makes up for the reduced calcium intake resulting in low rate of osteoporsosis. The preferences for the traditional methods of fracture management may also underscore published data (Nottidge, Akpanudo & Akinbami, 2011, Nwadiaro et al., 2008).

Table 5: Age-standardised hip fracture rates (per 100,000) in three countries in North and South America

Country	**Source**	**Age-adjusted rates/100,000 in Females(2010-2012)**	**Age-adjusted rates/100,000 in Males(2010-2012)**
Columbia	Latin America Regional audit 2012	234.9	116.5
USA	Ettinger et al 2010	260	122
Canada	Kanis et al 2012	290	131

Source: adapted from (Kanis et al., 2012) and the IOF Latin America Regional Audit 2012

Table 5 shows the age-standardised hip fracture rates in three countries in North and South America. Although the data were taken from two different continents, the hip fracture rates are comparable.

Interpretation: The hip fracture rates are comparable. In the Latin America Regional Audit of osteoporosis in 2012, the organisers reported scarcity of robust data and the lack of national databases and fracture registries in many countries in South America (Zanchetta, 2012).

Table 6: Age-standardised hip fracture rates (per 100,000) in some countries in Europe

Country	**Source**	**Age-adjusted rates/100,000 in Females(2012)**	**Age-adjusted rates/100,000 in Males(2012)**
UK	Kanis et al 2012	349	140
Italy	Kanis et al 2012	334	140
Spain	Kanis et al 2012	228	92

Source: adapted from (Kanis et al., 2012) .

Table 6 shows the age-standardised hip fracture rates in three countries in Europe. The hip fracture rates are comparable in the UK and Italy but lower in Spain.

Interpretation: The hip fracture rate was lowest in Spain. Spain is leading Europe in the number of Fracture Liaison Services (FLS) throughout the country. By the end of January 27, 2017 there were 33 clinics or hospitals listed in the *Capture the Fracture (CTF) Map of Best Practice*, an online map which reflects FLS around the world that have signed up to International Osteoporosis International`s (IOF) CTF programme (International Osteoporosis Foundation (IOF), 2018).

Summary: Tables 1 to 6 show the regional variations in hip fracture rates. They highlight the interactions of multiple risk factors: ageing, cultural and religious practices, dietary influences, availability of medical resources, environmental influences and other unidentified factors therefore the interpretations for the observations is not simplistic.

Wrist fractures show a different pattern of occurrence from hip and vertebral fractures. The incidence increases in white women from 45 to 60 years, followed by a plateau. This plateau might relate to altered neuromuscular reflexes seen with ageing, which are associated with a tendency to fall sideways or backwards, meaning that the fall is not stopped with an outstretched arm (Melton, et al 2001). Fracture of the proximal humerus is considered to be one of the most important fractures attributable to osteoporosis. In the elderly, it is the third most frequent fracture after hip fracture and Colles` fracture (Seeley, et al 1991, Lauritzen, et al 1993)

Pelvic ring fractures in the elderly are generally due to relatively trivial trauma and do not, as a rule, cause haemodynamic instability, nor are they associated with intrapelvic organ injuries of the surrounding soft tissues (Rommens, et al 2017). Burge et al reported that pelvic ring fractures in the elderly accounted for 75 of all osteoporosis-associated fractures (Burge, et al 2007). Andrich et al. reported an incidence of 22.4 osteoporosis-associated fractures per 10, 000 persons over 60 per year in Germany (Andrich, et al 2015), while a retrospective analysis revealed that the incidence of pelvic ring fractures among persons aged 80 or above in Finland rose over the 1970 - 1997 from 73 to 364 per 1 000 000 per year. Likewise, Sullivan et al. found that the number of pelvic ring fractures among elderly persons in the USA rose by 24% (from 26 500 to 33 000) over the period 1993 – 2010 (Sullivan, et al 2014).

1.2.3. Secular Trend in the Incidence of Fragility Fractures

Some causes have been suggested for the world-wide secular trends of fragility fractures: ageing population, vitamin D deficiency and urbanisation associated with relative global

socioeconomic prosperity. Changes in bone mineral density (BMD) do not appear to play major roles in some regions. For example, a study from Sweden showed that between 1970 and 2001, the age-specific incidence of hip fracture increased by 100% but there was no substantial increase in BMD (Ahlborg et al., 2004). Physical inactivity probably due to socioeconomic prosperity has been suggested. There is epidemiological evidence linking physical inactivity with the risk of hip fracture incidence (Berard, Bravo & Gauthier, 1997). Urbanisation has resulted in environmental pollution which blocks the sun rays (specifically UVB radiation) required for the synthesis of vitamin D in the skin, contributing to widespread vitamin D deficiency in some regions such as Asia (Mithal 2013). Vitamin D deficiency is now recognised as pandemic (Holick et al., 2008).

A systematic review found that in areas where data were available, the prevalence of low vitamin D was a problem in all age groups even in countries with sun exposure all year round (Palecus et al., 2014). The problem was greater in the Middle East particularly in girls and women. There was striking lack of data in most countries of South America and Africa. The high prevalence of vitamin D deficiency may be related to several factors such as reduced vitamin D photosynthesis in the skin of people with high melamin content or due to ageing, use of extensive skin coverage and scarce exposure to sunlight in individuals in Africa, the Middle East and Central and South America.

In addition the high rates of obesity worldwide could also have contributed because vitamin D may become `trapped` inside fat tissue so that less of it is available to circulate inside the blood (Vanlint 2013). Season appears to be a small cause of the problem as countries with

long winters have less deficiency rates overall compared to sunny countries. This is probably related to the fortification of staples, comsumption of fatty fish and regular use of vitamin D supplements.

Urbanisation has resulted in higher prevalence of harder surfaces on which people fall (Johnell et al., 2007). Sudden impact fractures happen when a bone takes a sudden hard hit that puts more stress on it than it can handle at once. Urbanisation may partly explain the changes in the risk in immigrant populations. For example, the African Americans in USA have lower incidence of fractures compared to Caucasians, but the incidence of hip fractures in Blacks in the USA is much higher than in African Blacks (Cauley et al., 2008, Cauley et al., 2010). Similarly, fracture risk is different in the Japanese population of Hawaii (Ross et al., 1991) and Chinese living in Hong Kong and Singapore compared with mainland China (Kanis et al., 2012).

Fractures incidences have been observed to be higher in colder days and winter seasons (Campbell et al., 1988, Nevitt et al., 1993a, Nevitt et al., 1993b, Douglas et al., 2000) but a 5-year local survey in Pilgrim Hospital, Boston England by this investigator (FI) using the National Hip Fracture Database (NHFD) found that 51% of the hip fractures occurred in warmer seasons of spring and summer months most likely because of the higher number of people given that east Lincolnshire is a holiday destination (Royal College of Physicians (RCP), 2017a).

But the greatest factor in the worldwide increase in fragility fractures is the unprecedented increase of the ageing population which has been observed in recent decades. Because of the global ageing population, it has been projected that over half of all hip fractures worldwide will occur in Asia by 2050 (Lau, Cooper, 1996). The projected increase in the population of the elderly and `old old` in some developed countries is presented in Table 7. From the age of 65 years, falls, osteoporosis and fragility fractures are common. To put this in context, approximately 75% of hip, spine and distal forearm fractures occur in people who are ≥65 years old.

At the biological level, ageing results from the impact of the accumulation of a wide variety of molecular and cellular damage over time. This leads to decrease in physical and mental capacity, a growing risk of disease and ultimately death (WHO 2018). Globalisation, technological developments, urbanisation, migration and changing gender norms are influencing the lives of people directly and indirectly leading to the increasing number of surviving generations.

Of the current world population of 7.5 billion, people aged 65 years and above account for 7.9% (Kanis et al., 2005b). Life expectancy has increased by about 30 years in many western countries during the last century (Christensen et al., 2009, Rossi, Rousson & Paccaud, 2013). It is estimated that the population of people aged 80 years and over in Europe will increase by between 160% in females and 239% in males in the next few decades (Kanis et al., 2005b).

Table 7: Elderly and 'Old old' population in some developed countries

Country	Elderly (65+) as a percentage of total population in 1997	Elderly (65+) as a percentage of total population in 2025	'Old old' (80+) as a percentage of total population in 1997	'Old old' (80+) as a percentage of total population in 2025
France	15.6	23.7	3.8	6.4
Sweden	17.5	22.7	4.9	6.8
United Kingdom	15.8	21.1	4.1	5.8
Russia	12.5	18.2	2.1	3.4
Ukraine	14.1	18.1	2.4	3.9
Romania	12.7	19.5	2.0	4.7
Australia	12.3	20.4	2.8	5.4
Japan	15.5	26.8	3.3	8.9
United States of America	12.7	18.5	3.2	4.3

Source: adapted from the 2nd edition Oxford Textbook of Geriatric Medicine (Grimley Evans et al., 2000).

Table 7 shows the percentage of elderly and 'old old' in some developed countries. The data show that the projected increase will be highest in Japan and lowest in some Eastern European countries and USA.

Interpretation: The proportion of people aged 65 years and over and 80 years and over is increasing in North America, Europe and Oceania.

Over the last 25 years, the number of people aged 85 years and over in the United Kingdom has more than doubled to 1.4 million and it is estimated that by 2035, this figure will rise to 3.5 million with people aged 85 years and over accounting for 5% of the total population (Office for National Statistics (ONS), 2014). The number of older Americans is steadily increasing and by 2030, 20% of the US population will be aged 65 and older (National Center for Health Statistics (NCHS), 2004). In Asia, a 7.6-fold increase in elderly is predicted between 2000 and 2050 (Mithal, Lau E, 2010). In 2000, approximately 46% of men aged 80 years and older were from Asia, this is projected to rise to 60% by 2050. The population over age 60 years in sub-Saharan Africa (50 countries) will increase by 90% between 2006 and 2030; older people currently account for less than 5% (Kinsella, 1993). The projected increase in the population of older people in some developing countries is shown in Table 8**.**

A recent study showed that there is more than 50% probability that by 2030, national female life expectancy will supersede the 90-year barrier, a level that was deemed unattainable at the turn of the 21st century (Kontis et al., 2017). The forecast is that life expectancy will be highest in South Korea, some western countries and some emerging economies. The *World Population Prospects*: *The 2017 Revision*, published by the United Nations Department of Economic and Social Affairs (United Nations 2017), provides a comprehensive review of global dermographic trends and prospects for the future. Among the ten largest countries worldwide, Nigeria is growing most rapidly. Consequently, the population of Nigeria, currently the world`s 7th largest, is projected to surpass that of the United States of America and become the third largest country in the world shortly before 2050.

Table 8: Proportion of persons aged 60 years and over in four developing countries

Countries	**Year 1970**	**Year 1995**	**Year 2020**
China	6.8	9.3	15.5
Brazil	5.3	7.7	13.5
India	5.9	7.2	11.0
Zimbabwe	4.2	4.3	6.2

Source: adapted from the 2nd edition Oxford Textbook of Geriatric Medicine (Grimley Evans et al., 2000).

Table 8 shows the proportions of persons aged 60 years and over in four countries. The data show that the projected increases are comparable in China, Brazil and India and lowest in Zimbabwe.

Interpretation: Within the next decade, countries in Asia and South America will experience an increase in the proportion of the ageing population. There will also be an increase in African countries but this will be slower. According to data from recent population predictions, the number of older persons – those aged 60 years or over – is expected to more than double by 2050 and to more than triple by 2100, rising from 962 million globally in 2017 to 2.1 billion in 2050 and 3.1 billion in 2100. Globally, population aged 60 or over is growing faster than all younger age groups.

Currently, Europe has the greatest percentage of population aged 60 or over (25 per cent). Rapid ageing will occur in other parts of the world as well, so that by 2050 all regions of the world except Africa will have nearly a quarter or more of their populations at ages 60 and above (United Nations 2019).

Compared to 2017, the number of persons aged 60 or above is expected to more than double by 2050 and to more than triple by 2100, rising from 962 million globally in 2017 to 2.1 billion in 2050 and 3.1 billion in 2100. In Europe, 25% of the population is already aged 60 years or over. That proportion is projected to reach 35% in 2050 and to remain around that level in the second half of the century. Populations in other regions are also projected to age significantly over the next several decades and continuing through 2100. Africa, for example which has the youngest age distribution of any region, is projected to experience a rapid ageing of its population.

Although the African population will remain relatively young for several decades, the percentage of its population aged 60 or over is expected to rise from 5% in 2017 to around 9% in 2050, and then to nearly 20% by the end of the century. Globally, the number of persons aged 80 or over is projected to triple by 2050, from 137 million in 2017 to 425 million in 2050. By 2100 it is expected to increase to 909 million, nearly seven times its value in 2017. Population ageing is projected to have a profound effect on societies, underscoring the fiscal and political pressures that the health care, old-age pension and societal systems of many countries are likely to face in the coming decades. The underlying causes of fragility fractures in the ageing population can be divided into two: trauma and weakness in bone strength. This will be the subject of the next narrative.

1.2.4 Causes of Fragility Fractures

The key causes of fragility fractures are falls (Cummings, Melton, 2002) and compromised bone strength (Cummings, Black, 1995, Grisso et al., 1991a, Grisso et al., 1991b, Cummings, Faulkner & Cauley, 1993) and both are common in care home residents (Kron M et al 2003).

Bone strength depends on the bone mass (BMD) and bone quality which in turn depends on a variety of the qualitative aspects of bone structure. Bone quality describes aspects of bone composition and structure that contribute to bone strength independently of BMD. These include bone turnover, microarchitecture, mineralisation, micro-damage and composition of the bone matrix (Compston, 2006).

A systematic review and meta-analysis on risk factors for falls in community-dwelling older people identified a total of 74 studies (Deandrea et al., 2010). The strongest associations were found for history of falls (OR was 2.8 for all fallers and 3.5 for recurrent fallers), gait problems (OR2.1), walking aids use (OR2.2), vertigo (OR1.8), Parkinson`s disease (OR2.7) and antiepileptic drug use (OR1.9). For other factors, the ORs were moderately above 1 and the ORs were generally higher for recurrent fallers than for all fallers.

A systematic review and meta-analysis for risk factors for falls in nursing homes residents (NHR) and hospitals inpatients (HI) found the following: for NHR, the strongest associations were history of falls (OR3.06), walking aid use (OR2.08), and moderate disability (OR2.08). For HI, the strongest association was found for history of falls (OR2.85). No association was found with age in NHR (OR1.00) while the OR for a 5 years increase in age of HI was 1.04. Female sex was associated with decreased risk (Deandrea et al., 2013). Although dementia was not specifically mentioned as a risk factor in the two systematic reviews, the risk factors which were identified are directly or indirectly associated with dementia

The risk factors for bone strength can be sub-divided into two: non-modifiable and modifiable. Modifiable risk factors are those that can be treated or modified by appropriate intervention, whereas the non-modifiable factors cannot be altered by any intervention. The evidence base for the list reported here is from the systematic literature review by the Scottish Intercollegiate Guideline Network (Scottish Intercollegiate Guidelines Network (SIGN), 2015) and meta-analyses (Kanis et al., 2005a).

The non-modifiable risk factors are age, gender, ethnicity, previous fracture, family history of fragility fractures and reproductive factors (age at menarche of 16 years and over and early natural menopause before the age of 45 years). The potentially modifiable risk factors are: bone mineral density (BMD), alcohol intake, weight, smoking, and physical inactivity; coexisting diseases: diabetes mellitus, inflammatory rheumatic diseases, gastrointestinal diseases, cystic fibrosis, epilepsy, human immunodeficiency virus, primary hyperparathyroidism and other endocrine diseases, chronic liver disease, neurological disorders (Alzheimer’s, Parkinson`s disease, stroke), depression, chronic kidney disease and asthma; pharmacological factors: anticoagulants, antidepressants, anticonvulsants, antipsychotics, aromatase inhibitors and tamoxifen, beta-blockers, benzodiazepines, hormonal contraception, gonadotropin-releasing hormone agonists, loop diuretics, acid suppressive drugs, statins, glucocorticoids, and antidiabetic agents.

1.2.4.1 Assessment of Bone Mineral Density (BMD)

T-scores have been traditionally used to define BMD. It is a measure of how closely bone density compares to that of an average 30-year old female (Meeta et al. 2013). The World Health Organisation (WHO) considers the following scores as the standard:

- T-score above -1 is considered normal bone mass
- T-score between -2.5 and -1 is low bone mass (also called osteopenia)
- T- score between -2.5 and below is considered osteoporosis
- T-score between -2.5 and below with a history of a fracture is considered severe osteoporosis

.

The original intention of WHO was to choose a threshold that would make osteopenia and osteoporosis uncommon at the time of the menopause, on the assumption that bone loss began at that time. Thus the diagnostic threshold of a T-score between -1 SD and -2.5 SD was anticipated to capture 50% of the population. It is now evident that bone loss occurs from the proximal femur at a much earlier age (Melton, et al 2009). The other measure which has been largely ignored is the Z-score which compares bone density with people of the same age and sex and is a more realistic assessment as it compares “apples to apples”

Osteoporosis is a condition characterised by a reduction in bone mass and density and increases the risk of fracture when a person falls. Osteoporosis has been dubbed the `silent epidemic` as it can often goes unnoticed until a fracture occurs. Osteoporosis is the most common metabolic bone disease and it affects up to 40% of postmenopausal women (Ray et al., 1997). The reference value is the NHANES III reference database for femoral neck

measurements in women aged 20-29 years (Looker et al., 1997). The NHANES is a population-based survey by the Centers for Disease Control and Prevention in the USA designed to collect information on the health and nutrition of the US household population. NHANES uses a stratified multistage and cluster sampling design to obtain a representative sample of the non-institutionalised civilian US population which involves detailed home interview and health examination conducted in a mobile centre. Beginning in 1999, the NHANES became a continuous annual survey rather than the periodic survey that it had been in the past (Centers for Disease Control and Prevention (CDC), 2001).

BMD using dual-energy absorptiometry (DEXA) scan is the current gold standard for the diagnosis of osteoporosis. But over 50% of women who sustained fragility fractures have BMD above the WHO-definition of osteoporosis (Nguyen et al., 2007b). Given the limitations of BMD in fracture prediction, molecular markers of bone metabolism known as bone turnover marker (BTM) have been suggested as novel tools which detect the dynamics of bone remodelling to complement the measurement of BMD in the detection and management of fragility fractures.

The adult skeleton is continuously remodelled; old bone is removed by osteoclasts and new bone is formed by osteoblasts. During skeletal growth, bone formation exceeds bone resorption resulting in net gain of bone. However, later in life bone resorption exceed formation particularly among oestrogen-deficient postmenopausal women and all older individuals. Prolonged bone loss leads to low BMD and eventually osteoporosis (Bauer 2019). BTMs are grouped into two based on the metabolic phase of bone: bone formation markers

and bone resorption markers. Detailed discussion of BTMs is beyond the remit of this thesis. Fragility fractures may result in adverse health outcomes to individuals and society and the impact will be the focus of the next discussion.

1.2.5 Costs and Health Impact of Fragility Fractures

Fragility fractures are associated with high morbidity and mortality (Cummings, Melton, 2002, Lips et al., 1997) and because its human and societal cost is projected to increase with the ageing population, the World Health Organisation (WHO) requested the Director-General to formulate a global strategy for the prevention of this disease (Johnell et al., 2005).

1.2.5.1 Morbidity Associated with Fragility Fractures

Hip fracture is the most serious type of fragility fracture taking up an average of 1.5 million bed days each year, which equates to more than 4,000 NHS beds (RCP, 2016). About 19% of orthopaedic beds were occupied by patients with fractured hip in 2016 (Moran, et al 2018). The number of bed days for hip fracture patients in Canada is predicted to increase from 465,000 in 1993/94 to 1.8 million by 2041 (Chen et al., 2009). Hip fractures account for substantial hospital admissions in the USA, of which 140,000 are nursing home admissions (Melton, 2003); this is projected to increase to 289,000 by 2030 (Stevens, Rudd, 2013). The degree of morbidity is related to age and the type of fracture. Chrischilles and colleagues showed that following hip fracture, 14% of patients aged 50 to 55 years were discharged to care homes compared to 55% of patients aged 90 years and above (Chrischilles et al., 1991).

A case-control study showed that hip fracture patients were 4.2 times more likely to be unable to function in the wider community two years after the fracture and 2.6 times more likely to be functionally dependent than controls (Norton et al., 2000). A report from Northern Sydney area in Australia showed that after 12 months' follow-up of community dwelling patients who had hip fractures, 76 % were unable to walk as well as before their fracture and 22% required nursing home admissions (March, Chamberlain & Cameron, 1996).

A meta-analysis on the long-term disability of hip fractures showed that 20% of the participants with a fracture were no longer able to shop independently and 42% had not returned to their pre-fracture mobility levels after a year (Bertram et al., 2011). One prospective study showed that only 8% could climb stairs compared with 63% before the fracture and 6% could walk half a mile compared with 41% before the fracture (Marottoli, Berkman & Cooney, 1992). A cause of the excess morbidity is new osteoporotic fractures which occur at a rate of 10.4 per 100 patients per year; this is 2.5 times as high as the rate in age-matched persons without previous hip fractures (Colon-Emeric et al., 2003a).

Some studies have demonstrated impairment of health status in patients with vertebral fractures (Pluijm et al., 2000, Cook et al., 1997). Osteoporotic specific questionnaires showed decreased quality of life in patients with vertebral fractures compared with controls and the quality of life decreased with increasing number of prevalent vertebral fractures. Men have greater functional impairment from vertebral deformities compared to women (Burger et al., 1997). The Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) is the most frequently used questionnaire for measuring health related quality

of life of patients with osteoporosis and vertebral fracture (Oleksik et al., 2000). The total QUALEFFO score is calculated as the sum of all the responses and then linearly transformed in the scale 0 to 100. The higher the score, the worse the health related quality of life (HRQOL).

The impact of spinal fractures appears to be greater with lumbar fractures compared to thoracic fractures (Pluijm et al., 2000, Cook et al., 1997). Patients with three thoracic fractures had a mean score of 35.6 ± 19.7, three lumbar fractures had a mean score of 53.2± 15.8, and people without fracture had a mean score of 25.6 ± 14.3 (Silverman et al., 2004). In contrast to fractures of the spine and hip, wrist fractures do not seem to be associated with increased morbidity. Although wrist fractures can impact some activities such as writing or meal preparation, few patients are completely disabled, despite overall reporting only fair-to-poor function at 6 months post fracture (Chrischilles, et al 1991).

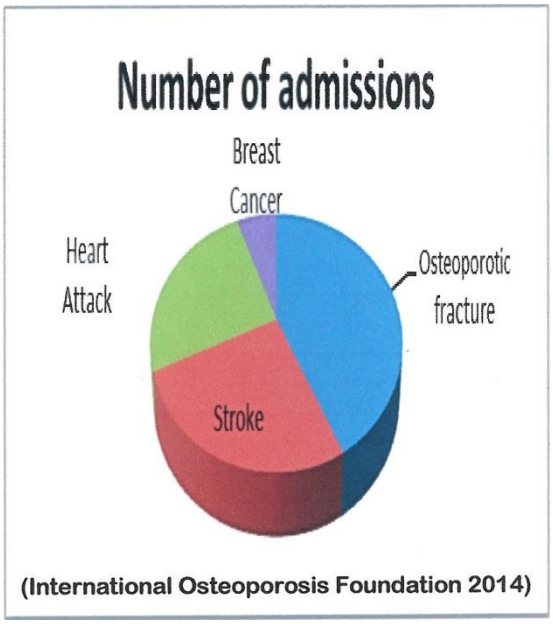
The morbidity associated with fracture of the proximal humerus is quite substantial, with functional capacity impaired for activities of daily living for an average of 2- 3 months. The long-term functional outcome is satisfactory in 80% of patients after a simple humeral fracture without displacement (Clifford, 1980). Nevertheless, displaced proximal humeral fractures may require hospitalisation and generally lead to long-term functional deficit (Mills, et al 1985). These cases require a mean hospitalisation length of 24 days, second only to hip fractures in the number of hospital days it causes (Lippuner, et al 1997). Fragility fractures of the pelvic ring in the elderly cause immobility and markedly impair quality of life (Oberkircher, et al 2018).

In a cohort of 10,000 50-year old white postmenopausal women, 7% of all survivors of fragility fractures had some degree of personal disability, 8% required long term institutional care, 50% experienced functional decline and 50% who were previously independent were disabled (Chrischilles et al., 1991).

Pain is present in many fractures, this is universal and it is a major impediment to recovery in hip fractures (Morrison et al., 2003). For a typical economy in the developed countries, the occupied bed days for patients 75 years and over with pain due to fractures are high and dwarf the combined numbers of heart attack, acute coronary syndrome and stroke (National Osteoporosis Society (NOS), 2013). One meta-analysis showed that assuming no pain prior to a hip fracture, 47% of patients reported pain one or more years post fracture, 23% reported mild pain, 24% moderate pain and 2% severe pain (Bertram et al., 2011).

Symptomatic vertebral fractures account for 52,000 and 2,180 hospital admissions each year in America and UK respectively and may result in spinal deformities (Cooper, Campion & Melton, 1992). In 2007, hospitalisation for osteoporotic fracture in Australia averaged 262 per day, or one person every 5-6 minutes (Fazzalari N, 2009). The proportions of hospital admissions due to heart attack, stroke, breast cancer and osteoporotic fractures are shown in figure 1. Consistent with the ageing population in the UK, the numbers of fracture neck of femur has increased (table 9). This has resulted in higher numbers of admissions for the condition and increase in the length of stay.

There has been a worldwide campaign to prevent cardiovascular disease (Go Red for women, WHO global health days and others) and cancer (Cancer Awareness Month, Blood Cancer Awareness, Breast Cancer Now and others) but not as much for fragility fractures which has a higher incidence. The data above support the need for the intensification of the current efforts at prevention of this global epidemic which deserves more publicity



Source: reproduced with the kind permission of the International Osteoporosis Foundation (IOF) (Singer et al. 2015).

Figure 1: Proportions of hospital admissions for stroke, heart attack, breast cancer and osteoporotic fractures in more than 1000 participating hospitals in the USA

Figure 1 shows the proportions of hospital admission contributed to by stroke, heart attack, breast cancer and osteoporotic fracture over a 12-year study period from 2000 to 2011. There were 4.9 million hospitalisations for osteoporotic fractures (43%), 2.9 million for heart attack (25%), 3.0 million for stroke (26%) and 0.7 for breast cancer (6%). Osteoporotic fracture accounted for the majority of the admissions with age adjusted outcome rate of 1124 admissions per 100,000 person years (Singer et al., 2015).

Interpretation: Osteoporotic fractures were more common causes of hospital admission compared to stroke, heart attack and breast cancer in the study.

Table 9: Number of hip fractures and length of stay in Pilgrim Hospital

Calendar Year	Number of hip fractures in England & Wales	Number of hip Fractures at Pilgrim Hospital	Number of patients with hip fracture from care home at Pilgrim Hospital (%)	Average length of stay in days for community-dwelling patients at Pilgrim Hospital	Average length of stay in days for patients from care home at Pilgrim Hospital
2011	46675	270	63(23.3)	17	19.8
2012	64580	337	63(18.6)	14.7	13
2013	67631	340	61(17.9)	12	11.5
2014	65160	349	53(15.4)	16.3	11.4
2015	65518	318	61(19.2)	16.2	16.2
2016	65700	336	70(21)	13.2	14.3

Source: adapted from the National Hip Fracture Database (NHFD), Royal College of Physicians (RCP), 2017b.

Table 9 shows that between 2011 and 2016, the incidence of hip fractures increased by 20,000 nationally and 66 locally. At Pilgrim hospital, care home residents accounted for 19% of fracture neck of femur admission. The average lengths of stay for community dwelling people and care home residents were 14.9 and 14.4 days respectively.

Interpretation: The number of hip fractures increased by about 42% nationally and 24% locally. Care home residents made up about a fifth of the fracture neck of femur admission at Pilgrim Hospital. The length of stay for both the community dwelling and care home residents were substantial given that for any medical condition, the average was 4.7 days in Scotland, 7.5 days in Wales (Karakusevic, 2016) and 9 days in Canada (Canadian Institute for Health Information (CIHI), 2011).

The NHFD is a National Clinical Audit which was established in 2007 as a joint venture of the British Geriatics Society (BGS) and the British Orthopaedic Association (BOA) designed to facilitate improvement in the quality and cost effectiveness of hip fracture care in England, Wales and Northern Ireland. The first website data entry was in 2007 and the first preliminary National report was in 2009 and approximately 19% of cases were reported, in 2010 approximately 54% of cases were reported, in 2011 approxitaely 76% of cases were reported.

In 2011, there were 176 data reports from the 191 participating hospitals. However in 2012, there were 188 participating hospitals and 95% of cases were reported and since then the average proportion of reports has been about 95%. This explains the increase in the national number reported between 2011 and 2012 and the plateaux of the figures since then. The increase in the number reported at Pilgrim Hospital suggests that the data collection was incomplete. This coincided with the visit of the Care Quality Commission (CQC) to the Hospital resulting in the drastic reorganisation of services in all the departments. Follwing this Pilgrim Hospital subquently went on to be the best Hospital in the country for the management of hip fractures for 2 sucessive years; 2012/13, and 2013/2014 (appendix S).

1.2.5.2 Mortality Associated with Fragility Fractures

Fragility fractures are associated with increased mortality. Hip fractures are particularly ominous because they are associated with the worst health outcomes and they account for the greatest burden of osteoporotic fractures (Cooper et al., 1993). A population based study from Rochester, Minnesota, USA showed that survival following hip fractures after 5 years was about 80% of aged-matched general population without fracture which may persist for up to 10 years before returning to general population mortality rates (Bliuc et al., 2009).

Hip fractures are associated with 3-month mortality of 5% to 27% (Todd et al., 1995) and a peak 12-month mortality of 15% to 19% for women and 25% to 35% for men (Magaziner et al., 1989, Forsen et al., 1999). No single factor or aspects of practice accounted for the differences in mortality observed but the following were the possibilities: casemix factors, nutritional status of the patients, multimorbities, cumulative effects of several aspects of the organisation of treatment and the management of fracture of the hip including thromboembolic prophylaxis and early mobilisation. Men have a 2-fold excess mortality following hip fracture within the immediate post-fracture period (Cooper, Campion & Melton, 1992); death is mostly due to underlying medical conditions (Boonen et al., 2004, Magaziner et al., 2000, Hannan et al., 2001) but one study showed that 24% of the deaths were related to the hip fracture itself (Kanis et al., 2003).

Worldwide an estimated 740,000 deaths annually are associated with hip fractures and the total life years lost from hip fractures was 951,000 years (Johnell, Kanis, 2004). Of these 67% were women with 50% occurring in developed countries (Western Europe, North America,

Japan and Australia). In the USA, around 31,000 excess deaths occur within 6 months of approximately 300,000 hip fractures annually (Anonymous, 1993). In the UK, survival post hip fracture for men is 63.3% compared to 90.0% for aged-matched males, and 74.9% compared to 91.1% for aged-matched females (Van Staa et al., 2001). Fewer than half of death were attributable to the fracture, the rest were a combination of fall and fracture bringing to light underlying ill-health (NICE 2009). These findings prompted the formation of the collaborative intiatives NHFD and the Blue Book (The British Orthopaedic Association 2007). The advantages of thses collaborative approaches are:

- Improvement in the overall standard of medical care
- Minimal delay to surgery due to medical problems
- Improved management of perioperative medical complications
- Better coordination of multidisciplinary team work
- Improved communication with patients and relatives
- Reduction in adverse outcomes

How to deliver these objectives are set out in the Blue Book (The British Orthopaedic Association, 2007).

The mortality after hip fracture is higher in institutionalised patients (Hannan et al., 2001, Brauer et al., 2009, Eastwood et al., 2002). A case-control study of 2005 elderly people in residential homes in Australia showed that mortality was initially the same within one year of surgery but after adjusting for sex, gender, type of institution, weight, immobility, cognition, comorbidities and the number of medications, the mortality was higher than in the control group. The hazard ratio (HR) post hip was 3.09 three months after surgery, 1.99 at between

three and nine months and 0.88 at more than nine months following surgery (Cameron et al., 2009). Table 10 shows the 30-day mortality of patients with fracture neck of femur in Pilgrim Hospital. The average 30-day mortality rates for care home residents, community dwelling patients in Boston and the national average for patients with fracture neck of femur from 2011 to 2015 were 9.3%, 8.5% and 7.5% respectively (Royal College of Physicians (RCP), 2017a).

Table 10: Mortality of fracture neck of femur in Pilgrim Hospital, Boston, UK

Calendar Year	Total NOF (n)	30-day mortality of patients from community	30-day mortality patients from care homes	National average 30-day mortality
2011	366	13.5	11.1	7.7
2012	328	7.4	14.3)	8
2013	353	7.6	3.3	7.6
2014	317	6.6	11.3	7.3
2015	350	7.5	6.6	7.1
Average 30-day mortality		**8.5**	**9.3**	**7.5**

Source: adapted from the National Hip Fracture Data Base (NHFD), Royal College of Physicians (RCP), 2017b. Neck of femur (NOF).

Interpretation: Table 10 shows that the average 30-day mortality rate for care home residents (9.3%) was higher than that of the community dwelling people (8.5%) and the national average (7.5%).

The marked reduction in the 30-day mortality in community dwelling older patients in 2011 and 2012 were due to the reorganisation of hip fracture services in 2011 following the CQC visit; Pilgrim hospital subsequently emerged as the best hospital in the UK for the management of hip fractures for 2 years in sucession 2012/13 and 2013/14 (http://wwwbostonstandard.co.uk appendix S).; the introduction of the Best Practice Tariff (BPT) which served as an incentive because the United Lincolnshire NHS Trust was experiencing severe financial difficulties at the time and lastly good intermediate care services. Admission avoidance by a hospital-at-home service is associated with a reduction in mortality, increased patient satisfaction and can reduce hospital use by 14 days (Shepperd et al 2008).

Studies have also shown premature mortality after non-hip fractures (vertebral, pelvis, distal femur, proximal tibia, proximal humerus, multiple ribs.) across all age groups (Center et al., 1999, Kado et al., 1999). For vertebral fractures, this persists for up to 5 years in both sexes (Cooper et al., 1993, Bliuc et al., 2009). In the UK General Practice Research Database (GPRD) study, the survival 12 months after vertebral fracture was 86.5% compared to 93.6% of aged-matched general population without fracture; after 5 years, survival decreased to 56.5% compared to 69.9% expected (Van Staa et al., 2001). Some studies have shown that the presence of multiple vertebral fractures increases the risk of death (Center et al., 1999, Kado et al., 1999, Jalava et al., 2003).There is no excess mortality following distal forearm fractures except in elderly men (Johnell, Kanis, 2004, Cooper et al., 1993, Center et al., 1999). The one-year mortality of osteoporotic pelvic fractures range from 9.5 % to 27% (Oberkircher, et al 2018).

The risk factors for osteoporotic fractures (osteoporosis and falls) are also independently associated with significant mortality and morbidity. For example, for each standard deviation (SD) decrease in bone mineral density (BMD), the mortality risk increases by approximately 1.5 fold (Cooper et al., 1993, Center et al., 1999, Cauley et al., 2000) and falls are a major cause of mortality in older people aged over 75 years (Health Education Authority 1999, 1999, United States Centers for Disease Control and Prevention (CDC), 2012).

1.2.5.3 Economic Impact of Fragility Fractures

The financial cost of fragility fractures is substantial. Cost rises progressively with age. Worldwide in 1990, the estimated cost was $34.8 billion; this is projected to rise to $131.5 billion (at an average cost of $21,000 per patient) by 2050 (Johnell, 1997). Costs vary worldwide. The direct medical expenditure for osteoporotic fractures in Europe was estimated at €36 billion annually, of this, half was accounted for by hip fractures and the cost is expected to double by 2050 (Kanis et al., 2005a). Hip fractures account for the highest proportion of the burden because of the longer period of hospitalisation, rehabilitation and post admission care (de Laet et al., 1996).

In the United States of America (USA), in 1990, an estimated $35 billion was spent on fragility fractures, this is set to rise to $131 billion by 2050 (Johnell, 1997). In 1995, the expenditure was $13.8 billion of which $48.7 billion was attributable to hip fractures (Ray et al., 1997). In Canada, the annual cost for hospitalisation due to hip fractures was estimated at $337.5 million (Goeree, O`Brien & Pettit, 1991). In Holland hip fractures accounted for about 85% of all fracture costs (de Laet et al., 1996).

Direct medical costs for fragility fractures to the UK healthcare economy was estimated at £1.8 billion in 2000, (i.e. approximately £6 million per day) with the potential to increase to £2.2 billion by 2025, most of these costs related to hip fracture care (Burge et al., 2001, Torgerson, Dolan, 2000). Table 11 shows the financial impact of hip fractures at Pilgrim Hospital, Boston for three consecutive years. The cost of one hip fracture was approximately

£14,000 including consumables. In 2011/12, the total cost of fracture neck of femur was nearly equal the combined cost for stroke and ischaemic heart disease.

Table 11: Cost of fracture neck of femur, stroke and ischaemic heart disease in Pilgrim Hospital.

	Pound Sterling in 2011/12	**Pound Sterling in 2013/14**	**Pound Sterling in 2014/15**	**Average**
Fracture neck of femur	7,314,252 .5	2,230,232.8	1,759,575.9	3,768,020.4
Stroke	4,672,705.8	3,644,692.4	3,230,658.2	3,849,352.1
Ischaemic heart disease	670,269.11	670,269.11	760,939.17	700,492.5

Source: Accounts Department of the United Lincolnshire Hospitals NHS Trust (ULHT 2017)

Table 11 shows that the financial burden was substantial in the three financial years. The data show that the financial impact of fracture neck of femur was much higher than ischaemic heart disease and comparable to that of stroke.

Interpretation: The average expenditure for fracture neck of femur (£3,768,020.4) was comparable to the combined average for stroke and ischaemic heart disease (£2,274,922.3). This is substantial given the financial challenges of United Lincolnshire Hospital Trust (ULHT). The budget deficit was £73 million in 2016/17 (United Lincolnshire Hospitals NHS Trust (ULHT), 2017).

There was a marked drop in expenditure for fracture neck of femur in 2013/14 and 2014/15. The possible explanations were the reorganisation of hip fracture services following the CQC visit in 2011/12 which resulted in identification of financial leakages and financial prudency. Following this, Pilgrim Hospital was adjudged the best hospital in hip fracture management in the UK for 2 sucessive years 2012/13 & 2013/14. (Appendix S) It is noticeable that the financial expenditure for stroke and ischaemic disease services did not change remarkably duration the same period

Countries in Asia have also incurred substantial costs in managing fragility fractures. In Chongqing, China, the average cost of hip fracture which was 3603 USD in 2007 has increased at a rate of 6% annually and it is estimated that by 2020, the average cost will rise to 7600 USD. In 2006, the Government of China spent 1.5 billion USD on hip fractures and estimates for 2020 and 2050 are 12.5 USD and 264.7 billion USD respectively (Mithal, Lau, 2009). The average hospital stay for hip fractures in Japan was 48.4 days in 2001; the inpatient costs including nursing care increased by between 6.34 USD and 7.58 billion USD by 2002. In Australia, the estimated cost of all osteoporotic fractures from 2000 to 2001 was 7.5 billion per annum (Australian Dollars) representing 1.2% of the Gross Domestic Product (GDP). The management of hip fractures accounted for 63% of the total healthcare expenditure (Polder et al., 1998). The costs of managing fragility fractures are also high in other countries in Asia such as the Republic of Korea, Malaysia, and Pakistan (Mithal, Lau E, 2010).

The cost of a hip fracture in Brazil is estimated at 3987 USD per patient with an average length of hospital stay of 11 days (direct cost is 12,000 USD in private hospitals). In Chile the direct hospital cost for treating a hip fracture is estimated at between 2000 USD and 7000 USD depending on whether the fracture is treated in a public or private healthcare setting (Society of Osteoporosis (SCHOMM), the length of hospitalisation for a hip fracture is 5 to 7 days with an average loss of wages of 45 days. The direct hospital cost of treating a hip fracture in Columbia is 6457 USD with an average hospital bed stay of 10 days. There are also indirect costs to the patient and families such as productivity loss associated with care (Zanchetta, 2012). As hip fractures predominantly occur in elderly people after the age of 80

years (Jones et al., 1994), the ageing population worldwide will experience increase in the number of hip fractures (Melton, 1993).

Vertebral fragility fractures seldom lead to hospitalisation. In Europe about 8% of vertebral fractures are admitted, in the UK about 2% are admitted (Finnern, Sykes, 2003). The admission rate in Sweden is higher with 10% for women and 15% for men. The cost of each hospital stay is about €3,900. This represents about 48% of the cost of a hip fracture (Finnern, Sykes, 2003). A cost analysis of symptomatic vertebral fractures in UK estimated the average additional health cost for the year prior and post-diagnosis was £165 for General Practitioner consultation, £134 for referrals and £2,314 for hospital admission i.e. a total of £2,612 compared to an estimated age-weighted cost of £771 in 1999-2000 (Kanis, 2002a).

1.2.5.4 Disability Adjusted Life Years (DALYs) Lost due to Fragility Fractures

The morbidity, mortality and cost incurred for fragility fractures can be expressed as the health burden which is the Disability Adjusted Life Years (DALYs) lost ie the quality of life lost (Johnell, Kanis, 2006). This is in contrast to the quality adjusted life years gained (QALY) ie the same quality of life gained although both DALY and QALY are measurements used in order to calculate time (in terms of life years) of an individual or a general population.

DALY is a metric used to estimate health loss due to disease, injuries and risk factors by age, sex and geography for time points. DALY is the most comprehensive effort which captures the mortality, morbidity and their relative importance. It quantifies health loss by combining premature death and non-fatal health outcomes (Murray et al., 2012). It is a measure of utility

and disutility and the favoured method by the WHO and the World Bank to assess the disability incurred by diseases including death and disability that arise in the survivors. It allows a method for the direct comparison of burden between different diseases. For fragility fractures, it integrates the years lost because of fracture and the disability in those who survive. A life lost equals one DALY (1=death, 0=perfect health). If the quality of life is halved by a fracture then that is 0.5 DALY. 1 DALY can be thought off as one lost year of health life.

Osteoporotic fractures account for a significant burden worldwide (Johnell, Kanis, 2006). 25% of the global burden from osteoporotic fractures occurs from hip fracture. In 2000, there were about 9 million fragility fractures worldwide of which 1.6 million were hip, 1.7 million forearm and 1.4 million clinical vertebral fractures. The total DALYs lost was 5.8 million accounting for 0.83% of the global burden of non-communicable disease and 1.75% in Europe (Johnell, Kanis, 2006). In the Americas and Europe, osteoporotic fractures account for 2.8 million DALYs annually (Anonymous. 2003). In Europe apart from lung cancer, fragility fractures accounts for more DALYs lost compared to common cancers (Johnell, Kanis, 2006).

The QALY concept allows combining the effects of health interventions on quantity and quality of the remaining life years into a single index. QALYs are calculated by multiplying the length of time spent in a certain health state by the utility score associated with it (Shepard 1999). The incremental cost-effectiveness ratio (ICER) is a statistic used in cost-effectiveness analysis to summarise the cost-effectiveness of a health care intervention. It is defined by the difference in cost between two possible interventions, divided by the difference in their effect.

It represents the average incremental cost associated with 1 additional unit of the measure of effect. The ICER can be used as a decision rule in resource allocation. If a decision-maker is able to establish a willingness-to-pay value for the outcome of interest, it is possible to adopt this value as a threshold. If for a given intervention the ICER is above this threshold it will be deemed too expensive and thus should not be funded, whereas if the ICER lies below the threshold the intervention can be judged cost-effective. This approach has been adopted in relation to QALYs; for example, the NICE adopts a nominal cost-per-QALY threshold of £20,000 to £30,000 (Appleby, et al 2007). For fragility fractures, the assessment of osteoporosis with dexascan and treatment with most of the osteoporotic medications fall below this threshold.

1.2.5.5 Carer`s Stress due to Fragility Fractures

Carer`s stress or care-giver stress is a complication of any long term medical condition on the carers. The term can be used interchangeably with carer`s burnout (Hamilton, 2011). It is a condition that strongly manifests exhaustion, anger, rage, or guilt resulting from unrelieved caring for a chronically ill patient. Although it is not listed in the *Diagnostic and Statitical Manuel of Mental Disorders,* the term is often used by many healthcare professionals. It comprises three components: emotional exhaustion – the depletion of emotional resources and a diminution of energy; depersonalisation (negative attitudes and feelings, insensitivity and a lack of compassion towards those who receive the service or care) and personal accomplishment (negative evaluation of one's work, which is usually associated with feelings of reduced competence and ineffectiveness) (Maslach, Jackson & Leiter, 1986).

It manifests in many ways: feelings of frustration, tiredness, anxiety, depression, ill health, poverty anger, guilt, loneliness, exhaustion, physical injury, elder abuse (I1iffe, Patterson & Gould, 1998). Burnout is a concern not only for the individual affected but also units and organisations in which the carer works (Bakker, Le Blanc & Schaufeli, 2005). Caring for an older family member with a fracture can take a lot of time and energy. This may involve organising time off work for medical appointments, making daily phone calls and organising services or finding someone trust-worthy to look after an older person. This may result in complaints and litigations. The carer may be a spouse who may have chronic ill health which limits their activities (Hamilton, 2011). The UK Government now recognises the need to support carers and the Department of Health has sponsored services in three geographical areas in England to address this. Most carers who received the support found it very valuable (Hills, 1991).

While there is anecdotal evidence for carer stress there is little robust data. A systematic review and meta-analysis of the impact of carer stress on subsequent institutionalisation of community-dwelling older people found the effect was small (Donnelly et al., 2015). Another systematic review of stress in staff caring for people with dementia living in 24-hour care settings did not show a high prevalence of psychological stress (Pitfield, Shahriyarmolki & Livingston, 2011). However, all the studies were small and used instruments with unsatisfactory psychometric properties. The number of fragility fractures will increase in the coming decades and a high proportion of older people who sustain these will be institutionalised, therefore a narrative on care home residents is germane to put this in context.

1.2.6 Fragility Fractures in Care Home Residents

1.2.6.1 General Considerations of Care Home and the Residents

The last few decades have witnessed an increase of the ageing population and their care has presented looming challenges in many countries. As elderly populations continue to grow, the number of older people with functional disabilities is also on the increase. Impairments in physical and mental functioning in elderly adults reduce healthy life expectancy (World Health Organization (WHO), 2014), healthcare costs and makes the need for long-term care inevitable in many cases (Lubitz et al., 2003). Consequently, in many countries, there is an increasing demand for nursing home care options. Care home residents are a distinct group with chronic medical problems which have assumed increased relevance because of the high healthcare burden.

A care home is defined as an institution which provides accommodation and care for people with complex needs who are unable to look after themselves (National Institute for Health Research (NIHR), 2016). The term care home inludess both nursing homes and residential homes. Nursing homes provide accommodation and assistance with personal care as well as 24-hour nursing care. Residential homes provide accommodation without nursing care, some homes provide both levels of care. Many care homes offer rehabilitation facilities (physiotherapy, occupational therapy and speech & language therapy) and recreational activities also. The level of care for the residents can change, more often from residential to nursing because of an increase in care needs.

Most care home residents are women who are over 85 years old. There is considerable overlap in health status and need and support amongst residents in all care homes. The median period from admission to care home to death is about 15 months, the average life expectancy is less than 2.5 years, but about 27% live for more than 3 years (National Institute for Health Research (NIHR), 2016). Given these, end-of-life care is a core component of care in many care home settings which can have impact on research, regardless of the research question.

The National Centre for Health Statistics of the Centers for Disease Control and Prevention in the USA (CDC) estimated 1.5 million adults over the age of 65 years are currently living in nursing homes; a number expected to triple by 2030 (Centers for Disease Control and Prevention, 2012). There are an estimated 450,000 people (0.64% of the population) living in care homes in the UK, this is 4% of the population aged 65 years and over; 9.7% of who are 75 years and over and 23.7% are 85 years and over (Office for National Statistics, 2011). A similar proportion (0.68%) has been reported in the Netherlands, where approximately 117,000 older people out of a national population of 17.08 million live in care homes (Verbeck – Qudijk 2012).

The proportion of care home residents is lower in developing countries: social, economic and cultural practices are responsible for this. In these countries, older people with care needs can rely on kinship networks to provide support, but with the established trend of population ageing and the rapid increases in the oldest age groups, the situation is changing. Studies from a wide range of developing communities indicate important shifts in inter-generational relations, whereby older generations are becoming less confident about receiving care and

support from younger family members (Aboderin, 2004, Bhat, Dhruvarajan, 2001) and there is evidence that care institutions are becoming an increasingly acceptable alternative to the traditional family care (Redondo, Lloyd-Sherlock, 2009).

A survey in India in 1984 showed that 91% of people said it was their duty to care for older parents; 10 years later, this had reduced to 77% (Jamuna, 2003). The survey also found no children supported the idea of sending older people to care homes in 1984, but 10 years later, 23% did. This changing social trend has contributed to the growing demand for care homes in the city of Buenos Aires, Argentina. According to the 2001 Census, 2% of Argentines aged 65 years and over, and 5% of people aged 80 years and over were living in care homes, almost all of which operated on a private for-profit basis (INDEC, 2001).

In the UK, 75% of care home residents are moderately disabled, with female residents having the higher proportion of disability. Shah and colleagues found that the mean age for nursing and residential homes was 84.9 and 86.1 years respectively compared to 74.7 for controls (Shah et al 2010). A health survey of 410,000 older people found 57% of women and 48% of men needed help with one or more `self-care` tasks and the following reasons were given for admission to care homes (Bebbington, Darton & Netten, 2001);

Physical health problems	69%
Mental health problems	43%
Functional disablement	42%
Stress on carers	38%

Lack of motivation	22%
Present home physically unsuitable	15%
Family break-down (incl. loss of carer)	8%
Need for rehabilitation	6%
Fear of being the victim of crime	4%
Abuse	2%
Loneliness or isolation	2%
Homelessness	1%

More than one reason may be given.

Oliver found that the common precipitants of care home admission were dementia, falls and fractures, and declining mobility and incontinence (Oliver 2014).

A survey found that local authority funded and self-funded residents differed in their levels of dependency and age when entering care; self-funded residents tended to be older and less dependent than publicly funded residents (Netten, Darton & Curtis, 2002).

The sources of admissions of the older person to care homes vary (Bebbington, Darton & Netten, 2001):

Admission from hospital	52%
Admission from a private household	29%
Admission from one form of care home to another (residential or nursing home)	13%
Admission from sheltered accommodation	6%.

Care home residents have high prevalence of cognitive impairment such as dementia (Alzheimer`s Society, 2013), depression (Godfrey, Denby, 2004) musculoskeletal problems (Arthritis Research UK, 2015), stroke (Martin, Meltzer & Elliot, 1998), Parkinson`s disease (Parkinson`s UK, 2015) and people at the end of life pathway. In a cross-sectional analyisis of 326 English and Welsh general practices, Shah and colleagues (2010) found that the prevalence ratios for dementia were 14.8 (95% CI 13.4 – 16.4) for nursing and 13.5 (95% CI 12.4 – 14.8) for residential homes compared to controls. Stroke and severe mental illness were commoner in nursing and residential homes but hypertension, respiratory and cancer diagnoses were slightly less common. Recorded disease prevalences in nursing and residential homes were similar (Shah et al 2010).

About 97,000 (17.8% of all those who die in England each year) are from care homes (Office for National Statistics (ONS), 2014) and 3,000 care homes in England are now registered for end-of-life care; 462 have received the Gold Standards Framework (GSF) accreditation, a Quality Hallmark that ensures the integrity and sustainability of the process (Care Quality Commission (CQC), 2015). The GSF is a systematic evidenced based approach to optimising the care for patients nearing the end of life and is widely used in the community and care home setting. The acute hospital training programme focuses on improving care provided by frontline generalist ward staff for all patients thought to be in the final months , weeks or days of life by introducing earlier identification and anticipation of needs and planning care in alignment with patient`s needs and preferences.

Hansen LC and colleagues found that care home environment allows staff to form closer relationships with residents and their families than is possible in a busy hospital environment thereby providing an appropriate environment for end-of-life care (Hanson, Gilliam & Lee, 2010). Care homes are often characterised by rigid schedules, high workloads, high staff turnover and large numbers of unregulated care providers with limited education and training (Mentes, Tripp-Reimer, 2002). Medical care is often provided by several General Practitioners (GP) whose offices are located off site, pharmacist visits are intermittent and only few care homes have advanced medical facilities on site.

There are an estimated 440,000 people living in 18,000 care homes in England (Commission for Social Care Inspection (CSCI), 2006). In Lincolnshire, there are 295 care homes representing 1.6% of care homes in England. London metropolis has the highest number. The UK Government specifies the minimum standard of care desired through the Care Standards Act and monitors implementation using the Care Quality Commission (CQC) in England, the Care Inspectorate in Scotland and the Care and Social Services Inspectorate in Wales.

1.2.6.2 Incidence and Prevalence of Fragility Fractures in Care Home Residents

People in care homes are 2 to 4 times more likely to have fragility fractures compared to community dwelling age matched counterparts (Crilly et al., 2010, Ronald et al., 2008). A population based study in Wales showed significantly higher risk of fragility fractures in nursing and residential homes than in comparable community dwelling older persons (Brennan et al., 2003). Hip fractures are particularly common and the risk of hip fractures are highest in the first months after admission to the care home and decrease with increasing

levels of care needs (Rapp et al., 2008). A plausible explanation is the reorientation in a new environment (toilet, furniture, lighting, etc.) which may result in increased risk of falls. Friedman and colleagues found that the fall rate of residents to be increased during the first 3 months after relocation to a new facility (Friedman et al., 1995).

Around a quarter of patients with hip fractures are admitted to hospital from care homes (Crilly et al., 2010, Ronald et al., 2008, National Institute for Health and Clinical Excellence (NICE), 2011b). Kane and colleagues found that the incidence of long bone fracture was 3.52 per 100 subjects per year; minor trauma fracture incidence was 0.84 per 100 subjects per year (Kane, Burns & Goodwin, 1995). Another study showed higher incidence rates of 10 fractures per 100 residents per year (Crilly et al., 2010).

Luthje reported an annual incidence rate of 91 per 100,000 hip fractures (Luthje 1991**).** Galagher and colleagues reported a hip fracture rate of 17 percent in men and 32 percent in women who were older than 80 years in Rochester, Minnesota, USA (Gallagher et al., 1980). Melton et al found hip fracture incidence was 2.5 times more in women who were older than 80 (Melton et al., 1982). Ytterstad reported an incidence rate of 70 per 1000 person years (Ytterstad, 1999). In the Auckland Hip Fracture Study, 42% of hip fractures occurred in care residents and the risk of hip fracture, unadjusted for age and sex was 10.5 times greater for care home residents compared with those living in their private homes (Butler et al., 1996). Two studies reported that the incidence rate of hip fracture in nursing home residents are more than five times higher than rates in community dwellers of the same age and sex (Ooms et al., 1994, Rudman, Rudman, 1989).

One publication of fragility fractures in care homes in Japan found hip fracture incidence of 14.9 per 1,000 person years for women and 9.7 for men. The incidences of forearm and upper-arm fracture were 1.9 and 5.1 for women and 0.5 and 2.1 for men respectively (Nakamura et al., 2010). Vertebral fractures have been documented in 30% of care home residents (Rodondi, Chevalley & Rizzoli, 2012). Nursing home residents have high prevalent fractures (Zimmerman et al., 1999) and have an increased risk of another fracture over the ensuring 2 years when compared to residents with no fracture history (Lyles, Schenck & Colon-Emeric, 2008). The different incidences reported show that fracture rates cannot be generalised in care home settings because of the different case mix and study methodologies. But, high fracture rates will be expected in institutistions that cater for dementia who are ambulant because of the higher propensity to falls.

1.2.6.3 Falls in Care Home Residents

The incidence of falls is reported to be about three times higher in care homes than in the community (Ytterstad, 1999) with an annual incidence from 600 – 3,600 per 1000 beds (Rubenstein et al 1996) This is because care home residents are generally frail and some have been admitted because of increased falls risk. Each year, a typical nursing home with 100 beds reports between 100 and 200 falls, half to three-quarters are unreported (ISHN 2017). A study of 56 care homes in the UK with a mean occupancy of 1,862 residents showed that there were 2,690 falls in a year, with mean falls rates as high as 3 per resident per annum in specialist residential homes for clients with dementia (Morse 1994). In 2006, the US Centers for Disease Control and Prevention (CDC) reported between 50% and 75% of older people in care homes in the USA sustain falls each year, twice the rate of community dwelling older

people, with 2 to 6% of the falls resulting in fractures (United States Centers for Disease Control and Prevention (CDC), 2012). A similar incidence was observed in about 60% of cohort in another study (Cryer, Patel, 2002). Kane and colleagues found an incidence of 1.5 falls per person per year (Kane, Burns & Goodwin, 1995).

Care home residents often fall more than once with an average of 2.6 falls each year (Rubenstein et al., 1990). About 35% of fall related injuries occur among residents who cannot walk (Thapa et al., 1996). About 1,800 people living in nursing homes die from falls each year, 10 to 20% of nursing home falls cause serious injuries; 2 to 6% are complicated with fractures (Rubenstein et al., 1988). The causes of falls may be related to dementia (van Staa, Leufkens & Cooper, 2002b), urinary incontinence (Colon-Emeric et al., 2003b), sarcopenia (low muscle mass) and frailty (Fiatarone Singh et al., 2009).

1.2.6.4 Osteoporosis in Care Home Residents

Osteoporosis is prevalent in the care home population with approximately 50% of men and 64% to 90% of women meeting the WHO criteria for the diagnosis (Zimmerman et al., 1999, Sallin, Mellstrom & Eggertsen, 2005, Toofanny et al., 2004). One study by Aspray and colleagues in Newcastle found a high prevalence using BMD at the calcaneus (Aspray et al., 2006). Vitamin D deficiency, a cause of low BMD is also common with 60% of nursing home residents having levels of 25, OH Vitamin D of less than 20ng/ml (Elliott, 2003).

Vitamin D also has neuromuscular functions; deficiency causes skeletal weakness which may result in more frequent falls thereby increasing fracture risk (Pfeifer et al., 2001, Gerdhem et

al., 2005). Gerdhem and colleagues found 25(OH) D levels correlated with physical activity, balance, gait speed and thigh muscle strength. Given that osteoporosis is very common in care home residents one can argue that the all care home residents should be offered pharmacological treatment but there is a caveat to such practice as some of the medications have potentially dangerous side effects, therefore only those who have been screened should be considered for such intervention.

1.2.6.5 Global Initiatives Aimed at Reducing Fragility Fractures

The global increase in fragility fractures has created concern and coalition of interested parties such as Fragility Fracture Networks (FFN) and the Falls & Fracture Alliance (FFA). Strategies have been developed for implementation of systemic approaches to fragility fracture prevention at state, provincial and national levels. During the first decade of this century, more than 50,000 consecutive fragility patients were assessed by the Glasgow Fracture Liaison Service (FLS). Consequently, hip fracture rates have reduced by 7.3% compared to a 17% increase in England where only 37% of localities operate FLS (Skelton, 2009).

Variants of this service such as Osteoporosis Co-ordinator Programme in Canada and Care Manager Programme in the USA, have been developed. The British Geriatrics Society in collaboration with the British Association of Orthopaedic Surgeons developed a guideline called the Blue Book which is aimed at improving the care for people with fragility fractures. As part of this initiative, the National Hip Fracture Data base (NHFD) was also created for better management and Ortho-geriatricians were harnessed with the tools needed to tackle secondary prevention of fractures and facilitate improvements in the quality and cost

effectiveness of hip fracture care. The successes recorded through these initiatives are rooted in risk assessment and health education programmes.

Other modalities of prevention and management of fragility fractures have also been developed (Scottish Intercollegiate Guidelines Network (SIGN), 2015). These are: exercise programmes, diet and pharmacological agents (alendronic acid, risedronate, zoledronic acid, ibandronic acid, cyclical etidronate, strontium ranelate, parathyroid hormone, calcitonin, denosumab, hormone replacement therapy (not relevant for care home residents), tibolone, raloxifene, Calcium and Vitamin D supplementation). Secondary prevention programmes have less chance of success once the irreversible process of osteoporosis has set in, therefore primary prevention through risk stratification should be the Holy Grail. The number of fragility fractures in care homes is likely to increase because of the ageing population; this makes the case for preventive programmes more compelling and strengthens the argument for a standardised risk assessment tool for this cohort.

1.2.6.6 The Need for Fragility Risk Assessment Tool for Care Home Residents

Adults in their eighth and ninth decades of life are less likely to be screened and treated for osteoporosis than younger individuals (Berry et al 2019). National (Teede, Jayasuriya & Gilfillan, 2007, Papaioannou et al., 2008), regional (McLellan, 2004, Hajcsar, Hawker & Bogoch, 2000) and local (Port et al., 2003) audits conducted across the world have shown that the usual standard of care results in 80% of fragility fracture patients neither being assessed nor treated for osteoporosis. In a community-based survey of 94 older hip fracture patients, 45% required treatments, 35% fulfilled criteria for investigation and reassessment and 20%

needed no future management. But in practice, only 27% received treatment, 4% had undergone DEXA assessment and were untreated and 69% had not been investigated and were untreated. In patients meeting the intervention threshold, only 33% of those who required treatment were receiving it (Elvey et al., 2014). More recently, the National Audit of Inpatient Falls (NAIF) has reported a drop in the number of Trusts that use falls risk tools from 74% in 2015 to 34% in 2017 (RCP, 2017). Also in a recent review of osteoporosis treatment, it was observed that individuals at high risk of fractures did not receive adequate treatment. Strategies to address this treatment gap such as nationwide implementation of the Fracture Liaison Service and enhanced adherence to therapy are needed; these are important challenges for the future (NICE 2018).

Many fractures are preventable but timely intervention depends on identifying the populations at risk. Care home residents are at greater risk of future fractures compared to community dwelling older people and risk assessment is a cost-effective measure for fracture prevention in this cohort (Cali, Kiel, 1995, Girman et al., 2002a). Currently, most fracture risk assessments are focused on older people living in the community (Cummings, Black, 1995, McGrother et al., 2002, De Laet et al., 1998). The following evidence supports the need for a specific fragility risk assessment in care home residents.

1.The benefits of osteoporosis medications may occur at 6 to 12 months, also the benefits for effective fall prevention interventions might be immediate. As age increases, the number needed to treat to prevent 1 hip fracture declines until the age of 80 years (Wells et al 2008). Despite a shorter life expectancy, a woman aged 90 years still has a substantially higher life-

time fracture risk and lower number needed to treat to prevent 1 hip fracture than a woman aged 70 years. Therefore, in contrast to cancer and other screening and preventive services, for which the benefits of screening cease beyond some age threshold, the effectiveness of fracture prevention increases with advancing age (Berry et al 2019).

2. Although the risk factors for fractures in noninstitutionalised populations are well known (Norton et al., 2000, Zarowitz et al., 2015, Newman et al., 2003, Cummings et al., 1995), those for care home residents are less well studied. In a prospective cohort study, the Fracture Risk Epidemiology in the Frail Elderly (FREE) study, designed to evaluate risk factors for falls and fractures in a population of 1894 older people (1433 women and 461 men) from 52 care homes and 30 hostels in Northern Sydney (Chen et al., 2008), it was found that some of the risk factors for fragility fractures in care home residents differed from those in community dwelling older people.

An increased risk of hip fracture was significantly associated with older age, cognitive impairment, history of fracture since age 50 and lower body weight in the care home residents and longer lower length (an index of mature skeletal stature) and poor balance in the intermediate-care hostel residents. However the existing fracture risk calculators do not include many comorbidities or frailty characteristics common in older adults that influence risk benefit assessment when considering pharmacological treatment as a preventive measure for osteoporosis (Berry et al 2019)

A study reviewed the prevalence of vertebral fracture among 151 oldest old nursing home residents using vertebral fracture assessment on dual-energy X-ray absorptiometry (DEXA) (Rodondi, Chevalley & Rizzoli, 2012). It was found that while the prevalence of osteoporosis and vertebral fractures was high (52% and 36% respectively), including these variables in a model did not markedly affect the fracture probability. Duque and colleagues therefore suggested that a medical history, which incorporates age and previous fractures, may be the most practical way to determine fracture risk in this cohort (Duque et al., 2016).

A systematic review and meta-analysis of fracture risk in long term care found that the addition of cognitive impairment and history of falls to FRAX (WHO fragility risk tool) were associated with small to moderate increases in fracture probability. This prompted the suggestion of the development of a specific fragility risk assessment tool for care home residents (Khatib et al., 2014, Girman et al., 2002b).

3. Some studies have demonstrated that elderly people at high risk of future hip and other fractures can be identified using bone mineral density (bone mass), particularly at the hip and over 90% of hip fractures occur in older people with low bone mass (Phillips et al., 1988). A large cross-sectional study showed continued bone loss between ages 65 and 90 years of approximately 0.7 to 1 % annually at the radius, calcaneus and hip with a similar loss of approximately 0.3% at the spine (Steiger et al., 1992, Steiger et al., 1995). Another study found bone mass continues at the spine, radius, femoral neck and heel for up to 20 years after menopause (Harris, Dawsonhughes, 1992). A longitudinal study of 100 women of between 65

and 80 years old showed that bone loss at the radius continues at approximately 1%/year at least up to the age of 80 years (Sowers et al., 1991, Sowers et al., 1992).

4. Bone loss not only continues but accelerates in old age (Jones et al., 1994, Chapuy et al., 1992). A large prospective study of 3,000 women aged 65 years and over showed that bone loss at the hip and calcaneus accelerates with increasing age (Ensrud et al., 1992, Ensrud et al., 1997). At the calcaneus, bone loss was 1.2%/year in people aged between 67 and 70 years, increasing to 2.8%/year in those who were over 85 years. At the femoral neck, the rate of loss increased from 0.4%/year for people aged between 67 and 70 years to 1.1%/year in those who are over 85years. Acceleration in bone loss rates was greater in other parts of the hip such as the trochanteric and the annual loss at this site increased from 0.4% in people of between 65 and 70 years to 1.7% in those over 85 years.

5. Minor traumas such as falls are common in older people. The proportion of older people falling is high and various incidences have been quoted. For people who are 65 years and above, the proportion sustaining at least one fall was 28 to 35% (Prudham, Evans, 1981, Campbell et al., 1981, Blake et al., 1988). This rises to between 32 and 42% in people who are 75 years and over (Tinetti, Speechley & Ginter, 1988, Downton, Andrews, 1991). A study from Australia reported that the incidence of falls in people who are older than 70 years may be as high as 49% (Hill et al., 1999). Also about 50% of those who fall do so repeatedly (Tinetti, Speechley, 1989, Rubenstein, Josephson & Robbins, 1994). Falls account for more than 90% of hip fractures and 87% of all fractures in elderly people (Melton, 1993, Grisso et

al., 1991c, Hedlund, Lindgren, 1987). The two major risk factors for fragility fractures are falls and osteoporosis and they are highly prevalent in older people.

6.There is now an increasing armamentarium of efficacious pharmacological therapies which reduce the rate of bone loss and fracture risk even after the age of 80 years (National Institute for Clinical Excellence (NICE), 2012b, Cummings et al., 2009, Black et al., 1996, McClung et al., 2001). The discovery of key pathways regulating bone resorption and formation has resulted in new approaches to treatment with medications with distinctive mechanisms of action. In people at high risk of fracture, the benefit versus risk profile is likely to be favourable for up to 10 years of treatment with bisphosphonates or denosumab. In people at high or inmminent risk of fracture, therapy with teriparatide or abaloparatide should be considered; however since the treatment duration with these drugs is restricted to 18 to 24 months, treatment should be continued with an antiresorptive drug (Compston et al., 2017).

Antiresorptive therapy with bisphosphonates or anabolic therapy with parathyroid hormone can reduce fracture risk by at least a third within 1 to 3 years (Delmas, 2002). Therefore accurately estimating the fracture risk is critical in identifying cost-effective medications for intervention (Kanis et al., 2005a, Kanis et al., 2001). Economic models suggest that it might be cost effective to treat older women for fracture reduction who have life expectancies of as little as 2 years (Pham et al 2011). If life expectancy is less than 1 year, pharmacologic osteoporosis treatment should not be provided (Berry et al 2019).

7. Finally concerns have been raised about serious side effects of antiresorptive therapy therefore many physicians prescribe these medications for a finite period usually of between 3 to 5 years. Reassessment of fracture risk at the end of this period is important since some people remain at high risk of fracture and require continued treatment whereas others may benefit from a drug holiday.

Patient and General Practitioner (GP) records often contain medical information that may be useful in evaluating fracture risk (e.g. age, sex, medications, comorbidities etc.). National (NHG Standaard Osteoporose, 2005) and international guidelines (Kanis, 2007) have recommended a case-finding approach for identification because it is cost-effective (Compston et al., 1998, Jonsson, 1998). Case finding is a strategy for targeting resources at individuals or groups who are suspected to be at risk. It involves actively screening high risk groups, rather than waiting for symptoms or signs of the active disease.

For several years, BMD alone was used to define susceptibility to fragility fractures until it was established that such `osteocentric` position does not explain many fragility fractures and that clinical risk factors (CRFs) were also important. Most fragility fractures occur in people without osteoporosis (Wainwright et al., 2005), because the sensitivity and specificity of BMD are low (Kanis et al., 2001, Henry et al., 2002, Siris et al., 2006). It is now recognised that BMD alone fails to capture other factors that influence bone strength such as bone quality (Bouxsein, 2003), bone turnover (Recker et al., 2004), mineral (Turner, 2002), non-mineral bone tissue composition (Wang et al., 2002), bone size, bone geometry and microarchitectural

properties (Seeman, 1997, Stauber, Muller, 2006), as well as postural reflexes and muscle strength deterioration (Wickham et al., 1989).

Several validated fragility risk assessment tools are now available which incorporate BMD and CRFs and express output as 10-year probability risk rather than a densitometric diagnosis based on BMD estimate (Kanis et al., 2008, Anonymous, 2013). In England and Wales, NICE issued revised guidance on the primary and secondary prevention of osteoporotic fracture in postmenopausal women in 2010 and 2011 which incorporates fracture risk assessment, osteoporosis treatment thresholds and treatment choices.

The appraisal committee stated that recommendations about treatment should not be based on absolute risk because the committee did not agree that all the CRFs used in FRAX were appropriate and that absolute risk was not directly related to cost effectiveness since different sites have different impacts on quality of life, costs and mortality (National Institute for Health and Clinical Excellence (NICE), 2011). The resultant Technology Appraisals require a DEXA scan although this is not considered necessary in women aged 75 years or older in whom osteoporosis may be assumed (National Institute for Health and Care Excellence, 2008). One study found that using this strategy better identified high risk patient groups (Johansson et al., 2004). Some opinion leaders argue that a model without BMD is nearly as good as one with BMD (Black et al., 2001a).

The situation is further compounded because it is not known if these risk models, many of which assess fracture risk over a 5 to 10 year period are applicable to care home residents

(Berry et al 2019). Care home residents are a distinct cohort and a risk profile which is calibrated, validated internally and externally exclusively for this group will be needed. Fracture risk is currently assessed opportunistically with no standardised assessment tool for care home residents and also there is no universal policy for screening. Amidst this confusion, the National Institute of Health and Care Excellence (NICE) support this investigator`s views that studies should be conducted to identify a specific fragility tool for care home residents (National Institute for Clinical Excellence (NICE), 2017).

1.2.7 Conclusion

Fragility fractures are common in older people and the health impact is substantial. The global increase in the ageing population has resulted in increased numbers of care homes residents who are particularly at high risk. There are now several validated fragility risk assessment tools which were designed for community dwelling older persons but it is not known if these are practicable for care home residents.

1.3 Aims and Objectives of this Project

Fragility fractures are common in care home residents and can be prevented by appropriate service provision, pharmacological treaments and physiotherapy. National guidelines recommend risk assessment to allow initiation of prophylactic measures. But the currently available risk assessment tools have been tested in community dwelling adults and not in care home residents. It is possible that one or more of the existing tools are also practicable in this population. The incidence of fragility fractures in care home residents in the UK was not available from published data but one study in Norway reported a rate of 70 per 1000 person

years (Ytterstad 1999). Assessment of the performance of fragility fracture tools thus requires a very large study.

1.3.1 Aim of this Study

The aim of this project was to identify fracture risk assessment tools which are practicable in care home residents and to determine which is the most suitable for use in this population.

1.3.2 Objectives

The objectives are:

1. To conduct a systematic literature review of the existing fragility risk assessments tools and select those that can be used in care home residents.

2. To develop a composite questionnaire which can be used to test the fragility fracture risk assessment tools in a care home population. This will be done by taking information from the systematic review to design the questionnaire. The Timed Up and Go Test (TUGT), a primary falls risk assessment tool was added to compare its performance with the fragility tools. The Charlson comorbidity Index (CCI) was also added because it may inform treatment decisions. The questionnaire and patient information sheets will then be assessed by consultation visits to two care homes.

3. To undertake an observational study of the feasibility and performance of the fragility fracture risk assessment tools identified in objective 1 in care home residents in Boston, Lincolnshire, England.

4. To design an Algorithm.

The details of the methods, results and discussion for each project will be presented sequentially as one informs the other.

Chapter 2 Identification of fragility risk assessment tools for care home residents: a systematic review

2.1 Abstract

2.1.1 Background

Fragility fracture risk assessment is important in the identification of older people who are at high risk. Many tools are now available for this purpose. Most of them were developed from community dwelling older people but it is not clear if any of these are practicable in care home residents. To address this knowledge gap, a systematic literature review was conducted.

2.1.2 Objectives

Two steps were followed in the systematic review:

1. First, identify existing fragility risk tools.

2. Second, identify those that can be used in care home residents.

2.1.3 Methods

1. A combination of electronic and manual searches was used to identify the tools. The electronic literature sources were: Cochrane Library, MEDLINE, EMBASE, CINAHL and AMED. Inclusion and exclusion criteria were applied and the relevant data collected with a data extraction form.

2. A priori criteria were used to select the tools that may be practicable in care home residents. These were:

- Prospective design/Systematicreview/Meta-analysis of the study
- Outcome measures of the study in the design of the tool
- Generalisability of the tool
- Cost – effectiveness & Pragmatism of evaluation of the tool

2.1.4 Results

1. A total of 1343 citations were identified for the review out of which thirty-three fragility tools were obtained. Four tools were derived from general literature review, two were from meta-analyses and twenty-seven were from original studies. There was considerable heterogeneity in characteristics among the tools.

Most of the tools were derived from North America, Europe and Oceania and were useable only in female Caucasians of 50 years and over. The majority of the tools were calibrated prognostic models for any major fragility fractures but they were not validated externally. Only few tools expressed their output in absolute fracture probability.

The distributions of the domains of the predictors in the tools from the original studies were as follows: demography 22 (76%), radiological investigations 20 (69%), comorbidities 19 (66%), physical limitations 12 (41%), life style factors 10 (34%), types of medications 6 (21%), living arrangements and biochemical indices 2(7%) each. The simplest tools included one or two risk factors whereas the complicated ones had more risk factors.

2. Four tools were found to be potentially practicable for care home residents by using the criteria for selection above. These were the World Health Organisation Fracture Risk Tool FRAX (independently and externally validated in many population-based cohorts), QFractureScores (independently and externally validated in 2 studies), Garvan nomogram (independently and externally validated in 3 studies) and Body Mass Index (BMI) (no published external validation studies). BMI is a common predictor in the first three tools. With the exception of BMI, their assessments are web-based and outputs are expressed as absolute fracture probability. Paper-based version of FRAX is also available.

2.1.5 Conclusions

Most of the existing tools were not validated and there was substantial heterogeneity in characteristics. Four of these are potentially practicable for care home residents. They are FRAX, QFractureScores, Garvan nomogram and BMI. They were derived from prospective cohorts, used any fragility fracture as outcome, they can be used for both sexes and they are attract no monetary cost for assessment.

2.2 Background

The marked increase in the numbers of fragility fractures and the accompanying health impact poses an immense burden to society in terms of morbidity, mortality and financial costs. Consequently, it is essential to accurately assess the individual patient`s fracture risk and where indicated, to initiate appropriate treatment that reduces fracture probability (Kanis et al., 2014). Risk assessment represents a cornerstone in this regard and one of the strategies is “case finding” screening for optimal identification of high risk individuals (NHG Standaard

Osteoporose, 2005, Kanis, 2007). Case-finding is widely accepted as a cost-effective method for identification of people suitable for treatment (Compston et al., 1998, Jonsson, 1998).

There are national guidelines for the management of fragility fractures (National Institute for Clinical Excellence (NICE), 2018, and NOGG 2017. NICE recommends FRAX or QFractureScores for assessment but NOGG intervention thresholds are based on FRAX probability. Although a number of factors were considered in the development of these guidelines, cost-effectiveness was central to their design as financial prudency featured in the terms of reference. Although the guidelines are simple to use and appeal to service providers, the scientific bases for their use are not robust.

A number of original tools are available for fracture risk assessment. Many of these were derived in different settings and used different outcome measures. The reliability, sensitivity, specificity and validity of many of them have not been tested in care home residents as many were developed from relatively healthy community dwelling older persons.

The World Health Organisation (WHO) and the International Osteoporosis Foundation (IOF) recommend that fracture risk should be expressed as a 10-year absolute risk using a combination of risk factors with or without BMD (Kanis, 2007). 10 years was chosen because this time frame is cost effective in modelling and allows 5 years on and 5 years off medications (Kanis et al., 2001). But the average life expectancy of care home residents is less than 5 years; consequently, this recommended metric of expression may not be useful for care home residents.

Care home residents are infirm and represent a distinct cohort; the majority have multi-morbidity resulting in considerable disability which increases fracture risk (Gordon et al., 2014). Thus, it is important to use validated measures to appraise their fracture risk and treatment options administered accordingly. The overarching aim of this project was to review the literature systematically and identify within the existing fragility risk assessment tools those that can be practicable for care home residents.

2.3 Methodology

To achieve the aim, two objectives were designed:

1. Identify the existing fragility tools through a systematic literature review.
2. Then identify within the tools identified in (1) those which can be practicable in care home settings using a priori criteria.

2.3.1 Methodology of the first objective of the systematic review: Identification of existing fragility tools

2.3.1.1 Search strategy

Two strategies were used for the search: electronic search and search using other resources.

2.3.1.2 Key words and search string on electronic databases

The following Medical Subject Headings (MeSH) terms were used: Osteoporosis, Fracture, Risk Assessment, Tool (Measure or Scale). These terms were chosen because they were the

most frequently used words relating to the subject of this research. The search string was: Osteoporosis AND Fracture AND Risk Assessment AND Tool OR Measure OR Scale in the following bibliographic databases:

COCHRANE LIBRARY (1993 to April 2014)

MEDLINE (1966 to April 2014)

EMBASE (1947 to April 2014)

CINAHL (1961 to April 2014)

AMED (1985 to April 2014)

Tools which were not reported in English language were excluded because of the difficulties with translation.

2.3.1.3 Searches in Other Resources

The reference lists of the full texts were inspected to identify studies that had been identified in the primary studies. Additional searches were carried out manually in grey literature on fragility fracture risk assessment tool publications in Keele University and the United Lincolnshire NHS Libraries, textbooks of fragility risk assessment tools, dossiers on fragility risk assessment tools in organisations such as the World Health Organisation, International Osteoporosis Foundation, pharmaceutical companies, conference abstracts (published and unpublished) and references provided by colleagues and opinion leaders on the subject.

The deadline for the searches was 30 April 2014 because the proposal for degree progression at Keele University had to be submitted by August 2014. All the relevant citations identified were exported to RefWorks.

2.3.1.4 Inclusion and Exclusion Criteria

The Population, Intervention, Comparison and Outcome (PICO) format was used to define the inclusion criteria (Moher et al., 2010). Tools which were derived from studies that recruited adults of either sex, any ethnic group in any setting, used fragility fractures as outcome and only the original tools were included.

Interventional studies were excluded because they have no bearing on model derivation. Case reports were excluded because they are too limited in scope. Osteoporosis and falls risk assessment tools were excluded because these are not the subjects of interest. Statistical models were excluded because they are not feasible for use in care home residents.

2.3.1.5 Method for the Selection of Studies

The citations obtained were screened in three stages. When the initial lists were obtained, duplicates were removed and the remaining screened for relevance from the title and abstract. Identified abstracts were scrutinised to ascertain whether they fulfilled the inclusion criteria. Where there were insufficient details in the abstract or where abstracts indicated that a study was likely to fulfil study criteria, the full text were retrieved. When it was unclear if an article fulfilled inclusion criteria, a second reviewer (AP) was consulted and any disagreements were resolved by discussion.

2.3.1.6 Data Abstraction and Quality Assessment

The relevant information was extracted by the author using a template designed for the study (appendix R). Methodological quality was assessed using Quality Assessment of Diagnostic Accuracy Studies tool (QUADAS Appendix O), as recommended by the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (Diagnostic Test Accuracy Working Group, The Cochrane Collaboration, 2009). This tool uses a scale where scores of 7 and more are high quality studies and scores less than 7 are considered low quality but no study was excluded based on the score.

2.3.2 Methodology of Second Objective of Systematic Review: Identifying Fragility Tools for Use in Care Home Residents

The next objective was to select the tools identified from objective one which can be used in care home settings. These tools were put through another elimination process using a priori criteria.

2.3.2.1 Criteria for Selection

The criteria which were used in the selection of the tools were:

2.3.2.1.1 Prospective Design/Systematic Review/Meta-analysis

The data for developing a prognostic model should ideally be derived from prospective cohort(s), consequently such models are dynamic and likely to be current and amenable to change (Moons et al., 2012). Prospective design assures that exposure was measured before

the occurrence of the index fracture(s) thus the risk is not static. A prospective study follows a group of individuals over some period until the development of the disease of interest (Porter et al., 1990). Prospective studies are well suited for the study of diseases such as fragility fractures and are typically ranked highest in the hierarchy of evidence (Porter et al., 1990).

Case-control or retrospective studies on the other hand start at the end point and go backwards in time to identify risk factors which the subjects (known as the cases) might have been exposed to in the past (Bowers, 1996). Any findings are compared with those obtained from a comparison group, called the controls. The most difficult part of a case-control study is choosing the controls. Ideally, the controls should be similar to the cases as much as possible (without having the disease) and they should be a sample from the same population as the cases. A major problem in the selection of appropriate controls is the presence of confounding variables. Another problem with case-control studies is that such retrospective studies rely on people`s memories which can lead to bias (those with the disease can often recall events which may relate to their illness better than those without), or on the accuracy of historic data, which may be unreliable. Although case-control studies have the advantage that the results are available much earlier, these may be unreliable. Thus, although retrospective cohort studies can address long term follow-up, these are usually at the expense of poorer systematically obtained data (Moons et al., 2009).

2.3.2.1.2 Outcome Measures of the Study

Many fragility fracture risk assessment tools use hip fractures as the only outcome measure because hip fractures are associated with the highest health burden. However hip fractures are

the `final endpoints` of fragility fractures, occurring about 30 years after menopause in women (Black, Cummings & Melton, 1992). The natural history of osteoporotic fractures varies according to fracture site. Wrist fractures are commonest between 45 and 60 years and ankle fractures peak in women between 50 and 70 years (Harvey, Dennison & Cooper, 2008). In contrast, vertebral and hip fractures peak later with sharp rise after 70 years for vertebral fractures (Harvey, Dennison & Cooper, 2008) while the average age for hip fracture is over 80 years (Harding, 2018).

Also the determinants that have been shown to predict hip fractures may not necessarily be extrapolated to other fractures because hip fractures occur at a later age and their mechanism may be different. In addition, hip fractures account for less than 20% of all osteoporotic fractures (Strom et al., 2011, Holmberg et al., 2006). Therefore using hip fracture as the only outcome measure may be synonymous with using the greater to predict the smaller such as using a major heart attack to predict angina or using a major stroke to predict a transient ischaemic attack. Consequently, only tools which predict `any` major osteoporotic fracture were selected.

2.3.2.1.3 Generalisability of the Tool

Fragility fractures occur in both sexes (Kanis et al., 2005b) therefore risk assessment and treatment should be offered to all appropriate residents consequently only tools useable in both sexes were included. Although the majority of patients who sustain osteoporotic fractures are women, a substantial proportion of all osteoporotic patients occur in males. About 40% of

women and 13% of men over 50 years will sustain at least one fracture during their remaining lifetime (Melton, 1993, Lips, 1997).

In 2005, there were approximately 1.45 million fractures in women older than 50 years and 594,000 fractures in men in the USA (Burge et al., 2007). Although men account for 29% of fractures, the medical costs associated with fractures in older men is substantial; $4.15 billion of the total $16.9 billion in cost for both sexes (Burge et al., 2007) and also males are more frequently affected by the serious consequences of hip fractures.

The 2001 and 2011 population census in England and Wales showed that there were changes in the resident care home population. Fewer women but more men aged 65 years and over were living as residents in 2011 compared to 2001. The population of women fell by around 9,000 (-4.2%) while the population of men increased by around 10,000 (15.2%). This is another reason why the tool chosen should be applicable to both sexes (ONS 2011).

2.3.2.1.4 Cost-effectiveness & Pragmatism of Evaluation

The last criterion for the selection was cost effectiveness and pragmatism of the assessment tool. Cost-effectiveness is an economic framework that explores the relationship between monetary inputs and the desired outcome. It is important to consider cost-effectiveness of screening tools in fragility fractures because of the estimated astronomical increase of the ageing population and the financial expenditure that could be incurred. In the development of predictive models, it is recommended that tests, especially those whose collection requires more burdensome and costly measurements, should not be evaluated on their individual

predictive abilities but rather on the incremental predictive value beyond established and easy to obtain predictors (Moons et al., 2012, Moons et al., 2009, Moons et al., 1999).

While striving to deliver the best healthcare, financial prudency should be considered during assessment: the NHS is currently running an aggregate budget deficit of £1.85 billion for the 2015/2016 financial year (King's Fund, 2016). NICE guidelines are geared towards improving outcomes for patients and ensuring efficient use of healthcare resources. For example, screening in secondary care based on BMD has been shown not to be cost-effective (Eddy, Johnston & Cummings SR, 1998).

The cost of a DEXA scan payable by commissioners in the UK is £69, the latest available reference cost for a DEXA scan incurred by providers was £77; in South Africa, it is $130 USD and between $60 and $100 in the USA. DEXA scans are expensive, their availability is restricted to major hospitals and the labour force required is also substantial (Eastell, 1998). DEXA machines range in cost from $25,000 to $85,000. In some countries, it is predominantly a research tool. DEXA scans are undertaken only in hospitals, and although the examination time is relatively short (between 5 and 7 minutes), the resident will be required to disrobe; the process and the logistics may be daunting for the frail elderly care home resident. Given these, any tool which involved an expensive or arduous investigation such as BMD was excluded.

2.3.3 Definition of Terms

Validity is the extent to which a tool measures accurately what it is designed to measure, sensitivity is the extent to which a test identifies people who truly have the condition of interest, specificity is the extent to which a test identifies people who truly do not have the condition of interest. Both sensitivity and specificity range from 0 to 100%. Because of the inter-relationship between sensitivity and specificity increasing one generally decreases the other. Both sensitivity and specificity can be integrated into a graph, the receiver operating characteristic curve (ROC).

ROC curve graphs sensitivity and specificity throughout the range of test values and quantifies the overall performance of the diagnostic test. Accuracy is measured by the area under the ROC curve (AUC). The AUC is a measure across all risk values and can range from 0 to 1; an AUC of 0.50 means that the diagnostic test has no ability to discriminate between persons with and without the disease of interest. The closer the AUC is to 1, the better the ability of the test to discriminate. A rough guide for classifying the accuracy of a diagnostic test is the academic point system (Metz, 1978):

0.90 – 1 = excellent (A)

0.80 – 0.9 = good (B)

0.70 – 0.80 = fair (C)

0.60 – 0.70 = poor (D)

0.50 – 0.60 = fail (F)

Reliability is the extent to which a scale produces results which can be replicated with different observers, responsiveness to change is the ability of the scale to detect change due to interventions or over time at all levels of the scale, format/language refers to the ease with which the tool can be used (Royal College of Physicians, 1992, Gupta, 2008).

Relative risk (RR) is the likelihood of an event in relation to all possible events. For example if a horse wins 2 out of every 5 races, its probability of winning is 2/5 (40%) (Last 2004).

Odds ratio compares events with nonevents. For eample if a horse wins 2 out of every 5 races, its odds of winning are 2 to 3 (expressed as 2:3) (Last 2004).

OR and RR are usually comparable in magnitude when the disease is rare. Howver an OR can overestimate and magnify the risk especially when the dsease is more common and should be avoided in such cases if RR can be used (Last 2004).

Care homes were defined as an institution which provide accommodation and care for people with complex needs who are unable to look after themselves. This includes both nursing and residential homes. Nursing homes provide accommodation, personal care, and 24-hour nursing care. Residential homes provide accommodation and personal care, but not nursing care. Some homes provide both levels of care. A dementia home is defined as a care home that provides care to patients with dementia.

2.4 Results

2.4.1 Step 1. Identification of existing fragility tools from the systematic literature review.

2.4.1.1 Electronic Search

The electronic search produced a total of 1504 articles including 30 following discussion with AP. When duplicates were removed this reduced to 1343. From the 1343, 1314 were rejected for the following reasons : 721 were rejected because their titles made it clear that they were irrelevant, 7 were rejected because they were case reports, 485 were rejected because they were experimental studies, 5 were rejected because they were articles about statistical models, 96 non-English articles were rejected because translation was not feasible. After this initial screening, 37 articles were left each resulting in the derivation of a tool, that is 37 tools. The abstract of the articles from which the tools were derived were screened; of these 7 were rejected because there were no performance characteristics in 5 and full text was not available in 2, leaving a total of 30.

2.4.1.2 Search from Other Resources

Manual search yielded 15 articles and from each, a tool was derived. Of these, 12 were duplicates leaving 3 articles from which 3 tools were derived. Grey literature search did not yield any publication**.**

2.4.1.3 :Total Number of Tools (electronic and other searches)

The flow chart for the retrieval of tools is shown in Figure 2.

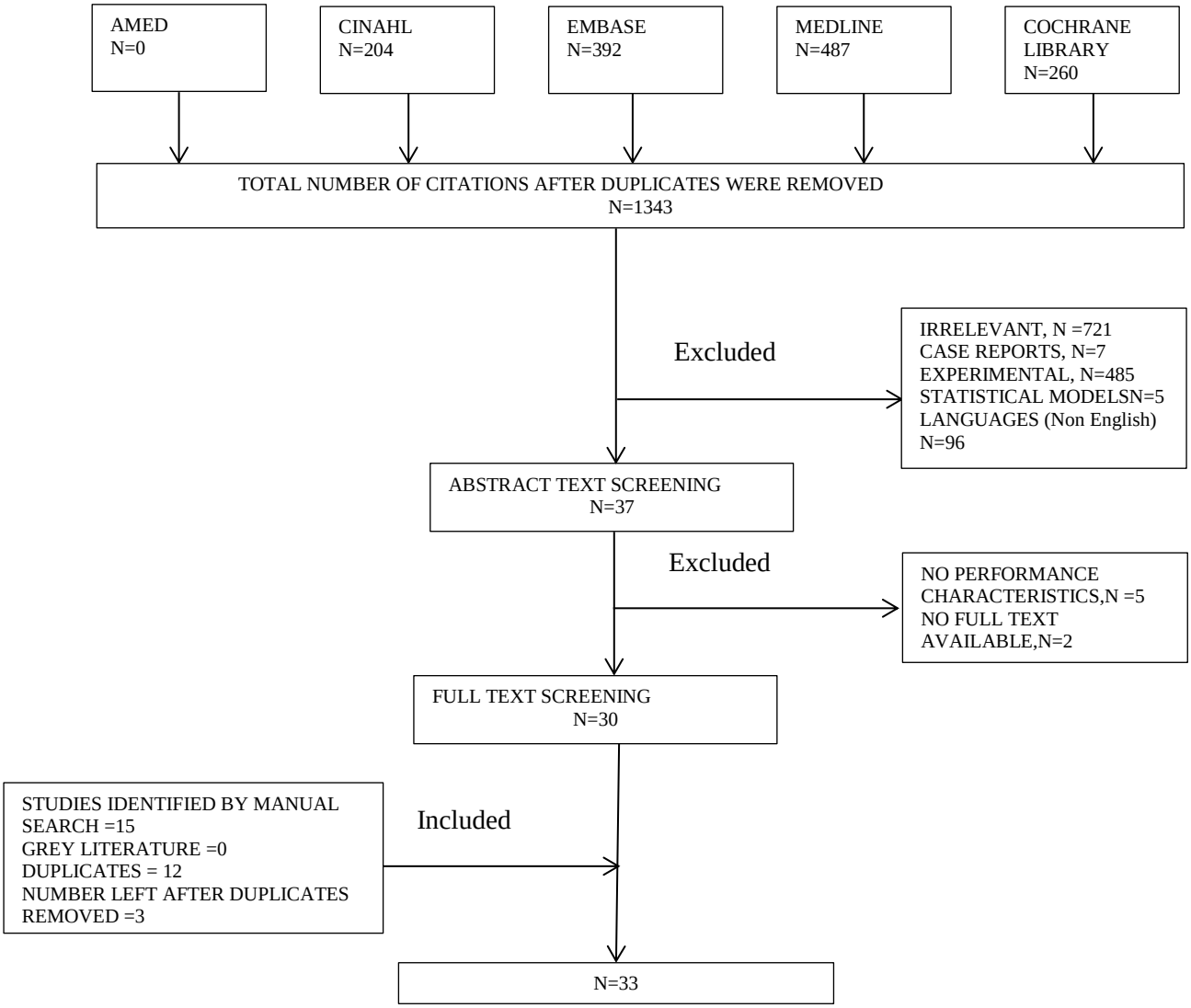


Figure 2: Flow diagram of search and study selection of the first part of the systematic literature review.

Interpretation Figure 2 shows that of the initial 1,343 articles identified, 33 fulfilled the criteria for the second part of the systematic literature review.

Finally, 33 tools were left. Of these, 4 tools were derived from literature review, 2 tools were derived from meta-analyses and 27 tools were derived from original studies. The tools selected are shown in table 12.

Table 12: The 33 tools derived from the first part of the systematic literature review

Tools derived from literature review (Tool no as list below)	Tools derived from meta-analyses (Tool no as list below)	Tools derived from original studies (Tool no as list below)
12,13,18, 29	1, 25	2-11,14 -17,19-24, 26-32,33

1. Bone mineral density (Marshall, Johnell & Wedel, 1996)
2. Markers of Bone Resorption Predict Hip Fracture in Elderly Women: The EPIDOS Prospective Study (Garnero et al., 1996)
3. A Simple Risk Score for the Assessment of Absolute Fracture Risk in General Practice Based on Two Longitudinal Studies (Pluijm et al., 2009)
4. Evaluation of a Hip Fracture Risk Score for Assessing Elderly Women: The Melton Osteoporotic Fracture (MOF) Study (McGrother et al., 2002)
5. An assessment Tool for Predicting Fracture Risk in Postmenopausal Women (Black et al., 2001a)
6. A triage strategy based on clinical risk factors for selecting women for treatment or bone densitometry: the EPIDOS prospective study (Dargent-Molina, Piault & Breart, 2005)
7. QFractureScores (Hippisley-Cox, Coupland, 2009)
8. Garvan nomogram (Nguyen et al., 2008)
9. A nomogram for individualizing hip fracture risk in men and women (Nguyen et al., 2007a)
10. Fracture Risk Score and absolute Risk of Fracture (FRISK) (Henry et al., 2011)
11. Added value of Bone Mineral Density in Hip Fracture Risk Scores (Burger et al., 1999)
12. Osteoporosis: Assessing the risk of a fragility fracture (National Institute for Clinical Excellence (NICE), 2012b)
13. Clinician`s Guide to Prevention and Treatment of Osteoporosis (NOF 1998) (Anonymous, 2013)
14. FRAX (Kanis, 2007)
15. Peripheral DXA measurements (Barr et al., 2005)
16. Homocysteine and fracture risk (Perier et al., 2007)
17. Osteoporotic Hip Fracture Combining Clinical Risk Factors and Heel Ultrasound (Hans et al., 2008)
18. Simplified System for Absolute Fracture Risk Assessment (CAROC) (Siminoski et al., 2007)
19. Prediction of Hip Fractures from Pelvic radiographs: (Gluer et al., 1994)
20. Prediction of hip fracture in elderly women (Porter et al., 1990)
21. Prediction of fracture Risk by radiographic Absorptiometry (RA) and Quantitative Ultrasound (Huang et al., 1998)
22. Risk factors for Hip Fractures in White Women (Cummings et al., 1995)
23. Use of clinical risk factors to identify postmenopausal women with vertebral fractures (Tobias et al., 2007)
24. Prediction of absolute risk of non-spinal fractures using clinical risk factors and heel quantitative ultrasound (Diez-Perez et al., 2007)
25. Body Mass Index(De Laet et al., 2005)
26. Use of Clinical Risk factors in Elderly Women with Low Bone Mineral density to Identify Women at Higher Risk of Hip Fracture (Dargent-Molina et al., 2002)
27. Assessment of osteoporotic fracture risk in community settings; a study of post (Tan et al., 2008)
28. Vertebral fracture risk (VFR) score (Lillholm et al., 2011)
29. Hip Geometry and Its Role in Fracture (Brownbill, Ilich, 2003)
30. Independent predictors of all osteoporotic-related fractures in healthy postmenopausal women (Albrand et al., 2003)
31. A simple clinical score for estimating the long-term risk of fracture in post-menopausal women (van Staa et al., 2006)
32. Factors Associated With 5-Year Risk of Hip Fracture in Postmenopausal Women (Robbins et al., 2007)
33. The Fracture and Immobilisation Score (FRISC) for risk assessment of osteoporotic and immobilisation in postmenopausal women-A joint analysis of the Nagano, Miyama, and Taiji Cohorts (Tanaka et al., 2010)

Interpretation

Table 12 shows that the majority (27/33 [82%]) of the tools were derived from original studies, 4/33 (12%) were from literature review and 2/33 (6%) were from meta-analyses.

The results of this part of the systematic review are presented in three sections: review articles, meta-analyses and original articles.

2.4.1.3.1 Review Articles

The review articles are shown in Table 13.There were 3 reviews of general guidelines on the management of fragility fractures and osteoporosis (National Institute for Clinical Excellence (NICE), 2012, National Osteoporosis Foundation (NOF), 1998, Siminoski et al., 2007) and one general review of hip geometry and its association with hip fractures (Brownbill, Ilich, 2003).

The general reviews recommended guidelines for risk assessment in the management of fragility fractures. The reviews were sponsored Government agencies and osteoporosis organisations and cost effectiveness was a prime consideration. The tool by NICE is applicable to both sexes, NOF is applicable to post-menopausal Caucasian females in the USA and the tool by Siminoski and colleagues is a recommendation by Osteoporosis Canada & the Canadian Association of Radiologists for both sexes.

The review of hip geometry and its association with hip fractures found that hip axis length. (HAL), neck shaft angle (NSA) and femoral neck width (FNW) show promise for enhancing fracture risk assessment in clinical settings. The review showed that both age and/ or loss of body weight are associated with changes in some geometric parameters which affect hip strength. It was shown that the greater hip strength in black men and women may be related to more favourable geometric parameters. Asian women who have a lower incidence of hip fractures compared to Caucasian women have a shorter HAL and a smaller NSA. The authors concluded that a longer HAL, wider NSA and FNW, increase the risk of hip fracture.

Table 13: Review articles of the systematic literature review from which four tools were derived

Author(s)	Year of review	Type of review	Title of article	Conclusion(s)
NICE	2012	General	Osteoporosis: assessing the risk of fragility fracture	Guideline for management recommended
NOF	1998	General	Osteoporosis: Review of the evidence for prevention, diagnosis and treatment and cost-effective analysis	Guideline for management recommended
Siminoski et al	2007	General	Recommendations of bone mineral density reporting in Canada: A shift to absolute fracture risk assessment	Guideline for management recommended
Brownbill RA et al	2003	General	Hip Geometry and Its Role in Fracture: What Do We Know so far	Parameters of hip geometry are helpful but more research is needed

National Institute for Health and Care Excellence (NICE), National Osteoporosis Foundation (NOF)

Interpretation

Table 13 shows that the review articles addressed different questions. NICE, NOF and Siminoski et al recommended guidelines for the management of osteoporosis and fragility fractures. Brownbill et al explored the role of hip geometry as a predictor of hip fractures and although some parameters of hip geometry may predict hip fractures, they suggested further research be conducted.

2.4.1.3.2 Meta-analyses

2.4.1.3.2.1 Meta-analysis of how Well Measures of Bone Mineral Density Predict Occurrence of Osteoporotic Fractures. (Marshall, et al 1996)

Aim

The aim of the study was to determine by a systematic review of the literature for all prospective studies if measurements of bone density in women could predict fractures of any type. The main outcome measure was the relative risk of fracture for a decrease in bone mineral density of one standard deviation below age adjusted mean.

Methods

Only women were included and two types of studies were used for the study: prospective cohort studies and case-control studies.

Prospective cohort studies

Table 14 shows a summary of the findings of the prospective cohort studies. There were twenty-five publications from 11 populations. The majority of the studies were from the USA (18 [72%]), 3(12%) were from Australia, 2(18%) were from Sweden and one each from the UK and Finland (1 [4%]). The studies were undertaken between 1977 and 1994 and the ethnicities of the participants were not stated. The population range was from 135 to 9704. The mean age range of the participants was from 57 to 83 years, the age was not reported in two studies. The follow-up was from 0.7 to 24 years equating to about 90,000 person years of observations.

There were more than 2000 incident fractures during the period of observation. The fracture sites were the forearm, hip, non-spine, vertebral, proximal humerus, distal forearm, proximal

femur wrist and any site. The authors stated that it was not possible to calculate the proportions of the fractures by site because definite numbers were not reported in 11 studies. The site of bone density measurements were different, the majority was in the proximal radius (8 [24%]), the distal radius and calcaneus (7 [21%]), the lumbar spine (3 [9%]), the middle radius, proximal femur and forearm (2 [6%]) and the spine and femoral neck 1 [3%]) each. The risks were reported as relative risk with the corresponding 95% confidence interval (CI) in all publications.

The range of the relative risk (RR) of 1SD deviation in BMD for all the studies was from 1.1 to 4.4. Most of the sites which were used for BMD measurements had predictive ability for a decrease of 1 SD in bone density of from 1.4 to 2.6. The measurement of BMD at the spine had predictive ability for a decrease of 1 SD of 2.3 (95% CI 1.9 to 2.8) while measurement at the hip had predictive ability for hip fractures of 2.6 (95% CI 2.0 to 3.5). The average total scores for quality of the studies ranged from 11.7 to 19.3 out a possible 25.

Table 14: Summary of the findings from the 25 prospective cohort studies of the predictive value of bone mineral density for fractures

Countries	**No of studies n (%)**
USA	18(72)
Australia	3(12)
Sweden	2(8)
UK	1(4)
Finland	1(4)
Population characteristics	**(min – max)**
Population size range of cohorts (n)	135 – 9704
Mean age of participants (years)	57 – 83
Duration of follow-up in (years)	0.7 – 24
Quality scores	11.7 – 19.3
Sites of BMD measurement	**n (%)**
Proximal radius	8(24)
Distal radius	7(21)
Calcaneus	7(21)
Lumbar spine	3(9)
Middle radius	2(6)
Proximal femur	2(6)
Forearm	2(6)
Femoral neck	1(3)
Fracture risk	**(min – max)**
Relative risk of fracture for 1SD decrease in BMD	1.1 – 4.4

Source: Marshall et al., 1996

This metanalysis includes prospective studies published between 1994 and 1997.

Interpretation

Table 14 shows that the majority of studies were conducted in the USA and there was a wide range in the sizes of the cohort and duration of follow-up, the participants in the studies were middle aged. The majority of the incident fractures occurred in the upper limbs. The range of relative risk of fracture for 1SD decrease in BMD was from 1.1 to 4.4.

Case-control Studies

Table 15 shows the summary of the findings of the case-control studies. There were twenty three studies and all were undertaken between 1991 and 1994. BMD measurements were estimated at the femoral neck in the majority (8 [36%]) and 5 (23%) each at the trochanter, Ward`s triangle and lumbar spine. The total number of cases was 1111 (minimum to maximum range 18 to 100).

The total number of controls was 1714 (minimum to maximum range 13 to 162). The range in bone mineral density between the cases and control was from minus 0.4 to minus 2.2. The differences in odds ratios of fracture for 1 SD decrease in BMD were as follows: femoral neck 1.5 to 9.0; trochanter 1.7 to 3.7; Ward`s triangle 1.5 to 4.8; and the lumbar spine 1.7 to 2.0.

Table 15: Summary of the findings from the 23 case-control studies of the predictive value of bone mineral density for fractures

Population characteristics	**(min – max)**
Cases (n)	1111 (18-100)
Controls (n)	1714 (13-162)
Differences in BMD between cases and controls	-0.4 - -2.2
Sites of BMD measurement	**n (%)**
Femoral neck	8 (36)
Trochanter	5 (23)
Ward`s triangle	5 (23)
Lumbar spine	5 (23)
Fracture risk	**Weighted average of OR per 1SD decrease in BMD†**
Femoral neck	2.68
Trochanter	2.79
Ward`s triangle	2.10
Lumbar spine	1.81

Source: Marshall et al., 1996
† confidence intervals were not stated in the publication

The case control studies include studies conducted between 1991 -1994

Interpretation
Table 15 shows that the majority of the BMD measurements were taken at the femoral neck. There was wide variation in the number of participants and BMD measurements in the cases and controls, the range was -0.4 to -2.2. The ORs for fracture for 1SD decrease in BMD were different between the sites of measurement.

2.4.1.3.2.2 Body Mass Index as a Predictor of Fracture Risk: A Meta-analysis (De Laet., et al 2005)

Aim

To quantify the effect of body mass index (BMI) on fracture risk in relation to bone mineral density (BMD), age and gender from an international perspective using worldwide data and BMI of 25 kg/m² as the reference

Methods

Baseline and follow-up data from 12 population-based cohorts comprising Rotterdam, EVOS/EPOS, CaMos, Rochester, Sheffield, Dubbo, EPIDOS, OFELY, Kuopio, Hiroshima and two cohorts from Gothenburg, Sweden were used. BMD was measured using different equipment. Fracture ascertainment was undertaken by self-report and or verified from hospital central databases. The study was done in 2004.

Results

The total population was 59,644 (75% were women). The follow-up was 252,034 person years (minimum to maximum 1,160 to 56,091), mean age 63.2 years (women 62.2 years, men 66.4 years), mean BMI was 26 kg/m² (women 25.9 kg/m², men 26.2 kg/m²), mean height 163.3 cm (women 160.4 cm, men 172.6 cm), mean weight 69.5 kg (women 66.9 kg, men 77.9 kg). There were 5,321 (any fractures), 1,141 (hip fractures), 3,318 (osteoporotic fractures) (table 16).

Table 16: Demography of the study population and outcome of fracture

Sex	Sample size [n (%)]	Person –years	Any fracture [n]	Hip fracture [n]	Osteoporosis fracture [n]	Age (mean years)	BMI (mean kg/m²)	Height (mean cm)	Weight (mean kg)
All men	14,887 (25%)	60,427	837	188	644	66.4	26.2	172.6	77.9
All women	44,757 (75%)	191,607	4,484	953	2674	62.2	25.9	160.4	66.9
Both	59,644 (100%)	252,034	5,321	1,141	3318	63.2	26.0	163.3	69.5

Source: De Laet., et al 2005: Body mass index (BMI)

Interpretation: Table 16 shows the ratio of men to women in the study: sample size 1:3, therefore the women were considerably more; study period 1:3, therefore women were followed-up for considerably longer duration; any fracture 1;5.4, therefore women had considerably more fractures of any type; hip fractures, 1:5.1, therefore women had considerably more hip fractures, osteoporotic fractures, 1:4.2, therefore women had considerably more osteoporotic fractures, age, 1.1:1, therefore men were older than women, BMI, 1:1, therefore men and women had similar BMI, height 1.1:1, therefore men were taller than women, weight 1.2:1, therefore the men were heavier than than the women.

Without adjusting for BMD, low BMI in men and women combined was associated with a significantly increased age-specific risk of fracture while at higher BMI values, the risk of fracture decreased (table 17). The risk ratio per unit increase in BMI was: for any fracture 0.98 (95% confidence interval 0.97 – 0.99), for osteoporotic fracture 0.97 (95% CI 0.96 – 0.98) and for hip fracture 0.93 (95% CI 0.91 – 0.94). The relative risk (RR) per change of BMI in men and women were similar ($p > 0.30$).

When BMD was adjusted for, the gradient of risk changed markedly and remained significantly different from unity only for hip fracture in women (i.e. the overall effect of BMI was mostly due to the influence of BMD). For age, any osteoporotic fracture, the gradient of risk per unit of BMI increased with advancing age (without BMD adjustment). In contrast, for hip fractures, the gradient of risk decreased with age although the trend was not significant. Overall, the RR for hip fracture decreased 0.93 per unit increase in BMI.

For BMI, the RR increased with decreasing BMI but the magnitude of the effect was greater for hip fractures than any osteoporotic or any fracture. Relative risk was markedly higher at lower values of BMI particularly with a BMI of 20 kg/m^2 or less. By contrast, between BMI of 25 kg/m^2 and 35 kg/m^2, the difference in RR was small. There were no significant differences in these relationships between men and women.

Table 17: Relative risk of fracture with and without Bone Mineral Density

BMI (not adjusted for BMD)	**Any fracture RR**	**Osteoporotic fracture RR**	**Hip fracture RR**
15	1.66	1.79	4.48
20	1.21	1.27	1.95
25	1.00	1.00	1.00
30	0.92	0.89	0.83
35	0.85	0.74	0.75
BMI (adjusted for BMD)	**Any fracture RR**	**Osteoporotic fracture RR**	**Hip fracture RR**
15	1.00	1.00	2.16
20	0.98	0.98	1.42
25	1.00	1.00	1.00
30	1.01	1.01	1.00
35	0.99	0.99	1.18

Source: De Laet., et al 2005: Body mass index (BMI); Bone mineral density (BMD); relative risk (RR)

Interpretation

Table 17 shows that when not adjusted for BMD, the relative risk (RR) for any fracture, osteoporotic fracture and hip fracture were high at BMI of 15 and 20 kg/m². There RR was no risk of fracture at BMI of 25kg/m². RR decreased when BMI were 30 and 35kg/m². When adjusted for BMD, the RR was practically nil for all BMIs except for hip fractures at BMI of 15 and 20 kg/m². This suggests that the major influence of BMI on fractures is mainly through BMD except for hip fractures at BMI of 15 and 20 kg/m².

2.4.1.3.3 Original Articles

2.4.1.3.3.1 Baseline Characteristics

Table 18 shows the baseline demographic characteristics of the population included in each of the original 27 studies identified in the systematic review. The publication dates show that the studies of fragility risk assessment tools has been ongoing for 20 years (1990 to 2010). The earliest study was undertaken in 1990 and the majority of studies were conducted between 2001 and 2010 (n=21 [75%]).

The studies were done in Europe (n= 20(74 %), North America (n=5 [19 %]) and Oceania (n=4 (15%). The highest number of publications was in the United Kingdom (n=7 (26%). There were no articles from South America, Asia or Africa.

The lowest age limit was 30 years in 2 (7%) studies and the highest was 103 years in 1 (4%) study. The majority of studies (n=18 [67%]) reported the participant`s mean age, most of which were above 65 years (n=15 [79%]). The remaining studies (n=5 [19 %]) reported age as range or participants equal to or above 60 years (n=1 [4 %]).

The majority of the studies (n=21 [78%]) recruited only female participants, while the remaining (n=5 [19%]) recruited both males and females. There were no studies exclusively in males.

The compositions of ethnic groups were as follows: Caucasians (n=10 [37%]), multiracial (n=3 [11%]), Caucasian and Aboriginal (n=2 [7%]) and mainly Caucasian in 1 (4%) study, ethnicity was not reported in 10 (37%) studies. There were no publications in other ethnic groups.

The majority of the studies (n=21 [78%]) included participants exclusively from the community, and the remaining studies (n=4 [15%]) recruited from both combined community and care home residents, only 1(4%) study recruited exclusively care home residents.

Summary: The demography of the participants shows that the studies were published between 1990 and 2010. All the studies were done in Europe, North America and Oceania with no studies reported in other geographical regions. Most of the participants were middle aged female Caucasians who were recruited from the community. There was only one study which was conducted exclusively in care homes and there were no studies exclusively in males.

Table 18 A: Demography of the participants of the original studies of the systematic review

Authors (s) and year of study	Country of study	Age (y) mean ±SD or (range)	Sex	Ethnicity	Setting(s)
Garnero et al., 1996	France	82.5±4.6	Female	Caucasian	Community (90%) Care home 10%)
Pluijm et al., 2009	Netherlands	74±9.1 76±6.7	Female	Not stated ? Caucasian	Community
McGrother et al., 2002	UK	77.9±6.1 70-103	Female	Not stated	Community/ care home
Black et al., 2001	USA	65-85	Female	99.7% Caucasian	Community
Dargent-Molina et al., 2002	France	80.5±3.7	Female	Caucasian	Community 90%/care home 10%
Hippisley-Cox et al., 2009	UK	42.7 30-85	Female (50.1%) Male (49.9%)	Multiracial	Community/care home
Nguyen et al., 2008	Australia	71±8 female, 70±6 male	Both;female 61.3% Male 38.7%	Caucasian 98.6% Aboriginal 1.4%	Community
Nguyen et al., 2007	Australia	≥60	Both;female 60% male 40%	Caucasian 98.6% Aboriginal 1.4%	Community
Henry et al., 2006	Australia	74±7	Female	Caucasian	Community
Burger et al., 1999	Netherlands	68.1±7.9	Both;Female 57.9% Male 42.1%	Not stated? Caucasian	Community
Kanis et al., 2007	UK	52-82	Both;female 77% male 29%	Multiracial	Community
Barr et al., 2005	UK	68±5.5 60-80	Female	Not stated	Community
Périer et al., 2007	France	62.2±9	Female	Not stated? Caucasian	Community

Table 18 B: Demography of the participants of the original studies of the systematic review

Authors (s) and year of study	Country of study	Age in years mean, SD, range	Sex	Ethnicity	Setting(s)
Hans et al., 2008	France/Switzerland	80.4±3.8 75.2±3.1 77.6±4.3	Female	Caucasian	Community
Gluer et al., 1994	USA	≥65	Female	Caucasian	Community
Porter et al., 1990	UK	83.4±6.2 84.6±6.4	Female	Not stated	Care home
Huang et al., 1998	USA	73.7±4.9 55-92	Female	Caucasian	Community
Cummings et al., 1995	USA	72±5	Female	Caucasian	Community
Tobias et al., 2007	UK	65-75	Female	Not stated	Community
Diez-Pérez et al., 2007	Spain	72.3±5.4	Female	Caucasian	Community
Dargent-Molina et al., 2005	France	80.5±3.8	Female	Caucasian	Community
Tan et al., 2008	Australia	71.3±5.8	Female	Not stated ? Caucasian	Community
Lillholm et al., 2001	Denmark	66.9±5.4	Female	Not stated ? Caucasian	Community
Albrand et al., 2002	France	31-89	Female	Caucasian	Community
Van Staa et al., 2006	UK	50-90	Female	Not stated	Community
Robbins et al., 2007	USA	50-79	Female	Multiracial	Community
Tanaka et al., 2010	Japan	63.4±11.1 59.5±11.3	Female	Not stated ? Japanese	Community

United Kingdom (UK)

Interpretation

Tables 18A and 18B show that the studies of fragility risk assessment tools have been ongoing for over 20 years. All the studies were conducted in Europe, North America and Oceania. Most of the participants in the studies are middle aged female Caucasians who were recruited from the community.

2.4.1.3.3.2 Methodology of the Studies

Table 19 shows the methodology of the twenty seven original articles which were identified in the systematic review. The majority of the studies (n=22 [82%]) were prospective, and the remaining were cross-sectional (n=2 [7%]), case-control (n=2 [7%]) and a combination of prospective and case-control (n=1 [4%]).

The majority of the studies (n=25 [93%]) recruited over five hundred participants. In two studies (n=2 [7%]), the study population was less than 130 and in one (n=1 [4%]), the participants were more than 2 million.

Most of the initial assessment of the participants (n=18 [67%]) were questionnaire-based. Of these, the majority (n=17 [94%]) were by a combination of questionnaire and physical examination, and the remainder (n=1 [4%]) by a combination of questionnaire and biochemical examination. The assessments of the remaining participants were solely by radiological examination in 4 (15%), review of medical record notes, biochemical indices and by a combination of physical and radiological examination in 1 (4%) study each.

Most of the studies (n=15 [56 %]) used any incident fracture at any site as the primary outcome measure and the remainder used the hip (n=10 [37%]) and the spine (n=2 [7%]). The method of verification of incident fractures was mostly by radiological report (n=20 [74%]), and the remainder were by self-report (n=2 [7%]), and combination of radiological and self-report in 2 (7%) studies. There were no records of how incident fractures were verified in the others (n=4 [14%]).

The follow-up of the participants were reported as years in the majority (n=25 [93%]) and person-years (n=2 [7%]) in the remaining studies. In the publications which reported follow-up as years, the duration of follow-up was three years and over in the majority (n=19 [70%]).

The authors analysed their data by using different statistical methods; Cox regression and logistic analysis in 22 (82%) studies, Bayesian model in 2 (7%) studies, correlation coefficient, Student`s t test, and Mann Whitney test in 1 (4%) study each.

Most of the authors (n=16 [59%]) included conflict of interest statements in the publications but the remainder (n=11 [30%]) did not. Most of the authors (n=19 [70%]) stated that they had obtained favourable ethical approval from the appropriate regulatory authorities and there was no documentation from the remainder (n=8 [30 %]).

Summary: The methodology of the studies shows that the majority (82%) were prospective. Most (93%) of the studies recruited over five hundred participants using questionnaire-based approach for the initial assessment. The primary outcome measures in just over half (56%) of the studies were incident fractures at any sites, these were often (74%) verified radiologically. In the majority (70%) of the studies, the follow-up duration of the participants was over three years. The majority (59%) of the authors included conflict of interest statement and most (70%) of them stated they had obtained ethical approval from the regulatory authorities.

Table 19A: Methodology of the original studies included in the systematic review

Author(s)	Design of study	No. of participants	Type of assessment at recruitment	Site of primary outcome measure of study	Method of fracture verification	Duration of follow-up (y)	Method of statistical analysis	Conflict of interest declared	Ethical approval for study Yes/No
Garnero et al., 1996	Prospective	7,598	Questionnaire/biochemical	Hip	Not stated	1.8	Correlation correlation	Not declared	Yes
Pluijm et al., 2009	Prospective	4,919	Questionnaire/physical	Any	Radiological	6-8.9	Cox regression	Not declared	Yes
McGrother et al., 2002	Prospective	1,289	Questionnaire/physical	Hip	Radiological	5.5	Logistic regression	Not declared	Not stated
Black et al., 2001	Prospective	9,704	Questionnaire/physical	Any	Radiological	5	Logistic regression	Declared	Yes
Dargent-Molina et al., 2002	Prospective	7,575	Questionnaire/physical	Any	Self-report	4	Cox regression	Declared	Not stated
Hippisley – Cox et a.,l 2009	Prospective	2,357,895	Medical records	Any	Radiological	15,947515 Person ys	Cox regression	Declared	Yes
Nguyen et al., 2008	Prospective	2,216	Questionnaire/physical	Any	Radiological	13	Bayesian model	Declared	Yes
Nguyen et al., 2007	Prospective	1,948	Questionnaire/physical	Hip	Radiological	13	Bayesian model	Declared	Yes
Henry et al., 2006	Cross-sectional	600	Questionnaire/physical	Any	Radiological	5.8	Logistic regression	Not declared	Yes
Burger et al 1999	Prospective	5,208	Questionnaire/physical	Hip	Radiological	3.8	Logistic regression	Declared	Yes
Kanis et al., 2007	Prospective	59,644	Questionnaire/physical	Any	Radiological/self-report	250,000 Person ys	Poisson regression	Not declared	Yes
Barr et al., 2005	Prospective	7.604	Radiological	Any	Self-report	1.5-2.1	Logistic regression	Declared	Yes

Table 19B: Methodology of the original studies included in the systematic review (continued)

Author(s)	Design of study	No. of participants	Type of assessment at recruitment	Site of primary outcome measure of study	Method of fracture verification	Duration of follow-up in ys	Method of statistical analysis	Conflict of interest declared	Ethical approval for study Yes/No
Périer et al., 2007	Prospective	671	Biochemical	Any	Radiological	10	Cox regression	Not declared	Not stated
Hans et al., 2008	Prospective	12,958	Questionnaire/physical	Hip	Radiological	3.2	Poisson regression	Not declared	Not stated
Gluer et al., 1994	Prospective/ Case control	9,704	Radiological	Hip	Radiological	3.3	Logistic regression	Declared	Yes
Porter et al., 1990	Prospective	1,414	Physical/radiological	Hip	Not stated	2	Student`s t test	Declared	Not stated
Huang et al., 1998	Prospective	560	Radiological	Any	Radiological/self-report	2.7	Logistic regression	Declared	Yes
Cummings et al., 1995	Prospective	9.516	Questionnaire/physical	Hip	Radiological	4.1	Cox`s regression	Not declared	Yes
Tobias et al., 2007	Cross-sectional	540	Questionnaire/physical	Spine	Radiological	Not stated	Logistic regression	Declared	Yes
Diez-Pérez et al., 2007	Prospective	5,201	Questionnaire/physical	Any	Radiological	3	Cox`s regression	Declared	Yes
Dargent-Molina et al., 2005	Prospective	7,512	Questionnaire/physical	Hip	Not stated	3.9	Cox`x regression	Declared	Yes
Tan et al., 2008	Case-control	104	Physical/radiological	Any	Radiological	Not stated	Logistic regression	Not declared	Yes
Lillholm et al., 2001	Case-control	126	Radiological	Lumbar spine	Radiological	6.3	Mann-Whitney test	Declared	Not stated

Table 19C: Methodology of the original studies included in the systematic review (continued)

Author(s)	Design of study	No. of participants	Type of assessment at recruitment	Site of primary outcome measure of study	Method of fracture verification	Duration of follow-up in ys	Method of statistical analysis	Conflict of interest declared	Ethical approval for study Yes/No
Albrand et al., 2002	Prospective	672	Questionnaire/physical	Any	Radiological	5.3	Logistic regression	Not declared	Yes
Van Staa et al., 2006	Prospective	366,104	Questionnaire	Any	Not stated	5.8	Cox`s regression	Declared	Not stated
Robbins et al., 2007	Prospective	93,676	Questionnaire	Hip	Radiological	7.6	Cox`s regression	Declared	Yes
Tanaka et al., 2010	Prospective	1,787	Questionnaire	Any	Radiological	5.3	Poisson regression	Not declared	Not stated

Interpretation

Tables 19A, 19B and 19C show the methodology of the original studies included in the systematic review. The majority were prospective. There were over five hundred participants in most of the studies; one study recruited over 2 million participants. The method of assessment of the participants during recruitment was mostly questionnaire-based. The primary outcome measures were incident fractures at any site and these were often verified radiologically. The follow-up period was over 3 years in the majority of studies. Regression methods of analysis were the commonest method of analysis. Most of the authors included conflict of interest statements and also stated they had obtained ethical approval for the studies from the appropriate review boards.

2.4.1.3.3.3 Findings from the Original Studies

Table 20 shows the results of the findings from the 27 original studies. The performance characteristics of the tools were reported as follows:

- Area under the receiver operating curve (AUC) of the receiver operating characteristics (ROC) curve 15 (54%)
- Sensitivity and specificity 3 (11%)
- Sensitivity and specificity and AUC 2 (7%)
- Odds ratios (OR) 2 (7%)
- Relative risk (RR) 2 (7%)
- C-statistics 2 (7%)
- There was no performance report in one 1 (4%) study

Most of the tools (n=19 [70%]) were not validated internally or externally (n=21 [78%]) and only 3 (11%) were validated both internally and externally. The output of the tools were reported as absolute probability (pseudocalibration as there are no current gold standards for comparison) in the majority (n=19 [70%]).

The output of the tools were reported as absolute risk in 13 (48%), RR in 2 (7%) and not stated in 12 (44%) studies. The models contained variable numbers of predictors with a range of 1 to 18. The commonest number of predictors was 1 (n=5 [19%]).

Few studies reported missing data (n=6 [22%]) and the loss to follow-up of the participants was reported in 2 (7%) studies.

Summary: The findings from the studies show that the majority used AUC to report performance, most of the tools were not validated internally or externally, only a few were validated both internally and externally. Most of the tools were calibrated and these were often undertaken by the authors. The metric of expression of the tools was often by absolute risk. The tools contained variable numbers of predictors but most of them had only one predictor. Few studies reported missing data and loss to follow-up of the participants.

Table 20 A: Findings from the original studies included in the systematic review

Author(s)	Performance characteristics of tools	Internal validation of tools?	External validation of tools?	Internal and external validation	Tool calibrated?	Authors involved in calibration?	Output of tools	No. of risk factors in tools	Missing data reported?	Loss to follow-up reported?
Garnero et al., 1996	Sen. 30-36 Spec. 81	No	No	No	No	NA	NA	2	No	No
Pluijm et al., 2009	c-statistic 0.77	Yes	No	No	Yes	Yes	10 y absolute risk	5	No	No
McGrother et al., 2002	ROC 0.82@3ys 0.77@5.5ys	No	No	No	No	NA	NA	6	Yes	Yes
Black et al., 2001	ROC 0.714 w BMD 0.77 wo BMD	No	Yes	No	Yes	Yes	5 y absolute risk	7 w BMD	No	No
Dargent-Molina et al., 2002	Sen. 37.3 Spec. 85.4	No	No	No	Yes	Yes	Not stated	6 w BMD	Yes	No
Hippisley-Cox et al., 2009	ROC 0.89(hip) in females, 0.86(hip) for males, 0.79 for other fractures in females, 0.69 for males	Yes	Yes	Yes	Yes	Yes	1-10 y absolute risk	18	Yes	No
Nguyen et al., 2008	ROC 0.85	Yes	Yes	Yes	Yes	Yes	5&10 y absolute risk	4	No	No
Nguyen et al., 2007	ROC 0.85	Yes	No	Yes	Yes	Yes	5&10 y absolute risk	4	No	No

Table 20B: Findings from the original studies included in the systematic review (continued)

Author(s)	Performance characteristics of tools	Internal validation of tools?	External validation of tools?	Internal & external validation	Tool calibrated?	Authors involved in calibration?	Output of tools	No. of risk factors in tools	Missing data reported?	Loss to follow-up reported?
Henty et al., 2006	Sen. 59.2 Spec. 64.8 ROC 0.66	No	No	No	Yes	Yes	5&10 y absolute risk	5 w BMD	No	No
Burger et al., 1999	ROC 0.88 w BMD, 0.83 wo BMD	No	No	No	Yes	Yes	4 y absolute risk	6	No	Yes
Kanis et al., 2007	Sen.60.8, spec. 65.6, ROC 0.68 (UK)	Yes	Yes	Yes	Yes	Yes	10 y absolute risk	12 w BMD	Yes	No
Barr et al., 2005	ROC 0.635	No	No	No	Yes	Yes	Not stated	1	No	No
Périer et al 2007	RR 1.03	No	No	No	Yes	Yes	Not stated	1	No	No
Hans et al., 2005	ROC 0.63-0.81	No	No	No	Yes	Yes	10 y absolute risk	7	No	No
Gluer et al., 1994	ROC 0.81	No	No	No	Yes	Yes	Not stated	1	No	No
Porter et al 1990	No induces reported	No	No	No	No	NA	NA	3	No	No
Huang et al., 1998	OR 1.5(vertebral fracture), 1.89 (non-spine) fracture, 1.72 (any fracture)	No	No	No	Yes	Yes	Absolute risk	1	No	No
Cummings et al., 1995	RR 0.6-2.8, RR 0.7-2.0 for base model +fractures+ BMD	No	No	No	No	NA	RR	17	Yes	No

Table 20C: Findings from the original studies included in the systematic review (continued)

Author(s)	Performance characteristics of tools	Internal validation of tools?	External validation of tools?	Internal & external validation	Tool calibrated?	Authors involved in calibration?	Output of tools	No. of risk factors in tools	Missing data reported?	Loss to follow-up reported?
Tobias et al., 2007	ROC BMD 0.68, 4 CRFs 0.74,BMD + 4 CRFs 0.78	Yes	No	No	No	NA	Not stated	5	Not stated	Not stated
Diez-Pérez et al., 2005	ROC 0.67-0.69	No	No	No	No	NA	Absolute risk	6	Not stated	Not stated
Dargent-Molina et al., 2005	Sen. CRFs vs BMD,51vs 34.9	Yes	No	No	Yes	Yes	Not stated	7	Not stated	Not stated
Tan et al., 2008	ROC 0.77	No	No	No	No	NA	Not stated	3	Not stated	Not stated
Lillholm et al., 2001	ROC 0.82	No	No	No	Yes	Yes	Not stated	1	Not stated	Not stated
Albrand et al 2002	OR 1.76 – 1.22	No	No	No	No	NA	Not stated	7	Not stated	Not stated
van Staa et al., 2006	ROC 0.86(hip), 0.69(vertebral), 0.60(others)	No	Yes	No	Yes	Yes	5 y absolute risk	6	Yes	Not stated
Robbins et al., 2007	ROC 0.80	Yes	No	No	Yes	Yes	5 y absolute risk	11	Not stated	Not stated
Tanaka et al., 2010	c-statistic 0.727	No	Yes	No	No	NA	RR	5	Not stated	Not stated

Sens.: sensitivity, Spec.: specificity, PPV.: positive predictive value, NA.: not applicable
RR.: relative risk, SD.: standard deviation, BMD.: bone mineral density
ROC.: receiver operating characteristic, WHO.: World Health Organisation, OR.: odds ratio
CRF.: clinical risk factor, BMI.: body mass index, w.: with, wo.: without

Interpretation

Tables 20 A, 20B and 20C show that the majority of the publications used the AUC under the ROC to report on the discriminatory capacity of the tools. The majority were not validated internally or externally. Most of the tools expressed output as absolute probability. Missing values and follow-up were often not reported.

2.4.1.3.4. Quality Assessment of the Studies

Tables 21 and 22 show the scores of the studies on QUADAS. A score of 7 and above out of the maximum possible of 14 is regarded as good quality study on this scale. The majority of the studies (n=22 [67%]) scored 7 and above each but there were variations in scores in each of the 14 domains.

The highest scores were in domains 2 and 10 (85%) and the lowest was in 3 (12%). The study with the highest score was De Laet et al., 2005 and the studies with lowest scores were NICE, NOF and Huang et al., 1998.

Table 21: Scores of the studies of the systematic review on the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)

Questions Yes/No/Unknown	Fracture risk assessment tools																																
	Marshall et al 1996	Garnero et al 1996	Pluijm et al 2009	McGrother et al 2002	Black et al 2001	Dargent-Molina et al 2006	Hippisley-Cox & Coupland	Nguyen et al 2008	Nguyen et al 2007	Henry et al 2006	Burger et al 1999	NICE CG 146 2012	NOF 1998	Kanis et al 2007	Barr et al 2005	Perier et al 2007	Hans et al 2008	Siminoski et al 2005	Gluer et al 1994	Porter et al 1990	Huang et al 1998	Cummings et al 1995	Tobias et al 2007	Diez-Perez et al 2007	De Laet et al 2005	Dargent-Molina et al 2002	Tan et al 2008	Lillholm et al 2011	Brownhill et al 2003	Albrand et al 2002	Van Staa et al 2006	Robbins et al 2007	Tanaka et al 2010
Was the Spectrum of patients representative of the patients who will receive the test in practice?	N	N	N	Y	N	N	Y	N	N	N	N	Y	N	Y	N	N	N	N	N	Y	N	N	N	Y	Y	N	N	N	U	U	N	N	N
Were selection criteria clearly described?	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y
Is the reference standard likely to correctly classify the target condition?	N	N	U	U	U	U	U	U	U	U	N	U	N	U	N	N	Y	U	N	U	U	N	Y	U	Y	U	N	Y	U	U	U	U	U
Is the period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?	U	N	U	U	U	Y	U	U	U	U	Y	U	Y	U	Y	Y	Y	N	Y	U	U	U	Y	U	Y	Y	Y	Y	U	Y	U	Y	Y
Did the whole sample of a random selection of the sample, receive verification using a reference standard of diagnosis?	Y	Y	U	Y	Y	Y	U	Y	Y	Y	Y	N	U	Y	Y	Y	Y	N	Y	U	N	U	Y	U	Y	Y	Y	Y	U	Y	U	Y	Y
Did patients receive the same reference standard regardless of the index test results?	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	N	U	Y	U	Y	Y	Y	Y	U	Y	U	Y	Y
Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?	Y	Y	U	U	Y	Y	U	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	U	U	U	Y	Y	Y	Y	Y	Y	U	Y	U	Y	Y
Was the execution on the index test described in sufficient detail of permit replication of the test?	Y	Y	N	Y	N	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	U	Y	Y	N	Y
Was the execution of the reference standard described in sufficient detail to permit its replication?	N	Y	N	N	N	N	U	Y	Y	Y	Y	N	N	U	Y	Y	Y	Y	Y	U	U	U	Y	Y	Y	Y	Y	Y	U	Y	U	N	Y
Were the index test results interpreted without knowledge of the results of the reference standard?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	U	Y	Y	U	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y
Were the reference standard results interpreted without knowledge of the results of the index test?	Y	Y	U	Y	U	Y	U	Y	Y	Y	Y	N	N	U	U	U	Y	Y	Y	U	U	U	Y	U	Y	Y	Y	Y	U	Y	Y	Y	Y
Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	N	Y	Y	U	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	U	U	U	U	U	U	U	N	U	Y	U	U	U	U	U	U	Y	Y
Were uninterpretable/Intermediate test results reported?	N	N	N	Y	Y	U	Y	U	U	U	U	N	N	Y	U	U	Y	U	U	U	N	U	U	U	Y	U	Y	U	U	U	Y	U	U
Were withdrawals from the study explained?	N	N	Y	Y	Y	N	Y	U	U	U	Y	N	N	Y	Y	U	U	U	Y	U	N	Y	U	U	Y	Y	U	U	U	U	Y	U	U
Total	6	9	4	8	7	8	8	9	9	7	11	2	2	10	9	8	11	5	10	4	2	4	9	6	13	10	10	10	0	9	5	8	10

N= no , Y= yes, U= unknown

Interpretation: Table 21 shows that the scores on QUADAS indicate that the majority of the tools were of good quality but there were variations in many domains.

Table 22: Summary of the responses on the Quality Assessment of Diagnostic Accuracy Studies

Questions	Yes	No	Unknown
Was the spectrum of patients representative of the patients who will receive the test in practice? n (%)	7 (21)	24 (73)	2 (6)
Were selection criteria clearly described? n (%)	28 (85)	4 (12)	1 (3)
Is the reference standard likely to classify the target conditions correctly n (%)?	4 (12)	9 (27)	20 (61)
Is the period between the reference standard and the index test short enough to be reasonably sure that the target condition did not change between the two tests? n (%)	15 (46)	2 (6)	16 (49)
Did the whole sample of a random selection of the sample receive verification using a reference standard of diagnosis? n (%)	22 (67)	3 (9)	8 (24)
Did patients receive the same reference standard regardless of the index test results? n (%)	25 (76)	4 (12)	4 (12)
Was the reference standard independent of the index test? (i.e. the index did not form part of the reference standard) n (%)	23 (70)	2 (6)	8 (24)
Was the execution of the index test described in sufficient details to permit replication of the test? n (%)	25 (76)	7 (21)	1(3)
Was the execution of the reference standard described in sufficient details to permit its replication? n (%)	18 (55)	8 (24)	7 (21)
Were the test results interpreted without knowledge of the results of the reference standard? n (%)	28 (85)	2 (6)	3 (9)
Were the reference standard results interpreted without knowledge of the results of the index test? n (%)	20 (61)	2 (6)	11 (33)
Were the same clinical data available when the test results were interpreted as would be available when the test is used in practice? n (%)	14 (42)	4 (12)	15 (46)
Were uninterpretable test results reported? n (%)	8 (24)	6 (18)	19 (56)
Were withdrawals from the study explained? n (%)	12 (36)	6 (18)	15 (46)

Quality Assessment of Diagnostic Accuracy Studies (QUADAS)

Interpretation

Table 22 shows that although the majority of the responses to the questions on QUADAS were `yes`, the response relating to the reference standard were low which highlights the fact that currently there is no single diagnostic test for fragility fractures. For fragility fracture risk assessment, FRAX is the most widely used. Many publications did not report on uninterpretable test results and withdrawals which threaten validity of the data.

2.4.1.3.5. Characteristics of the Tools

Table 23 shows the distribution of the predictors in the tools. They were grouped into 8 domains:

- Dermography; refers to the characteristics such as age, sex, ethnicity
- Radiological investigations; refers to the radiological investigation and fractures
- Comorbidities; refers to the presence of one or more diseases in the same person
- Physical limitations; refers to difficulty performing any physical activities
- Life style; refers to behavioural and social issues that may impact health such as alcohol, smoking
- Types of medications; this refers to the different drugs which may have effect on falls and musculoskeletal health
- Living arrangement; refers to the way someone organises how and where they live
- Biochemical indices; a number of biochemical indices are related to falls and musculoskeletal health

The most common was demography (n=22 [76%]). In this domain, the distribution of the risk factors was as follows: age 15 (52%); body mass index/weight 13 (49%); gender 9 (31%); ethnicity 3 (10%); and height after 25 years 1 (3%).

The next domain was the result of radiological investigations (n=20 [69%]). The distribution of predictors in this domain was as follows: axial BMD 10 (35%); broad band ultrasound attenuation (BUA) 6 (21%); vertebral morphology 3 (10%); peripheral BMD 2 (7%); and X-ray pelvis 1 (3%).

Comorbidities was the next commonest domain (n=19 [66%]). The distribution of the risk factors were as follows: history of prior fractures 15 (52%); history of falls 9 (28%); diabetes mellitus 3 (10%); rheumatoid arthritis 2 (7%); other causes of osteoporosis 2 (7%); dementia 2 (7%); and history of back pain 1 (3%); cancer 1 (3%); asthma/copd 1 (3%); IHD/stroke 1 (3%); chronic liver disease 1 (3%); chronic kidney disease 1 (3%); Parkinson`s disease 1 (3%); malabsorption 1 (3%); endocrine problems 1 (3%); and history of early menopause 1 (3%).

The next domain was physical limitations (n=12 [41%]). The distribution of the risk factors were as follows: use of the arms to stand up 3 (10%); visual defects 3(10%); use of walking aids 2(7%); reported poor health 2 (7%); grip strength 2 (7%); gait speed 2 (7%); poor circulation in the feet 2 (7%); poor trunk manoeuvre 1(3%); assistance with activities of daily living (ADLs) 1 (3%); tachycardia 1 (3%); and the ability to tandem walk 1 (3%).

The next domain was life style factors (n=10 [34%]). The distribution of the risk factors were as follows: history of smoking 7 (24%); physical activities 3 (10%); alcohol history 2 (7%); calcium intake less than 250mg/day 1 (3%); and history of taking great amount of caffeine 1(3%).

The next domain was the types of medications taken by the patient (n=6 [21%]). The distribution were as follows: oral corticosteroids 3 (10%); anticonvulsants 2 (7%); recent use of CNS drugs 2 (7%); and oestrogen only HRT 1 (3%).

The last two domains were living arrangements (living in a care home) and biochemical indices (bone turnover markers) which contained 1 (3%) risk factor each.

Summary: There was considerable heterogeneity in the broad categories of the predictors of the tools. The most common were demographic variables. The next were radiological

investigations, comorbidities, physical limitations, life style factors, the types of medications, living arrangements and biochemical indices in that order.

Table 23A: Characteristics of the tools identified in the systematic review

Variables	Marshall et al 1996	Garnero et al 1996	Pluijm et al 2009	McGrother et al 2002	Black et al 2001	Dargent-Molina et al 2006	Hippisley-Cox & Coupland	Nguyen et al 2008	Nguyen et al 2007	Henry et al 2006	Burger et al 1999	Kanis et al 2007	Barr et al 2005	Perier et al 2007	Hans et al 2008	Gluer et al 1994	Porter et al 1990	Huang et al 1998	Cummings et al 1995	Tobias et al 2007	Diez-Perez et al 2007	De Laet et al 2005	Dargent-Molina et al 2002	Tan et al 2008	Lillholm et al 2011	Albrand et al 2002	Van Staa et al 2006	Robbins et al 2007	Tanaka et al 2010
Demographic Details																													
Age			X		X	X	X	X	X		X	X								X	X		X			X	X	X	X
Gender							X	X	X		X	X					X		X				X	X					
Ethnicity							X	X																				X	
Body Mass Index or Weight			X	X	X	X	X			X	X	X			X							X					X	X	X
Height after 25 years																			X										
Life Style Factors																													
Smoking			X		X		X				X	X			X													X	
Alcohol							X					X																	
Calcium intake < 250mg/day																					X								
Taking great amount of caffeine																			X										
Physical activity																			X							X		X	
Living arrangement																													
Care home							X																						
Community																													
Physical Limitations																													
Use of walking aid			X								X																		
Poor trunk manoeuvre				X																									
Reported poor health																			X									X	
Use of arms to stand up					X										X				X										
Instrumental ADL assistance						X																							
Grip strength						X																				X			
Visual defects						X													X				X						
Tachycardia																			X										
Ability to do tandem walk																							X						
Gait speed																	X						X						
Poor circulation in feet				X																				X					
Family History																													
Family history of fracture					X		X					X									X					X		X	

Table 23B: Characteristics of the tools identified in the systematic review (continued)

Variables	Marshall et al 1996	Garnero et al 1996	Pluijm et al 2009	McGrother et al 2002	Black et al 2001	Dargent-Molina et al 2006	Hippisley-Cox & Coupland	Nguyen et al 2008	Nguyen et al 2007	Henry et al 2006	Burger et al 1999	Kanis et al 2007	Barr et al 2005	Perier et al 2007	Hans et al 2008	Gluer et al 1994	Porter et al 1990	Huang et al 1998	Cummings et al 1995	Tobias et al 2007	Diez-Perez et al 2007	De Laet et al 2005	Dargent-Molina et al 2002	Tan et al 2008	Lillholm et al 2011	Albrand et al 2002	Van Staa et al 2006	Robbins et al 2007	Tanaka et al 2010
Comorbidities																													
Prior fracture			X			X	X	X	X	X		X			X					X	X			X		X	X	X	X
Epilepsy				X			X																						
Diabetes Mellitus							X								X													X	
History of Fall							X	X	X	X					X						X		X				X		
Dementia							X										X												
Cancer							X																						
Asthma/COPD							X																						
IHD/Stroke							X																						
Chronic Liver disease							X																						
Chronic Kidney disease 4 or 5							X																						
Parkinson`s Disease							X																						
Rheumatoid Arthritis							X					X																	
Malabsorption							X																						
Endocrine problems							X																						
Other causes of secondary osteoporosis												X							X										
History of early menopause																													
History of back pain																				X									X
Radiological Features																													
Axial BMD	X	X				X			X	X	X	X												X		X			X
Geometric and structure of femur																													
X-ray pelvis																X													
BUA Index															X		X	X	X		X			X					
Vertebral morphology				X																X					X				
Hip Geometry																													
CT models																													
Peripheral BMD													X					X											
Biochemical Features																													
Bone turnover markers		X																											
Serum Homocysteine														X															
Medications																													
Use of oral steroids				X								X																X	
Taking oestrogen only HRT							X																						
Antidepressant							X																						
Anticonvulsant							X												X										
Recent use of CNS drugs																			X								X		

X= present

Interpretation : Tables 23A and 23B show that QFractureScores (Hippisley-Cox et al,2009) had the highest number of predictors which were distributed in most of the domains. BMD (Marshall et al, 1996) had only one predictor which was in the radiological domain. The predictors in the other tools were in between.

2.4.2. Summary of Findings

Thirty three tools informed this review: 4 general literature based review based tools, 2 meta-analyses based tools and 27 original study based tools. The main findings from the reviews were:

General literature review based tools. Of the four tools, three were synthesised by opinion leaders. The articles which they reviewed and their quality (quantity risk of bias) were not stated and guidelines were subsequently produced for their use. In the fourth article, the author suggested that hip geometry was a promising tool for predicting hip fractures and more research was needed. This researcher awarded scores of between 0 and 5 to the methodology on QUADAS.

Meta-analyses based tools. The first of the two meta-analyses was conducted in 1994 and the tool was based on the relative risk of fragility fracture in females, age adjusted sustaining fragility fractures for 1 SD difference in BMD. The articles which were used were published from 1985 to 1994. Two types of studies were used: prospective cohort studies (11 of them) and case-control studies (8 of them). All the measuring sites had had similar predictive abilities (RR 1.5 [95% Confidence interval 1.4 to 1.6]) for decrease in bone mineral density except for measurement at spine for predicting vertebral fractures (RR 2.3 [11.9 to 2.8]) and measurements at the hip for hip fractures (RR 2.6 [2.0 to 3.5]). The quality of scores for the prospective studies ranged from 11.7 to 19.3 out of a possible 25 but the assessors did not state the quality of the case-control studies. This researcher rated the quality of the entire meta-analysis as poor and awarded 6 on QUADAS.

The second meta-analysis based tool, BMI was conducted in 2004 and it explored the effects of BMI, BMD, age and sex on the risk of fractures using international population-based

cohorts. The data were robust that low BMI increase fracture risk while BMI of 25kg/m² and above is protective. The authors did not report quality assessment of the studies they used; this researcher awarded a score of 13 on QUADAS.

Original study based tools. A total of 27 tools were identified. All the tools were derived in developed countries between 1990 and 2010. The majority (82%) of the tools were derived from prospective studies. Just over a half (57%) used any incident fractures as primary outcome which were verified radiologically in the majority (71%). Although the majority of the authors included conflict declaration, 39% did not. Most (71%) of the authors stated they had ethical approval from the appropriate review board and there was no such documentation in 29%. This author`s assessment of the quality of the studies ranged from 2 to 13 out of a possible 14.

2.4.3. Step 2 Selecting Tools for Care Home Residents

2.4.3.1. The selection process

The flow chart is shown in Figure 3. When the first criterion (was the design of the study prospective, systematic review or meta-analysis?) was applied, 24 (82.7%) fragility tools remained. When the second criterion (is the tool useable for any fragility fracture?) was applied, 14 (58%) fragility tools were left. When the third criterion (is the tool applicable to both sexes?) was applied, 4 (28.6%) fragility tools were left. When the last criterion (is the tool cost effective or pragmatic for care home residents?) was applied, 4 tools were left; they are FRAX, QFractureScores, Garvan nomogram and body mass index (BMI).

1. Marshall et al., 1996
2. Garnero et al., 1996
3. Pluijm et al., 2009
4. McGrother et al., 2002
5. Black et al., 2001
6. Dargent-Molina et al., 2002
7. Hippisley Cox & Coupland 2009
8. Nguyen et al., 2008
9. Nguyen et al., 2007
10. Henry et al., 2006
11. Burger et al., 1999
12. NICE Clinical guide 146
13. NOF 1998
14. Kanis et al., 2007
15. Barr et al., 2005
16. Perier et al., 2007
17. Hans et al., 2008
18 Simoniski et al., 2007
19 Glüer et al., 1994
20 Porter et al., 1990
21 Huang et al., 1998
22 Cummings et al., 1995
23 Tobias et al., 2007
24 Diez-Perez et al 2007
25 De Laet et al., 2005
26 Dargent-Molina et al., 2005
27 Tan et al., 2008
28 Lillholm et al., 2011
29 Brownbill et al., 2003
30 Albrand et al., 2002
31 Van Staa et al., 2006
32 Robbins J et al., 2007
33 Tanaka S et al., 2010

Was the study prospective or systematic review or meta-analysis? If yes accepted

1. Marshall et al., 1996
2. Garnero et al., 1996
3. Pluijm et al., 2009
4. McGrother et al., 2002
5. Black et al 2001
6. Hippisley Cox & Coupland 2009
7. Nguyen et al., 2008
8. Nguyen et al., 2007
9. Burger et al., 1999
10. Kanis et al., 2007
11. Barr et al 2005
12. Perier et al., 2007
13. Hans et al., 2009
14. Glüer et al., 1994
15 Porter et al., 1990
16 Huang et al., 1998
17 Cummings et al., 1995
18 Diez-Perez et al., 2007
19 De Laet et al., 2005
20 Dargent-Molina et al., 2005
21 Albrand et al., 2002
22 Van Staa et al., 2006
23 Robbins J et al., 2007
24 Tanaka S et al., 2010

Was any fragility tool the endpoint? If yes accepted

1. Marshall et al., 1996
2. Pluijm et al., 2009
3. Black et al 2001
4. Hippisley Cox & Coupland 2009
5. Nguyen et al., 2008
6. Henry et al., 2006
7. Kanis et al., 2007
8. Barr et al., 2005
9. Perier et al., 2007
10. Huang et al., 1998
11. Diez-Perez et al., 2007
12. De Laet et al., 2005
13. Van Staa et al., 2009
14. Tanaka S et al., 2010

Is the tool practicable in both sexes? If yes accepted

1. Nguyen et al., 2008 (Garvan nomogram)
2. Hippisley Cox & Coupland 2009 (QFractureScores)
3. Kanis J et al., 2007 (FRAX)
4. De Laet et al., 2005 (Body Mass Index)

Is the tool cost effective/ pragmatic for care home residents? If yes accepted

1. Nguyen et al., 2008 (Garvan nomogram)
2. Hippisley Cox & Coupland 2009 (QFractureScores)
3. Kanis J et al., 2007 (FRAX)
4. De Laet et al., 2005 (Body Mass Index)

Figure 3: Flow diagram of the second part of the systematic review showing the selection of the tools for use in care homes

Interpretation

Figure 3 shows that of the 33 tools, when the first criterion was applied 24 were selected, when the secord criterion was applied, 14 were selected, when the third criterion was applied, 4 were selected and when the last criterion was applied, the 4 tools were found practicable for use in care home residents. They were FRAX, QFractureScores, Garvan nomogram and body mass index (BMI).

2.4.3.2. The Characteristics of the Selected Tools

The predictors in the tools are shown in Table 24.

FRAX has twelve predictors these are: age, sex, smoking status, alcohol history, weight, height, diabetes mellitus, parental history of fractures, history of prior fractures, rheumatoid arthritis, malabsorption, endocrine disorders, and oral corticosteroids. The output of the tool is 10 year absolute probability which can be computed with or without BMD. The sociodemographic predictors in FRAX account for half of the risk factors and the remaining are comorbidities.

QFractureScores has twenty-six predictors these are: age, sex, ethnic status, smoking history, alcohol status, diabetes mellitus, past history of fractures, parental history of fractures, living in care home, history of falls, dementia, cancer, asthma/copd, heart attack/angina/TIA, chronic liver disease, chronic kidney disease, Parkinson`s disease, rheumatoid arthritis, malabsorption, endocrine disorders, epilepsy/anticonvulsants, antidepressants, corticosteroid tablets, oestrogen HRT only, body mass index (height, weight). The output is as annualised absolute fracture risk for 10 years. The comorbidities in QFractureScores make up 70% of the predictors while the sociodemographic risk factors account for the rest.

Garvan nomogram has five predictors these are: age, sex, previous history of fractures, history of falls and femoral neck BMD. The output of the tool is as 5 or 10 year absolute probability. When the femoral neck BMD is not available, body weight can be used as surrogate. If the body weight is used, the demographic predictors in Garvan nomogram account for 60% while the comorbidities account for the rest.

BMI is the only predictor in the fourth tool. Body weight or body mass index is common to all the tools. Age, sex, previous history of fractures and history of falls are common to FRAX, QFractureScores and Garvan nomogram. Age, sex, smoking status, alcohol status, diabetes mellitus, parental history of fractures, previous history of fractures, rheumatoid arthritis, malabsorption, endocrine disorders, oral corticosteroid use, weight, and height are common to FRAX and QFractureScores.

FRAX, QFractureScores and Garvan nomogram have output of 10 year absolute probability but only QFractureScores has annualised fracture risk for 1 to 10 years.

Summary: The four fracture risk assessment tools selected for use in care home residents contain variable numbers of predictors. QFractureScores has the highest while body mass index has the lowest. Body mass index/weight is a common predictor in all four. All the models except BMI are calibrated and the outputs are expressed as 10-year absolute probability. Only QFractureScores has annualised absolute risk score for one to ten years and it is also the only model which includes the type of living accommodation as predictor.

Table 24: The predictors of the 4 tools identified from the second part of the systematic review.

Variables	FRAX	QFractureScores	Garvan nomogram	Body mass index
Age	X	X	X	
Sex	X	X	X	
Ethnic status		X		
Smoking status	X	X		
Alcohol status	X	X		
Diabetes mellitus	X	X		
Parental history of fractures	X	X		
Previous history of fracture	X	X	X	
Living in care home		X		
History of falls		X	X	
Dementia		X		
Cancer		X		
Asthma		X		
COPD		X		
Heart attack/angina/TIA		X		
Chronic liver disease		X		
Chronic kidney disease		X		
Parkinson`s disease		X		
Rheumatoid arthritis	X	X		
Malabsorption	X	X		
Endocrine disorders	X	X		
Epilepsy/anticonvulsants		X		
Antidepressants		X		
Corticosteroid tablets	X	X		
Oestrogen HRT only		X		
Body mass index		X		X
Height (cm)	X	X		
Weight (kg)	X	X	X	
Femoral neck BMD	X		X	
10-year fracture probability	X	X	X	

X=present
COPD=chronic obstructive pulmonary disease
TIA=Transient ischaemic attack
BMD Bone mineral density

Interpretation

Table 24 shows that the predictors in the four tools were different. QFractureScores had the highest and BMI the lowest. BMI was a common predictor in FRAX, QFractureScores and Garvan nomogram.

2.5 Discussion

The key findings of this systematic literature review were:

1. In the first part, 33 fragility assessment tools were identified of which 4 were literature review based, 2 were meta-analyses based and 27 were original studies based.

2. In the second part of the review 4 of the 33 tools identified in the first part were practicable for care home residents; these were FRAX, QFractureScores, Garvan nomogram and BMI.

The discussion that follows will be presented in four sections: section 1 will be the review articles, section 2 will be the meta-analysis, section 3 will be the original studies and section 4 will be discussion of the four tools which were finally selected for care home residents.

2.5.1 Review Articles

The two national guidelines (NICE and NOF) cited earlier were developed from general literature review by opinion leaders. The international validity of candidate risk factors and the extent to which they can identify a reversible risk is amenable to an evidenced-based approach. There are well-established methods for evaluating the quality of evidence of different approaches (Khan K, 2003). The lowest level of evidence is provided by expert committees or clinical experience i.e. level V11 evidence. Systematic reviews and meta-analysis represent the gold standards because they constitute level I evidence and provide more robust evidence than general literature reviews.

The publication by Brownbill and colleagues identified some indices of hip geometry as predictors of hip fractures in females (HAL, FNW and NSA). It was suggested that the different incidence rates in hip fracture in females may be explainable by these but it is not known if these measurements also predict other fractures. While these measurements may be useful in a subset of the population, further studies are needed to assess their usefulness as predictors of fragility fractures.

2.5.2 Meta-analyses

2.5.2.1 Meta-analysis of How Well Measures of Bone Mineral Density Predict Occurrence of Osteoporotic Fractures

The aim of the meta-analysis to determine the ability of measurements of bone density in women to predict later fractures; a combination of prospective cohort and case-control studies were used. The main outcome measure was the relative risk of fracture for a decrease in BMD of one standard deviation below age adjusted mean. The results were similar in the two groups, therefore the authors concluded that measurement of BMD can predict fracture risk but cannot identify individuals who will have a fracture.

The study had some strengths; first the design (meta-analysis) of the study. Meta-analysis of high quality randomised controlled studies that show consistent effects is the gold standard in evidence based intervention and the inclusion of an internal control is important for the highest level of evidence (Khan K, 2003). But the demonstration of a significant risk for 1SD decrease of BMD in postmenopausal women would not provide enough evidence for a similar degree of risk in males because a sample frame that does not capture the population in which the test would be applied results in a lower level of evidence (level II studies and below).

The results of the group analyses were similar; the different designs (prospective cohort and case-control) indicate consistency of the relative risk of fracture for fractures in women. However, case-control studies are efficient only for studies aimed at finding the independent predictors of an outcome out of a larger set, not for developing a prediction model. This is because this design does not allow for estimation of absolute risks because the correct baseline risk or hazard cannot be retrieved from the data except by using a nested case-control or case-control design (Moons, 2010, Biesheuvel et al., 2008).

This meta-analysis had limitations: the restriction of the search language to English may have omitted some publications. It compared BMD with a group of Swedish women but mortality and fracture rates vary between populations which may underestimate or overestimate risk. Also, the studies were conducted in the developed countries (USA, Sweden, UK, Finland, and Australia) which suggest that the findings may not be applicable to other geographical settings.

The ethnic composition of the participants was not stated; ethnic composition is important because of the known differences in fracture risk. Also, the results may not be applicable to males as only females were included. Therefore, from a clinical perspective, the participants are not representative of those who will receive the test in practice. In addition, different techniques were used in the baseline assessment of the BMD; BMD measurements between techniques are not transferable and comparable because the correlation coefficients between skeletal sites are too low for predictive purposes and population variances differ as do apparent rates of bone loss.

Although BMD is the gold standard for the diagnosis of osteoporosis, the technique of estimation has some limitations; DEXA provides a two-dimensional projection of a three-dimensional structure, therefore it cannot capture bone geometry or microarchitecture. Consequently, the BMD values obtained with DEXA do not represent the true volumetric bone mineral density but rather a projected areal bone mineral density, DEXA estimation is confounded by bone size because it cannot distinguish between increased BMD values arising from thicker bones (geometric change) and those arising from increased tissue mineral density (material change). DEXA estimates can be distorted by aortic calcification, soft-tissue calcification, and other artefacts in an older individual who are at greater risk of fracture. DEXA does not distinguish the contributions from trabecular and cortical bones.

DEXA provides static information and may not detect any differences for several years after osteoporosis treatment (Bonnick, Shulman, 2006, Delmas, 2000, Roux et al., 2005) and the assessment is not pragmatic for care home residents who will be required to disrobe. DEXA scans are expensive, their availability is restricted to major hospitals and the cost of examination is substantial. The labour force required is also immense (Eastell, 1998). In some countries, it is predominantly a research tool. DEXA machines range in cost from $25,000 to $85,000. DEXA machines are not portable unlike quantitative ultrasound (QUS). Given these limitations, BMD is not recommended as a sole predictor for fracture assessment.

It is unclear whether uninterpretable tests and withdrawals were reported in the studies which were analysed. The analyses were based on relative risk but this approach does not include the background risk of the individual patient beyond age and gender-adjustments, therefore it is an imperfect estimate of the absolute risk for an individual over a given period. This researcher`s quality assessment score on QUADAS was 6.

2.5.2.2. Body Mass Index as a Predictor of Fracture Risk

The findings were convincing that low BMI is associated with a substantial increase in fracture risk of similar magnitude in men and women whereas high BMI is protective. The risk associated with low BMI was present at most ages for all types of fractures but was strongest for hip fracture. At BMI of 30 kg/m² and 35 kg/m², BMD appears to have less influence on hip fractures given the RRs reported. It is plausible that the impact of the force of impact may be more important at these values of BMI because the bigger the mass, the greater the gravitational force.

The strength of the study was that it was an international prospective cohort study with prolonged periods of follow-up. The limitations were: cohorts in Middle East, South America

and Africa were not included therefore it is not known how the findings apply to people in these continents. BMD assessments were done by different methods which may also affect the estimates. Lastly fracture assessment was sometimes by self-report which may have introduced some bias if these were not verified by X-ray reports.

2.5.3 Original Articles

2.5.3.1 Main Findings

The results show fragility tool derivation has been ongoing for many years. 33 fragility tools were identified, but only 6 (18%) were externally validated in a population-based setting (Fracture Risk Index, FRAX, QFractureScores, Garvan nomogram, Simple Clinical Score and FRISC). There was only one study that recruited elderly female participants exclusively from the care home and geriatric settings (Porter et al., 1990). All the studies were conducted in developed countries and most of them recruited only postmenopausal female Caucasians.

2.5.3.1.1 Historical Perspective

About two decades ago, BMD provided the most useful proxy measure for fracture assessment (Ross et al., 1990) but it has since been recognised that clinical risk factors play significant and independent roles (Cummings, Black, 1995, Burger et al., 1999, Dargent-Molina et al., 1999). Epidemiological studies show that most fragility fractures occur in osteopenia patients i.e. patients with normal BMD (Wainwright et al., 2005). Using WHO criteria, it has been demonstrated that the risk prediction algorithms that do not include bone mineral density are almost as good as those that do (Black et al., 2001b). Only 34% of women and 21% of men who sustained non-vertebral fracture had BMD in the osteoporotic range (Schuit et al., 2006), only half of elderly women with incident hip fracture had BMD in osteoporotic range at baseline (Wainwright et al., 2005) and only 10 to 44% of bone fractures can be attributed to low bone mass (Stone et al., 2003).

Also BMD explains less than 50% of the variation in whole-bone strength (Melton, 1993, Dufresne et al., 2003, Cummings, Bates & Black, 2002). The National Osteoporosis Risk Assessment Study showed that 82% (1852) of 2259 postmenopausal women with a fracture after 1-year of follow-up had T-score above -2.5 and 67% (1514) had a T-score greater than -2.0 (Siris et al., 2004). Similarly, in the Rotterdam Study only 56% (280 of 499) of the non-vertebral fractures in women and 79% (115 of 1450 in men occurred in people with T-score in the osteoporotic range (Schuit et al., 2006). Analysis of data on trials of antiresorptive drugs showed improvement in spinal BMD during treatment accounted for only a small part in the observed reduction in risk of vertebral fracture (Cummings, 2002, Sarkar et al., 2002).

2.5.3.1.2 Geographical Setting

Most studies were conducted in Europe, North America, and Australia therefore it is questionable if the models derived can be used in other geographical settings such as Asia, Africa or South America. The setting of model derivation has an influence on demographic variables because of the differences in environment and cultural practices (sunlight exposure, diet, education, religion). Tools are dependent on the accuracy of epidemiological data used to derive them; therefore tools validated in one population may not necessarily be useable in others. Studies over the last decades have demonstrated geographical variation in the incidence of hip fracture across continents as well as among different parts of a region (Johnell et al., 2007, Johnell et al., 1992). For example, the incidence of hip fracture is highest in Sweden and North America with almost seven-fold lower rates in Southern European countries and hip fracture rates are lower in Asia and Latin American populations.

2.5.3.1.3 Design of Study

The majority of studies were prospective; this has merit because of the time dependent nature of fragility fractures. Prospective studies usually have fewer potential sources of bias and confounding variables. (Bowers, 2000). Consequently, the Guideline Development Group recommends that research in the development of fragility risk tools should be prospective (Guideline Development Group, 2012). The majority of the participants in the studies were community based. Given this, most of the tools may not be useable in the high-risk frail elderly such as care home residents.

2.5.3.1.4 Number of Participants in Study

Many of the studies recruited over 500 participants; this numerical value has some merit as it increases the study power and makes statistical inferences more robust. The larger the study sample, the more it reflects the source population, and the less the performance in the study sample deviates from the performance that would theoretically be found in the source population. To increase the statistical power of a test, it is important that there are a large number of randomly selected participants. For a 95% confidence interval (which means that there is only a 5% chance the sample results differ from the true population average), a good estimate of the margin error (or confidence interval) is given by the equation: $1/\sqrt{N}$ where N is the number of participants or sample size (Niles, 2006). In medical research, a study sample is supposed to be a random draw from a larger (theoretical) target or source population. However, the selection of participants in the majority of the studies was not random casting doubt on the representativeness of the study population.

To reduce the margin of error to plus or minus 5%, 500 randomly selected participants is suggested but no firm guidelines exist on sample size requirements to develop or validate studies (Collins, Michaelsson, 2012, Vergouwe et al., 2005) and effective sample size is not

driven by the number of subjects but the number of events. Empirical simulations have found that at least 100 events are required to validate a prediction model (Vergouwe et al., 2005). Many of the studies did not report the number of incident events therefore it is not known if these studies were underpowered.

2.5.3.1.5 Age of the Participants

Most studies recruited people of 50 years and over, the age at which fragility fractures commonly begin to occur; this has merit. Age is a powerful independent risk factor for fragility fractures. At the age of 50 years, approximately 75% of people hospitalized for vertebral fractures have fractures attributable to low energy injuries, increasing to 100% by the age of 90 years (Johnell, 2005). In women with osteoporosis (T-score of minus 2.5), the probability of hip fracture is five times greater at the age of 80 years than at the age of 50 years (Kanis JA et al 2008). But surprisingly, age was largely ignored as a predictor in some models.

2.5.3.1.6 Sex of the Participants

Most tools were derived from females; while it is established that the incidence rate of fragility fractures is higher in females, an increasing proportion of males also sustain fragility fractures (Kanis et al., 2001, Cummings, Bates & Black, 2002, Kanis, 2002b, Compston, Rosen, 2006, Morales-Torres, Gutierrez-Urena & PANLAR, 2004), therefore many of the tools may not be useable in both sexes.

2.5.3.1.7 Race/Ethnicity of the Participants

Most studies did not state the ethnicity of the participants; about 37% were derived from Caucasians only therefore their application is not generalizable to other ethnic groups. Worldwide, the incidence of hip fractures varies with ethnicity (Kanis, 2002b). Rates of hip

fractures are highest in Northern European countries where the 10-year relative probability of hip fractures averaged for age and sex is 1.25 in Sweden compared to 0.62 in Singapore and 0.08 in Chile (Kanis, 2002b). Persons of African ancestry, have very low rates of hip fractures (GRIFFIN et al., 1992). One large-scale multi-ethnic longitudinal study showed that African-American and Asian women had lower risks of fracture than white women, after adjusting for weight, BMD, and other clinically important factors (Barrett-Connor et al., 2005).

There is much less ethnic variability in morphometric vertebral fractures worldwide. The prevalence of vertebral fractures in women older than 65 years is 70% for white women, 68% for Japanese women, 55% for Mexican women and 50% in African American women (Cauley et al., 2008, Cummings, Melton, 2002, Clark et al., 2009). Epidemiological data show that Asian ethnicity is associated with lower BMD values compared to other ethnicities when adjusted for body mass index (Goh, Low & DasDe, 2004). Low BMD values were also obtained in Sub-Sahara region in Black-African women from Gambia but fragility fractures are rare in this population (Aspray et al., 1996). This contrasts with Black Americans and Brazilians who have higher BMD than Caucasians, after adjustment for socioeconomic status (Siqueira, Facchini & Hallal, 2005).

2.5.3.1.8 Fracture Outcome of the Study

Most of the studies used any osteoporotic fracture as outcome which suggests that the majority of the tools could be used for predicting any fragility fracture. About 37% of the tools used hip fracture limiting their application. Vertebral fractures typically occur earlier and are an established risk factor for hip fractures (Kanis et al., 2005a). Therefore, from a fragility prevention perspective, a risk assessment that predicts vertebral fracture may be more useful.

2.5.3.1.9 Methods of Verification of Outcome of Study

The majority of studies verified fractures radiologically which provided robust evidence for fracture. About 18% were by self-report which may have introduced response bias and cast doubts on the results. Although self-report represents a cheap way of collecting data, they rely on the honesty of the participant. Even when a participant is trying to be honest, they may lack the introspective ability to provide an accurate response to a question. Also participants may have varying understanding or interpretation of a research question. Ideally to avoid possible bias, it is suggested that the outcome measurement should be blinded to or independent of any knowledge of the predictors under consideration (Moons et al., 2012).

2.5.3.1.10 Duration of Follow-up of the Participants

For the development of prognostic models, the duration of follow-up for the outcome data collection should be clearly defined. In this review, about 50% of the models were derived following 4 or more years of follow-up. This has merit because of the time dependent nature of fragility fractures. The European Medicine Agency (EMA) recommends that a period of 2 to 5 years should be allowed for evaluation of osteoporotic medications (European Medicines Agency (EMA), 2005).

2.5.3.1.11 Validation of the Tools

Few tools were validated internally, externally or both. Both internal and external validations are recommended in the development of tools (Leslie, Lix, 2014). Internal validation refers to the process of assessing the reproducibility of the risk in the same population and confirms that no other data other than the study sample are being used. Internal validation can be assessed by generating a random subset from the sample population and evaluating performance in another subset of the same population. Prediction models can be expected to perform optimistically in the data sample from which they are developed compared with the

performance found when tested in new but comparable individuals. External validation refers to the generalisation of the model in other populations. External validation can be assessed by comparing the efficacy of the model in a different population to the one in which the model was developed. The validation cohort may be from the same geographical region (e.g. same country or region) but at a different point in time.

2.5.3.1.12 Methods of Statistical Derivation of the Tools

The majority of tools were derived using appropriate statistical techniques (logistic regression and Cox regression models). Parametric or semi-parametric models for producing risk estimates include linear regression for continuous outcomes (e.g. for prediction of BMD scores) and logistic or Cox proportional hazards regression models for dichotomous outcomes (e.g. fractures or no fractures (Callas, Pastides & Hosmer, 1998). The logistic model is adopted when the observation time for risk estimation of the event of interest is fixed for each participant while the Cox model is often adopted when the duration of the observation period for the event of interest varies.

The Cox model also computes for competing risks such as fracture, death or study closing date. Since many of the risk factors for fractures are also the risk factors for death (e.g. old age, medical comorbidities), failure to consider competing mortality may result in inflation of fracture probability. For example further analysis in a study found that in subgroups with high mortality (men, age >80 years, presence of diabetes), the failure to account for competing mortality overestimated fracture probability by 16-56% with the standard non-parametric (Kaplan-Meier) method and 15 to 29% with the standard parametric Cox model (Leslie et al., 2013).

2.5.3.1.13 Method of assessing Discriminatory Ability of the Tools

The discriminative abilities of the tools were expressed using the area under curve (AUC) of the receiver operating characteristics (ROC) and the performances of the tools were modest. Discrimination (the model`s ability to distinguish between people who do or do not have the condition of interest) is a key component in the predictive ability of a tool. The ability of a model to discriminate between people with and without the outcome can be summarised using the AUC of the ROC or the c-statistic (Ikeda, Ishigaki & Yamauchi, 2002, Harrell, Lee & Mark, 1996) as the appropriate method to estimate the accuracy of species distribution in models (Fielding, Bell, 1997, Pearce, Ferrier, 2000, Manel, Williams & Ormerod, 2001, McPherson, Jetz & Rogers, 2004).

ROC curves were developed during World War II to assess the performance of radar receivers in signal detection (to estimate the trade-off between hit rates and false alarm rates), and were subsequently adopted in biomedical applications, mainly for comparing the performance of diagnostic tests (Pepe, 2000). In spite of its wide use and generally good performance (Bradley, 1997), research efforts have been devoted to calculations of AUC variations to provide measure of variance or to estimate the AUC`s statistical significance (Provost, Fawcett, 2001, Fawcett, 2004, Ferri et al., 2005, Forman, Cohen, 2005). Consequently, some authors have begun to question the indiscriminate use of AUC as the standard measurement metric (Termansen, Collin & McClean, 2006, Lobo, Jimenez-Valverde & Real, 2008).

Kanis et al have criticized the use of AUC arguing that ROC curves should not be used because ROC curves are traditionally applied to diagnostic criteria and not predictive algorithms (Kanis et al., 2012). It was argued that that there is a mistaken belief that ROC capture all that is required to judge the performance characteristics of a test ignoring the three fundamental limitations of such analysis: lack of sensitivity of ROC to additional variables,

inappropriateness of comparing AUCs across studies and the inability of ROC to determine the use of a clinical tool to identify risk categories for intervention.

Other researchers support Kanis's view stating that AUC scores ignore the actual probability scores because it is insensitive to transformations of the probabilities that preserve their ranks (Ferri et al., 2005). Also it is argued that AUC is a discrimination index that represents the likelihood that a presence will have a higher predicted value than an absence (Hosmer, Lemeshow, 2000) regardless of the goodness of fit of the predictions (Vaughan, Ormerod, 2005). Therefore, it is possible that a poorly fitted model (overestimating or underestimating all the predictions) has a good discrimination and a well-fitted model has poor discrimination.

Baker and Pinsky argue that ROC summarises model performance over all conditions including regions rarely needed in practice, for example, the extreme right and left of the curve (Baker, Pinsky, 2001). Also AUC weights omission (false negatives) and commission (false positives) errors equally, but in many applications of distribution modelling, omission and commission errors may not have the same importance (Fielding, Bell, 1997, Peterson, 2006). Finally, Pontius and colleague argue that ROC plots do not provide information about the spatial distribution of model errors since it is impossible to decide if the biases are homogeneously distributed across the modelled territory, or if the lack of distribution is due to the incapacity to predict specific regions correctly (Pontius, Schneider, 2001). Although these arguments are persuasive, there is currently no alternative to the ROC.

2.5.3.1.14 Calibration of the Tools

Many of the tools were calibrated. Calibration is the agreement between observed and predicted event rates for groups of individuals and it is important for a risk model. Calibration is also useful for comparisons of accuracy between prediction models (Collins, Mallett & Altman, 2011, Mallett et al., 2010). The Brier score provides an indication of the agreement

between an observed binary outcome and the predictive probability of that outcome i.e. calibration and discrimination. Scores can range from 0 to 0.25 for a non-informative model assuming 50% incidence of the outcome; lower Brier scores indicate improved model accuracy (Brier, 1950, Blattenberger, Lad, 1985).

A perfectly calibrated model is one in which the observed and the predicted event rates of interest are the same. Calibrations in most of the studies were undertaken by the authors without independent evaluators; this makes it difficult to exclude bias. Calibration is most valuable if conducted by an independent third party who can provide an impartial perspective. There are two benefits to having an independent evaluation; first, the independent evaluator asking the questions will pose them in such a way as to gather maximum insights from interviews without the bias that might be introduced by the innovator and second, the respondent is more likely to share profound insights with an independent third party whereas they might be reluctant to do so with the innovator.

2.5.3.1.15 Output of the Tools

Few studies expressed their output in the format suggested by WHO and IOF i.e. absolute risk estimates (Kanis, 2002b). The absolute risk of a disease is the risk of developing it over a time period based on the population relative risk (PRR). The absolute risk estimates provide a clinically meaningful dimension of the actual risk of fracture and a more robust basis for intervention. Ten years was chosen by the WHO because this time frame is cost effective in modelling and allows 5 years-on and 5 years-off treatment (Kanis et al., 2001, Siris, Delmas, 2008, AnkjaerJensen, Johnell, 1996).

However the use of this metric has resulted in treatment recommendations that contradict those of some national guidelines such as NICE and the National Osteoporosis Foundation

(NOF). For example using FRAX, a fifty-year old postmenopausal woman with a BMI of 24.1 kg/m², and no clinical risk factors, and a T-score of -2.5 SD meets the threshold for pharmacological therapy based on the T-score. However, the fracture probabilities calculated with the WHO model (8.7% for major osteoporotic fracture and 2.5% for hip fracture) are below the treatment threshold. Conversely, an 80-year-old postmenopausal woman with the same body mass index, a parental history of hip fracture, and a T-score of -1.0 SD has a 10-year risk of 26% and 9.9%, for a major osteoporotic fracture and a hip fracture respectively; a level of risk at which treatment should be considered using FRAX but there is no strong evidence to support treatment of patients with this level of BMD.

The situation is further compounded because the 10-year absolute fracture probability may not be applicable to the frail elderly care home resident whose life expectancy is on average 5 years. Tools are dependent on the accuracy of the epidemiological data which are used to derive them and validation in one population may not apply in others. Many of the models are more applicable to groups of individuals rather than to an individual, because they were developed based on the concept of risk stratification in which continuous variables were categorised into subgroups. The risk grouping approach attempts to create homogenous groups of individuals which may in fact be impossible and unnecessary, because there may be variation in other risk predictors. At the patient level, an individual is likely to be unique in risk profile therefore the risk of fracture for the individual should take that uniqueness into account. The different methods of fracture risk expression highlight the diversity of views and calls for a consensus approach.

2.5.3.1.16 Governance Issues of the Publications

About 40% of the authors received research grants from pharmaceutical companies. It is not clear if these incentives had influence on model derivation and validation. While 53.9% of the

studies received favourable ethical approval about 40% did not. This indicates a breach of the Declaration of Helsinki (WMA, 2013) and failure to comply with the International Guidelines for Good Medical Practice (IGCP) which may be perceived as fraudulent. The Declaration of Helsinki is a set of ethical principles regarding human experimentation developed for the medical community by the World Medical Association (WMA). It is widely regarded as the cornerstone document of human research ethics and the International Conference on Harmonisation provides guidelines for good clinical practice (Guideline for Good Clinical Practice-ICH, 2016).

2.5.3.2 Methodological Quality

Many the studies were adjudged to be of good quality on QUADAS. QUADAS is recommended for quality assessment by the Cochrane Group (Diagnostic Test Accuracy Working Group, The Cochrane Collaboration, 2009). It is challenging to use all the generic items in the QUADAS check list when assessing studies of fragility risk tools because there is currently no reference standard. In this systematic review there were many methodological shortcomings and similar observations have been reported in other studies (Nelson et al., 2010, Rubin et al., 2013, Rud et al., 2007, Steurer et al., 2011). For example, one publication by Kanis et al observed that many external validation studies of models did not incorporate death hazard when assessing tool performance (Kanis et al., 2012).

The final models/algorithms were often presented clearly and in the majority of the tools, it would be possible to collect the risk predictors in clinical practice. However, these attributes were overshadowed by the poor quality of data collection. For example, it was unclear if all participants answered all questions or whether some were intermediate, uninterpretable or missing. Only a few studies reported missing data and one of them handled it by using

multiple imputation methods (Hippisley-Cox, Coupland, 2009). Missing data can threaten internal and external validity of the risk model.

Excluding the participants with missing values from the analysis reduces the effective sample size and the participants with the completely observed data are then not a random subsample of the original study sample (Little, Rubin, 1987, Moons et al., 2006). Ignoring missing observations can reduce statistical power to detect associations of the outcome and predictor variable and lead to erroneous inferences about the strength of association as well as affecting the predictive ability of the model. Few studies reported participants' withdrawals: thus there exists the possibility of inadequate or biased estimates of the performances of the tools in these studies. The absence of methodological transparency in some of the studies means that the scores obtained on QUADAS were at best approximations.

2.5.4 The Fragility Assessment Tools

The tools identified in this review have different predictors with the majority having four and above. There is no consensus on the numbers of variables to be included in a model. Four was chosen in this study because that was the modal value. The systematic review by Nayak and colleagues used five as threshold (Nayak et al., 2014). In the selection of predictors, it is important that predictive models contain an appropriate number and range of risk factors which should be easy to identify in clinical practice. The usefulness of a prediction model is dependent amongst others on the diagnostic accuracy and ease of use (Kanis, 2007). Risk factors should be unambiguous and easy to determine.

Most of the models included baseline demographics: age, gender, BMI, weight, and ethnicity. The age is particularly important because epidemiological data show that fragility fractures are commonest after 50 years especially in women after menopause (Van Staa et al., 2001, Kanis,

2012, Office of the Surgeon General (US), 2004) and age has the strongest known association with BMD and fragility fractures (Rubin et al., 2011).

About half of the tools included BMD as a predictor. But the detection rates (sensitivity) for fractures using BMD are low as 96% of fragility fractures occur in women without osteoporosis (Kanis et al., 2001), reference has been made to this earlier. The low sensitivity and specificity of BMD as predictor of fragility fractures was underpinned in some tools in which the fracture probability can be calculated with and without BMD estimation (Kanis et al., 2001, Kanis, 2007, Nguyen et al., 2008).

The next commonest group of predictors included in many tools was comorbidities of which prior fracture and falls were in the majority. This has merit because it has been recognised since the 1980s that fractures beget fracture. About 50% of patients presenting with hip fractures have sustained fractures in the past (Gallagher et al., 1980, Edwards et al., 2007). Two meta-analyses concluded that a prior fracture is associated with a doubling of future risk (Klotzbuecher et al., 2000, Kanis et al., 2004). Women with prevalent vertebral deformities have a risk of sustaining a subsequent vertebral fracture of five times that of a woman without prevalent vertebral deformities (Black et al., 1999). With regards to falls, approximately 95% of hip fractures are caused by falls (Nyberg et al., 1996) and most osteoporotic fractures result from trauma (Winner, Morgan & Evans, 1989).

It was surprising that both diabetes mellitus (DM) and dementia did not feature in many risk models given that they are common in older people and are now established risk factors for fragility fractures. The prevalence of diabetes mellitus is increasing worldwide (Borissova et al., 2015, Nguyen et al., 2015). Its prevalence is higher in the elderly than in younger people (Sloan et al., 2008). Casperson and colleagues estimate that diagnosed and undiagnosed DM affects about 10.9 million US people aged 65 years and over and this is projected to reach

26.7 million by 2050 (Caspersen et al., 2012). There are about 60 million people with DM in the European region or about 10.3% of men and 9.6% of women aged 25 years and over (WHO Regional Office for Europe, 2017). One meta-analysis showed that both type 1 and type 2 DM are associated with significantly increased risk of hip fractures in both sexes (Janghorbani et al., 2007).

Dementia and fracture are common problems in the elderly population. About 0.5% of the global population (or more than 35 million people) worldwide have dementia. The population of people with dementia is expected to double within the next 20 years (Querfurth, LaFerla, 2010, Sousa et al., 2009). Dementia is associated with increased risk of falling and low BMD (Friedman et al., 2010, Amboni, Barone & Hausdorff, 2013) both of which are risk factors for fragility fractures. In one study in Taiwan, during a 3-year follow-up period, 264 patients with dementia (18.7%) and 1098 patients without dementia (15.6%) sustained incident fractures. Dementia was found to be independently associated with increased risk of hip fractures (adjusted HR 1.92, 95% CI 1.48-2.49) (Wang et al., 2014). A systematic review and meta-analysis on fracture risk in long term care found that falls and cognitive impairment are associated with increased risk of fractures (Khatib et al., 2014)

In conclusion, there was significant heterogeneity in study characteristics, predictor variables, outcome assessment and follow-up periods therefore a meta-analysis could not be undertaken.

2.5.5 Findings from Other Studies

The discussion in this section will focus on FRAX, QFractureScores, Garvan nomogram and body mass index (BMI) because they were identified as the fragility tools which may be practicable in care home residents in this systematic review. FRAX, QFractureScores and

Garvan nomogram are the best studied fragility tools which used robust theoretical aspects for development and validation (Leslie, Lix, 2014).

2.5.5.1 FRAX

FRAX is the most widely tool used globally. It has been validated in many population-based cohorts and incorporated in many national guidelines (Austria, China, Germany, France, Italy, Japan, Spain, Sweden, Switzerland, Turkey, USA, Argentina, Belgium, Finland, Hong Kong, Lebanon, New Zealand and UK) (Kanis et al., 2013, Silverman SL, 2010) and it is recommended by NICE (National Institute for Clinical Excellence (NICE), 2012b). There are country and region specific versions available at the University of Sheffield website (*http://www.shef.ac.uk/FRAX*). It is available in many languages including English, Chinese, French, German, Italian, Japanese and Spanish. FRAX gives an absolute rather than a relative risk score. The extensive epidemiological data from various geographical areas in the world has permitted separate models to be constructed for different regions for example in very high risk geographical areas (e.g. Scandinavia), high risk (e.g. Western Europe), moderate risk (e.g. southern Europe), and low risk (e.g. developing countries).

In the UK, FRAX 10-year fracture probability output is linked to the National Osteoporosis Guideline Group (National Osteoporosis Guideline Group (NOGG), 2008) guidance which offers a management algorithm to prompt a decision about treatment; the green zone recommends lifestyle advice; amber zone recommends DEXA scan to refine the risk and a red zone recommends that pharmacological intervention should be considered. FRAX has 12 predictors and most of these are dichotomised. The responses are computed to give a sum total in percentage, 0 to 100. The higher the score, the higher the fracture risk. Although FRAX is web-based, paper chart versions are available where access to computers is limited (www.shef.ac.uk/FRAX).

FRAX can be used with and without BMD. In countries where DEXA scans are not available, FRAX without BMD can be used. In the countries where DEXA scans are limited, FRAX without BMD can be used for a selection of patients for DEXA assessment. FRAX is internally and externally validated. It has modest performance using ROC and it is reliable and easy to use. Although FRAX has utility as a clinical tool it has some limitations:

1. It does not incorporate fall, a major cause of fragility fractures. The reason given is that fall is not amenable to pharmaceutical intervention and the definition of fall is not universal. But most fragility fractures result from falls and an increased propensity to fall is a risk factor for fractures (Dargent-Molina et al., 1999, Genant et al., 1999). The multidisciplinary intervention study by Close and colleagues (1999), in the Prevention of Falls in the Elderly Trial (PROFET) showed that some falls in the elderly are preventable; this might involve medication review (Close et al., 1999). Also, Calcium and Vitamin D supplementation have been associated with significant improvement in musculoskeletal function with a reduction in the risk of falls decreasing by 49% (Latham et al., 2003).

2. Some of the predictor variables in FRAX such as alcohol and steroid use do not take account of dose-response. There is robust evidence that the risk associated with excess alcohol and glucocorticoids are greater at higher doses. Daily doses of oral glucocorticoids (OG) between 2.5 and 5 mg increased fracture risk by 50% (van Staa, Leufkens & Cooper, 2002a). Hip fracture risk rose from 1.77 at daily doses of 2.5 to 7.5mg and 2.27 at 7.5mg or greater. Clinical vertebral fracture risks were 2.29 for a daily dose less than 2.5mg, 2.59 for 2.5mg to 7.5mg and 5.18 at 7.5mg or greater.

3. The risk of fracture is higher with any parental fragility fracture. A parental history of any fracture is associated with a modest but significant increased risk of any osteoporotic fracture (RR=1.18, 95% CI=1.06-1.31) and hip fracture; RR=1.49, 95% CI 1.17-1.89 (Kanis et al., 2004). A stronger association was observed for a maternal history of hip fracture with RR of up to 1.5 for any fracture and RR of up to 2.0 for hip fracture (LaFleur et al., 2008). However, a large-scale Finnish study failed to find a significant genetic contribution to fall-related osteoporotic fractures (Kannus et al., 1999).

4. Participants were relatively healthy community dwelling adults therefore the performance of the tool in the frail elderly such as care home residents is not known.

5. It is established that the risk of fractures increases with the number and type of previous fractures sustained (Klotzbuecher et al., 2000) but this is not factored into FRAX. Also, FRAX underestimates the risk of vertebral fractures because many of them are not detected clinically.

6. Rheumatoid arthritis is included in FRAX permutation because its effect is considered over and above that accountable for by BMD alone. However, inflammatory conditions such as psoriatic arthritis, systemic lupus erythematosus (SLE), spondyloarthritis and many drugs such as heparin, anti-retroviral agents and poor nutrition which have similar effects on BMD are not included in FRAX.

7. FRAX cannot be used for patients who are under treatment for osteoporosis because pharmacological therapy reduces fracture risk without changes in BMD (Saag, Geusens, 2009).

8. Only a few clinicians use FRAX. Some years ago, few Clinicians went on line to access FRAX because it is web-based but that is likely to change with the advent of the Electronic Patient Record (EPR) system by the National Programme for Information Technology (NPHT) launched in 2007 (HOC 2007).

9. FRAX is not designed for use in people under the age of 40 years or over the age of 90 years; therefore it does not accurately predict fracture risk across all age groups (Browner, 2007).

10. The lack of flexibility of FRAX remains a critical limitation. A flexible tool should allow the adjustment of risk gradients and the inclusion of new risk factors either agreed locally or internationally. For example, FRAX allows for input of femoral BMD only regardless of values at other sites.

2.5.5.2 QFracture Scores

QFractureScores (Hippisley-Cox, Coupland, 2009) is recommended by NICE. The derivation and validation cohorts were large. Missing data were accounted for and fracture probability can be computed yearly for 10 years making it very valuable for people with short life expectancy such as care home residents. The discriminative ability of QFractureScores is modest and it is reliable and responsive to change (Leslie, Lix, 2014). It has been independently and externally validated in the UK (Collins, Mallett & Altman, 2011) and Israel (Dagan et al., 2017). QFractureScore has 29 predictors and like FRAX most of them are dichotomised. The computation is web-based and it is presented as a percentage from 0 to 100, the higher the score the higher the fracture risk.

QFractureScores has some limitations: it consists of a number of predictors which makes assessment cumbersome (Rubin et al., 2013). QFractureScores is the most complex of the four tools; it has 31 clinical risk factors in the updated version (QFracture-2016) therefore the applicability of the tool in clinical setting is questionable. The usefulness of a tool is dependent to some extent on the ease of use. Also, in the development of QFractureScores, the risk factors were only assessed at baseline, not taking into account any changes in risk factor status during follow-up. For example a person who developed an incidental stroke would be incorrectly classified during the follow-up.

2.5.5.3 Garvan nomogram

Garvan nomogram (Nguyen et al., 2008) showed modest efficacy. Garvan nomogram is responsive to change and a simple tool to use. Fracture risk assessment is within the repertoire of many frontline practitioners (Rubin et al., 2013). Garvan nomogram has 6 predictors. When BMD is not available, body weight can be substituted. Garvan nomogram is web-based and like FRAX and QFRactureScores, the output is presented as a percentage; 0 to 100, the higher the score, the higher the fracture risk. The two versions (one with BMD and the other with weight if BMD is not available) give options for application particularly where BMD assessment is not available (Leslie et al 2014). Fracture probability can be computed for 5 years and 10 years. These advantages make it an attractive fragility tool for care home residents.

The limitations of Garvan nomogram are: although it has been independently validated in Canada (Langsetmo et al., 2011), Norway (Ahmed et al., 2014) and Israel (Dagan et al., 2017), it has only been calibrated for an Australian population, it does not include other risk factors as FRAX and QFractureScores therefore it might underestimate fracture risk when other relevant clinical risk factors are present, it is useable only in people older than 60 years and it

does not include an explicit compelling mortality risk adjustment (Leslie et al., 2013), consequently the fracture probability may be overestimated.

2.5.5.4 Body Mass Index

BMI is a recognised risk factor for fragility fractures and it is a predictor in many fracture prediction models. It was derived from a meta-analysis of 12 prospective population-based cohorts, the same as FRAX. There are no publications on external validation.

There is an association of fracture risk with low BMI and age: in younger people, low BMI may be associated with physical fitness and lower risk of fracture but in the elderly, fractures are more common because of frailty and the negative effects of relative gonadal deficiency on the bone. The risk is strongest for hip fractures but the association is not linear being higher at lower BMI (De Laet et al., 2005). BMI is easy to use and it is routinely assessed in most care homes during admission and follow-up. A limitation of BMI is that it can be influenced by changes in height: for example height loss associated with vertebral collapse, thus in people with significant height loss, fracture risk can be underestimated. The other limitations of BMI are discussed in chapter 4.

2.5.6 Strengths and Limitations of this Systematic Review

This systematic review had some strengths. To my knowledge this is the first systematic review to identify the fragility risk tools for potential use in care home residents and the methods used followed the analytical methods and standards established by the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) group. Additionally, the methodological qualities of the studies were assessed using QUADAS.

The study also had limitations: although effort was made to include the totality of published literature on the subject, it is possible that some studies escaped detection particularly those that were published after the literature search was performed. All the publications were reviewed initially by only the researcher and a second opinion was sought only when there were uncertainties therefore some relevant citations may have been missed. Also a meta-analysis of the included studies was not performed due to considerable heterogeneity in the study characteristics.

2.6 Conclusion

This systematic review identified 33 existing fragility risk tools of which four may be useable in care home residents. These tools are FRAX, QFractureScores, Garvan nomogram and BMI. Apart from BMI, all the tools are web-based (FRAX has paper-based version) and express fracture risk as absolute probability. They contain varying numbers of predictors of which BMI is common. In the next project, a questionnaire will be developed using all the predictors from the tools and acceptability tested in two care homes in preparation for the observational cohort study.

2.7 Addendum

As the initial literature search on which this project is based was conducted in 2014 a further, updated, search was conducted to determine whether any new fragility fracture assessment tools have been reported and evaluated since. The period of search was from 15/04/2014 to 19/07/2019. Identical search terms, search strings and databases (section 2.3.1.2 in thesis), were used and only publications in English language were included as in the previous search. The same criteria and procedures as in the initial search (section 2.3.1.4 in thesis) were used for the screening and the selection of publications and all the decisions were independently verified by the same second reviewer, AP.

A total of 989 publications were identified and 550 were left after duplicates were removed. Of these 289 were rejected because their titles indicated that they were irrelevant, 40 were rejected because they were experimental studies, 28 were rejected because they were statistical models, 2 were rejected because they were case reports and 191 publications were rejected because they contained tools which I had reviewed previously. A total of 11 full journal publications were reviewed and of these 2 have informed the addendum, in addition a 5th paper was identified from the reference list of Walter and colleagues (2017). Eight papers were rejected as they did not meet the criteria. There were 3 papers that suggest microRNAs have a future potential but the biomarkers are yet to be isolated (Walter et al., 2017, Hellmeier et al., 2016, & Bedene et al., 2016). In community dwelling older adults, the FRAX remains less sensitive than suggested in the literature (Atkinson et al et al., 2015, Duncan et al., 2014 & Holloway et al., 2015).

MicroRNAs define the physiological nature of the cell and play significant roles in the diverse biological processes such as cell differentiation, proliferation, death, immunity and metabolism (Wahid et al., 2014). Aberrantly expressed miRNAs can be used as biomarkers for the diagnosis of a variety of diseases including osteoporotic fractures. A number of miRNAs have been discovered. At the cellular level, miR-21 and miR-148a are known to play specific roles in bone homeostasis. Seeliger and colleagues discovered 9 upregulated circulating miRNA (miR-21, miR-23a, miR-93, miR-100, miR-122a, miR-124a, miR-125b, and miR-148a) that could significantly distinguish between serum samples of osteoporotic and non-osteoporotic fractured patients in a cohort (Seeliger et al.2014). Kocijan and colleagues (2016) found that a set of 19 miRNA was consistently upregulated in three subgroups of 46 premenopausal women, 52 postmenopausal women and 55 males and that these were excellent discriminators of patients with low-traumatic fractures with area under the curve of between 0.81 and 0.89. Over a lifetime, estimating miRNA could avoid 57,919 fractures compared with

DEXA, 31,285 fractures compared with FRAX and 133,394 fractures compared with no monitoring (Walter et al 2017).

Analyses of miRNA have the advantage that they are minimally invasive requiring only blood samples; therefore they could be useful for care home residents. But there are a number of confounding variables with their estimation and diagnostic thresholds are yet to be established. Also the cost effectiveness of miRNA profiling is not yet known (Walter et al 2017), therefore if I had identified this tool as a predictor before now, it would not have been selected as a tool for use in care home residents. However, these biomarkers could open a novel method for the diagnosis and response to treatment of fragility fractures but more research is needed.

For the identification of high risk people, many guidelines recognise that widespread screening is currently neither feasible nor desirable and therefore adopt the case-finding strategy. The National Institute for Health and Care Excellence (NICE) has recently released new guidance for fragility fractures (NICE 2016). The guidelines state that fracture risk should be considered in the following circumstances : in all women aged 65 years and over and all men aged 75 years and over, in women aged under 65 years and men aged under 75 years in the presence of risk factors such as previous fragility fracture, current use or frequent use of oral systemic glucocorticoids, history of falls, family history of hip fracture, other causes of secondary osteoporosis, low body mass index less than 18.5 kg/m², smoking and alcohol intake of more than 14 units per week for women and more than 21 units per week for men. NICE guideline recommends that fracture risk should be estimated using diagnostic tools such as FRAX or QFractureScores.

The Scottish Intercollegiate Guidelines Network (SIGN 2015) recommends that the assessment should be carried out preferably using QFractureScores because of the extensive validation of QFractureScores in the UK population. The National Osteoporosis Guideline Group (NOGG) recommends the fracture risk assessment should be undertaken with FRAX and vertebral fracture assessment should be considered in postmenopausal women and men age > 50 years if there is a history of ≥ 4 cm height loss, kyphosis, recent or current long-term oral glucocorticoid therapy, or a BMD T-score ≤ - 2.5 (NOGG 2018). In the United States, the National Osteoporosis Foundation (NOF 2008) recommends FRAX and uses these risk factors for case-finding: previous fragility fractures (vertebral or non-vertebral), low body weight (less than 127Ibs [58kg] for USA citizens) and a family history of fragility fractures. But in my study, I found that both FRAX and QFractureScores were ineffective in care home residents. Vertebral fracture assessment was not done in my study because it was not practicable.

Chapter 3. Consultation Visits to Two Care Homes to Determine the Acceptability of a Fragility Risk Assessment Questionnaire

3.1 Abstract

3.1.1 Background

Fragility fractures are common in care home residents and risk assessment is important in identifying high risk people in this cohort. The last project identified four tools FRAX, QFractureScores, Garvan nomogram and BMI as useable in this group. A composite questionnaire was then developed using the pdf versions of these tools but it was unclear if it would be feasible given the inherent difficulties conducting research in care home residents. The aim of this consultation project was to sample the views of care home staff and residents on the questionnaire and the information leaflets in two care homes in Staffordshire, UK.

3.1.2 Aims

Three steps were used:

. First, design a composite questionnaire and information leaflet;

. Second, identify two care homes in Staffordshire;

. Third, undertake consultation visits.

3.1.3 Methods

A composite questionnaire was designed by including all the predictors from the four tools as they appeared in the PDF versions. Next care homes were identified through the internet by using the key words `care homes, Newcastle-Under-Lyme` and then contact their managers requesting consultation visits. If the care managers agreed to this, the research documents were sent by postal mail ahead of the scheduled visits.

3.1.4 Results

Two care homes were identified from the yield and the care managers agreed to the visit on the first telephone contact. Two group consultations and four individual consultations with care residents took place. Following the feedback, the composite questionnaire and the information leaflets were modified to reflect the views of the participants.

3.1.5 Conclusions

The project was valuable as it provided useful feedback which resulted in the modifications of the documents in preparation for the observational study.

3.2 Background

It has already been demonstrated that fragility fractures are common in care home residents; however, there is no standardised fracture assessment tool in this high-risk cohort. In the last project, the following tools were shown to be usable in this group: FRAX (Kanis et al., 2008), QFractureScores (Hippisley-Cox, Coupland, 2009), Garvan nomogram (Nguyen et al., 2008) and Body Mass Index (De Laet et al., 2005). A composite questionnaire comprising the covariates in these tools is important in simultaneously evaluating their performance. Prompted by the proposal that women should be involved in the design and conduct of research into breast cancer, I decided to adopt a similar approach with care home residents (Thornton, 1993, Baum, 1993).

Conducting research in care home residents could be daunting (Hall, Longhurst & Higginson, 2009, Luff, Ferreira & Meyer, 2011). They are a distinct group compared to community dwelling older people of the same age in almost every way including mortality (Nimmo, Peterkin & Coid, 2006), health status (Sinclair et al., 2001) and needs (Petty, Scrivener, 1998).

Also care managers and care home staff are the residents` `gate keepers` and it is impossible and impolitic to conduct research without them as identifying residents and gaining access requires their involvement. Research ethics committee chairpersons frequently field questions from researchers wanting to know when and why gatekeeper permission should be sought.

Conscientious and well-informed negotiations with gatekeepers are required in order to honour the ethical obligations to conduct appropriate stakeholder engagement before and during research, along with respect for autonomy of institutions and their employees/clients/service recipients. Therefore it was important to evaluate the acceptability of the composite questionnaire and associated research documents in residents and care home staff prior to the observational study. Two care homes were identified in North Staffordshire for the consultation.

Consultations are valuable in many aspects of research including the design, conduct and analysis of the data obtained. There are recommended guidelines for consultations (Cabinet Office, 2018) and the method employed depends on the type of study. Generally, consultations can be divided into two types: quantitative, for example, surveys, and qualitative, for example interviews and focus groups. Quantitative and qualitative methods, although different, are complimentary. Often the best and most useful consultation is developed using a combination of the two.

The type of consultation chosen for this feasibility study was qualitative, comprising individual and group consultation. This design was driven by the type of setting and the hope of bringing together the strengths of the two approaches. For care home residents, individual interview was preferred because of the logistical problems of getting the participating residents together at the same time. For care staff, group consultation was chosen because they are the advocates of the residents.

Individual interviews are one-to-one discussions, framed around an area. Because only one person is being interviewed, it gives in-depth, detailed personal information and identifies new issues that may not have been thought of. A group consultation is a small number of people (typically 8 to 12) brought together to consider a topic or issue. It is indicated when looking for qualitative or descriptive feedback aimed at generating new ideas and identifying issues for larger consultation practices.

Group consultations are usually led by facilitators. Their advantages include: ability to involve service users directly in discussion or dialogue about a specific issue; permitting individuals to freely express their views in an informal environment; generating detailed and quick feedback on a specific issue; skilled facilitators can respond quickly to non-verbal signals and direct the consultation accordingly (Derbyshire County Council, 2017). The disadvantages of group consultation are: there can be disagreements and irrelevant discussion which distract from the main focus. Some participants may find a group consultation intimidating; participants may feel under pressure to agree with the dominant view. This study will explore the experiences, attitudes, opinions and feelings of the residents and care staff toward the questionnaire and information document designed for the next project.

Care home residents are a vulnerable cohort because often they are physically and mentally challenged and their life expectancy is short. Bebbington and colleagues found that 79% of all older people admitted to care homes have high levels of physical frailty and 44% have some degree of cognitive impairment (Bebbington, Darton & Netten, 2001). Consequently, the ethos in many care homes is end-of-life care. Given this, the researcher was unsure how the proposed research and documents would be perceived by both care home staff and residents. The aims of the feasibility project therefore were:

1. To determine if the assessment process will be acceptable to the residents and carers;
2. To determine whether the documents are workable;
3. To determine if the whole process is feasible.

3.3 Methodology

Three steps were followed:

1. Design the questionnaire and information leaflet;
2. Identify two care homes in Newcastle-Under-Lyme;
3. Undertake the consultation study.

3.3.1 Design of the Questionnaire

3.3.1.1 Selection of Items for the Questionnaire

A structured composite questionnaire that captured all the covariates in each tool FRAX, QFractureScores, Garvan nomogram, and BMI was designed by copying them exactly as they appear in the PDF versions. This was to enable evaluation of their performances simultaneously. The questionnaire also included the type of setting (RH, NH, dementia) as this will be required during data analysis; the contact details of the settings, consultee and the General Practitioner as these will be required to schedule appointments; the clinical outcomes (falls, fractures, falls & fractures, mortality and duration of recruitment for each participant) as these will be required for data analysis; the date of recruitment and proposed date of termination for each participant as these will ensure timely follow-up. Timed Up & Go Test (TUGT) and Charlson comorbidity index (CCI) were included, the rationale for their inclusion are discussed next.

3.3.1.1.1 Timed Up and Go Test (TUGT)

The TUGT (Podsiadlo, Richardson, 1991) is a standard falls risk assessment tool that was included for comparison of falls risk with the fragility tools. There are many tools for assessing falls risk in older people. Three systematic reviews identified varying numbers. The first identified 25 but found insufficient evidence that any screening instrument exists for predicting falls (Gates et al., 2008). The second identified 21 tools but did not undertake assessment of their efficacy (Perell et al., 2001). The third identified 45 and found that the Berg Balance scale in combination with self-reported imbalance to be the best (Jarnlo, 2003) but using this tool in this observational study was not feasible because of the anticipated challenges of obtaining self-reported history of imbalance from cognitively impaired residents who will be recruited.

The TUGT assesses gait and balance and is recommended by the American Geriatrics Society, the British Geriatrics Society and the American Academy of Orthopaedic Surgeons Panel on Fall Prevention (Anonymous, 2001) as well as the National Institute for Health and Care Excellence (NICE, 2013). It measures the time that a person takes to rise from a chair, to walk 3 metres, to turn around, to walk back to the chair and to sit down. The TUGT was developed as a simple test to assess basic mobility in older people and requires both static and dynamic balance. It is can be used in primary care settings as no special equipment is required. The original TUGT validation study identified that people who complete the test in 30 seconds or more tend to require assistance with climbing stairs and leaving the house. However, more studies identified that compared with the prototype model reference standard, a TUGT cut-off of 12 seconds or more had a high specificity for identifying very few false positives (Bischoff et al., 2003) and a meta-analysis of 21 studies showed that the mean (95% confidence interval) TUGT time for individuals at least 60 years of age was 9.4 (8.9-9.9) seconds (Bohannon, 2006).

3.3.1.1.2 Charlson Comorbidity Index (CCI)

The Charlson Comorbidity Index (Charlson et al., 1987) was included to guide treatment decisions because of the relatively short life expectancy of care home residents. The current guidelines do not explicitly address life expectancy; it is an important consideration when choosing preventive treatment. There is substantial heterogeneity in life expectancy among older adults. Median life expectancy for an 80 year-old woman is approximately 10 years; however, for women in the "healthiest" quartile, life expectancy is more than 14 years, whereas for women in the "sickest" quartile, life expectancy is less than 5 years (Pham et al 2011).

Clinicians tend to overestimate survival, and so it is recommended to use standardised tools such as life tales or ePrognosis (University of California, San Francisco) to estimate remaining life expectancy instead. The CCI is another method for predicting mortality by classifying or weighting comorbidities. It has been used in a number of studies to stratify patients in order to control the confounding influence of comorbid conditions on overall survival (Wahigren et al 2011).

A systematic review of comorbidity indices identified 54 articles and the two most commonly used were the Elixhauser comorbidity measure (ECM) (Elixhauser et al., 1998) and Charlson Comorbidity Index (CCI) (Sharabiani, Aylin & Bottle, 2012). Comparatively, Elixhauser appears to have better performance in all aspects of validity. ECM used administrative data to identify 30 International Classification of Diseases (ICD) comorbidities that had a major impact on short-term outcomes in acutely hospitalised patients but the feasibility of collecting ICD coded comorbidities from care home nursing records persuaded this researcher to choose the CCI instead.

The CCI predicts the mortality for a patient who may have a range of comorbid conditions, a total of 22 are included in the model. The CCI score at 12 months may be useful when considering pharmacological intervention or not. Patients with anticipated death of 12 months or less are not suitable for osteoporotic medications but palliation and end of life care (The Gold Standard Framework (GSF) Team, 2018). Information on the demographic and medical covariates can be obtained from the case files and the CCI calculated on-line (Vaugier, 2018).

3.3.2 Identification of the Care Home in Staffordshire

Identification of the care homes was done online on Google using the key words `care homes, Newcastle-under Lyme`.

3.3.3 Consultation Meeting with the Care Managers and Residents

The care managers of the homes identified were contacted by telephone and the reasons for the proposed visit were discussed. These were to obtain the views of staff and residents with mental capacity on the composite questionnaire and information leaflet. Two sets were posted, one for care home nursing staff, the other for residents who have mental capacity and have been identified by the care home manager as persons interested in looking at the material and giving advice on format and content. The care managers were asked to make extra copies of the documents for distribution to nursing staff and residents who they had identified.

3.3.3.1 Consultation with Care Home Staff

Two consultations following the same pattern and using the same format were scheduled four months apart. The consultations took place in the offices of the care managers between 0930hrs and 1030hrs on 27/04/2013 and 27/08/2013. The following people attended each meeting: the investigator/facilitator, the care manager and other care staff (nurses and care assistants) employed by the homes. The lead supervisor of this research was present in one of

the meetings. When the group consultation meeting was about to start, all the sound systems were switched off, a brief introduction was made by this researcher and the meeting was declared open for general discussions.

3.3.3.2 Consultation with the Residents

The meeting took place with each resident in their private rooms immediately after the group consultation and a carer was in attendance. The meeting with the residents took place separately. The residents were seated either on the chair or bed and put at ease by the carer who introduced the investigator, FI. When the resident made it clear they were happy to be consulted, the researcher stated the purpose of the visit and asked the residents for their opinion concerning the research documents which they had received earlier using a structured interview.

3.4 Results

3.4.1 The Questionnaire

Table 25 shows the composite questionnaire which includes all the predictors of the four tools as well as other variables detailed in the methodology section. They are: age, date of birth, sex, weight, height, prior fracture, parental fragility fracture, smoking status, alcohol history, ethnicity, nursing or care home, medication use, history of rheumatoid arthritis, diabetes mellitus, dementia, previous fractures, previous falls, cancer, asthma or COPD, chronic kidney disease, chronic liver disease, Parkinson`s disease, malabsorption syndromes, endocrine problems, epilepsy, 10 year absolute fracture risk, time to complete each tool, TUGT, number of comorbidities, CCI, outcome measures, type of care home, contact details of care homes/relatives/GP, recruitment date and proposed date of termination. Ethnicity questions

and categories were those used by the Office of Population Censuses and Surveys (OPCS) (Office of National Statistics (ONS), 2018).

QFractureScores has the highest numbers of predictors of 29, BMI has only one 1 predictor. FRAX has 12 predictors and Garvan nomogram has 6 predictors. BMI is a common predictor in all the tools.

The composite questionnaire consists of sixty seven questions which can be subdivided into two categories: predictors in the tools (n=44 [66%]) and other variables (n=23 [34%]).The majority of the questions relating to the predictors are dichotomised (n=24 [58%]).

Table 25: The composite questionnaire derived from the pdf versions of FRAX, QFractureScores, Garvan nomogram and BMI

A. FRAX

Number	Variables
1	Age
2	Date of birth (Year, Month, Day)
3	Sex (Male, Female)
4	Weight (kg)
5	Height (cm)
6	Previous fracture (No, Yes)
7	Parental Fractured Hip (No, Yes)
8	Current smoking (No, Yes)
9	Glucocorticoids (No, Yes)
10	Rheumatoid arthritis (No, Yes)
11	Secondary osteoporosis (No, Yes)
12	Alcohol 3 or more units/day (No, Yes)
13	10-year absolute probability
14	Time to complete FRAX in minutes

B. QFractureScores

Number	Variables
1	Age (30-99)
2	Sex (Male, Female)
3	Ethnicity (White or not stated, Indian, Pakistani, Bangladeshi, Other Asian, Black Caribbean, Black African, Chinese, Other Ethnic group)
4	Smoking (Non-smoker, ex-smoker, light smoker (less than 10), moderate smoker (10-19), heavy smoker (20 or over)
5	Alcohol status (None, <1 unit per day,1-2 units per day, 3-6 units per day, 7-9 units per day, > 9 units per day)
6	Diabetes (None, Type 1, Type 2)
7	Do either your parents have osteoporosis/hip fracture? (No, Yes)
8	Do you live in a nursing or care home? (No, Yes)*
9	Have you had a wrist, spine, hip or shoulder fracture? (No, Yes)
10	History of fall? (No, Yes)
11	Dementia? (No, Yes)
12	Cancer? (No, Yes)
13	Asthma or COPD? (No, Yes)
14	Heart attack, angina, stroke or TIA? (No, Yes)
15	Chronic liver disease? (No, Yes)
16	Chronic kidney disease (No, Yes)
17	Parkinson`s disease? (No, Yes)
18	Rheumatoid arthritis or SLE? (No, Yes)
19	Malabsorption e.g. Crohn`s disease, ulcerative colitis, coeliac disease, steatorrhea or blind loop syndrome? (No, Yes)
20	Endocrine problems e.g. thyrotoxicosis, hyperparathyroidism, Cushing`s syndrome? (No, Yes)
21	Epilepsy or taking anticonvulsants? (No, Yes)
22	Taking antidepressants? (No, Yes)
23	Taking steroid tablets regularly? (No, Yes)

24	Taking oestrogen only HRT? (No, Yes)
25	Body mass index
26	Height (cm)
27	Weight (kg)
28	10-year absolute probability
29	Time to complete QFractureScores in minutes

C. Garvan Nomogram

Number	Variables
1	Sex (Male, Female)
2	Age (60-96 years)
3	Fracture since age of 50 (Excluding major trauma e.g. car accidents)(0.1,2, or ≥3
4	Falls over last 12 months (0, 1, 2 or ≥ 3)
5	Weight (kg)
6	10-year absolute probability
7	Time to complete Garvan nomogram in minutes

D. Timed Up & Go Test

Number	Variables
1	TUGT (Actual time taken for test)
2	Time to complete TUGT in minutes (including preparation)
3	Participant unable to undertake

E. Other variables in the composite questionnaire

Number	Variables
1	Number of comorbidities
2	Charlson`s Comorbidity Index
3	Falls in study
4	Fractures in study
5	Falls and fractures in study
6	Outcome of participant
7	Name of care home
8	Type of care home
9	Telephone number of care home
10	GP of participant
11	Telephone number of Participant`s GP
12	Next of kin of Participant (NOK)
13	Telephone number of NOK
14	Date of recruitment of participant
15	Proposed termination date of participant

Table 25 shows the composite questionnaire derived from the pdf versions of FRAX, QFractureScores, Garvan nomogram and BMI. Panel A shows items for FRAX, panel B items for QFracture Score, Panel C the Garvan Nomogram, panel D the Timed Up & Go Test TUGT), and panel E other variables. *In this table the term care home is used to refer to a residential home. The term is taken form the original paper describing the score and has not been changed, but has been interpreted as referring to a 'residential home'.

Interpretation

There were 68 variables in the composite questionnaire. QFractureScores had the highest number and the TUGT the least. The majority (78% [53/68]) of the variables were derived

from the tools. Forty one percent (28/68) of variables in the composite questionnaire were dichotomised.

3.4.2 Identification of the Care Homes in Staffordshire

Two care homes were identified in Newcastle-Under-Lyme: the G and Q nursing homes. They were located about 0.5 miles from the office of the lead supervisor (CR) therefore she attended one of the meetings. The two care homes provided RH, NH and dementia care.

3.4.3 Consultation with Care Staff and Residents

3.4.3.1 Consultation with Care Staff

The care managers welcomed the visit and were happy to make the time because they felt falls and fractures were common problems in care homes. A total of 8 people attended the two group consultations comprising two care managers and 6 carers, they were all female.

For the questionnaire, one comment was that a question which has been asked earlier should not be repeated because it is time wastage and may cause irritation to some residents. Generally, the participants felt the research documents were adequate.

For the information leaflet, the participants felt that two versions should be produced: a summary version and a more detailed section, both in bold bigger font (e.g. 16) (appendix E and G). This is for the benefit of residents whose vision may be impaired and attention span is limited. Otherwise the care home staff felt that the information leaflet was comprehensive and usable. It was suggested that for residents without mental capacity, contact with the consultee should be through the care managers so that confidentiality is not breached. If the consultee was agreeable to be contacted, then the researcher would discuss the study by telephone and if

they are happy to act on behalf of the resident, the research documents including the consultee form should be posted in a stamped self-addressed envelope.

For the observational study, they suggested that the researcher should attend general resident/ relative meetings because this would provide a reasonable forum to discuss the research with more people thereby enhancing the chances of recruitment. Also, it was suggested that any time the researcher visits the resident, a care nurse should be in attendance to inspire confidence and prevent elder abuse. Each meeting lasted for about one hour. At the end the author expressed gratitude to the participants.

3.4.3.2 Consultation with Residents

A total of 4 care home residents participated in the interview and they were all females. All four residents were happy with the documents and willing to participate in the observational study if invited. Midway during the consultation, one of the residents drifted off to sleep. The meetings lasted for about 30 minutes each. At the end, the researcher expressed gratitude to the residents and nurse for their time.

3.5 Discussion

The feedback from the feasibility consultation provided valuable insight that helped in refining the questionnaire and information leaflet. Also, the views expressed assisted in planning the best methods to approach potential participants and consultees for the planned observational study.

There are recognised weaknesses with group consultations, these include: the danger of one or two people influencing the group and the process requires trained facilitators and assistant

facilitators. Consultations are not statistically reliable and the small numbers of participants involved mean it is extremely difficult to extrapolate the results to a whole population with any degree of confidence. It can be time consuming therefore people may not attend. Also it requires a quiet/private location for optimal concentration and the diversity of opinion expressed may make it difficult to condense the results (Derbyshire County Council).

The group consultations in this study were not `hijacked` by any persons. All the participants told the investigator that they had opportunity to express their opinions freely in a cordial, non-threatening atmosphere although I had no formal training in facilitating. Group size theory suggests eight to be the perfect group dynamic but there are discussions as to whether this includes the facilitator/assistant. In this project there were 5 in each meeting. The feedback from each meeting was similar but it is not known if they captured the opinion of the greater majority of care staff. The interviews with the residents were one to one because of the logistical problems of getting many residents together in a quiet room at the same time. Although these had the advantage of privacy there might have been restraints because residents may have had difficulty expressing their opinion freely to a stranger. Organising these meetings was time consuming because of the different schedules of the participants.

There are few publications on consultation methods in care homes. One systematic review by Bradshaw and colleagues explored living well in care homes (Bradshaw, Playford & Riazi, 2012). In the review, 31 studies were identified from which four themes affecting the quality of life of care home residents emerged. One of the four themes was relevant to this project: close relationship with peer residents within the care home. Although connectedness was not explored in this study, it is conceivable that the four residents who participated were sociable and could engage with others.

Four non-systematic reviews explored the improvement in the quality of life through consultation methods. All four found that by taking time to explore the views of care staff, they could engage and strategize with residents about the implementation process. Participants clearly appreciated being involved in the decision-making process relating to the planning and implementation of interventions. These findings highlight the importance of using a participatory approach when engaging care staff in research activities during the planning phase, to encourage them to be more involved in the decision making and to acknowledge their contributions as being a meaningful component of the project (Kaasalainen et al., 2010). Also, these meetings promote effective communication and build positive relationships between researchers and care staff.

Van de Pol and colleagues (2015) found staff gained practical inspiration from participating in relevant research if it contributes to advancing their practical knowledge (van de Pol, Marjolein Helena Johanna et al., 2015). Mentes & Tripp-Reimer (2002) found that consultation methods assist researchers to realise the normal routines in the care home and provide important information about which parts of the intervention are too time consuming for staff. The study by Wilson and colleagues highlighted the importance of collective engagement through consultation in identifying leadership and organisation of care in building reciprocal relationship between residents, families and care staff (Wilson, 2009). These observations underpin the need to be mindful of the strong influence of the practice environment when trying to implement new strategies. The findings from the consultation visits for the project are consistent with the views which have been expressed and encourage prior consultation with residents and care home staff when conducting research in this setting.

3.5.1 Limitations of the Project

The project had some limitations. Firstly, the group and individual consultation consisted of few and highly selected people therefore it is not known if the views expressed represent the generality. Secondly, the researcher is not a trained facilitator; therefore all aspects of the subject may not have been explored. The researcher was also the facilitator; this may have unduly influenced the participants. Aware of this potential bias, the investigator had participants review their opinion, checked for alternative explanations, reviewed the findings with peers and allowed free discussion by the participants and only intervening to bring the discussion back to the subject. Thirdly, the project was conducted in Staffordshire and it is not known if the views expressed are representative of similar groups in Lincolnshire where the observational study was conducted. Finally, family members were not represented in the meetings therefore their views were not captured.

3.6 Conclusion

This study demonstrated that using two consultation methods at the planning stage of the research is useful in evaluating the acceptability of the questionnaire and information leaflets. The available publications support the rationale for this project. By synthesising the opinions expressed by the care home residents and care staff, important adjustments that facilitate the research process were made. Staff and residents welcomed the opportunity to engage with the researcher and suggested the best ways of implementing the proposed observational study.

Chapter 4. Observational study of falls and fractures in a care home population

4.1 Abstract

4.1.1 Background

The systematic review of fragility fracture risk assessment tools in chapter 2 identified 33 fragility fracture assessment tools but only four were practicable in care home residents. These were FRAX, the QFractureScore, the Garvan nomogram and BMI all of which were derived from community-based older people. These tools were designed to predict fractures, not falls.

Care home residents are distinct and it is not known if these tools will be practicable in this cohort. The aims of this pilot study were the following: to determine the recruitment rate of care home residents for the study; to identify if the existing fragility risk assessment tools and the Timed Up and Go Test, a falls risk assessment tool (TUGT) predict falls, fractures and combined falls and fractures in care home residents and and to determine if the tools are easy to use by determining their duration of assessment.

4.1.2 Methods

This was an observational prospective cohort study. Inclusion criteria were: adults living in a care home from whom informed signed consent could be obtained directly or indirectly from a consultee. Exclusion criteria were: residents on the end of life pathway and non-English speaking residents when interpreters could not be obtained. Participants were recruited from 18 care homes in Boston, Lincolnshire, and followed up for 12 months. The outcome measures were falls, fractures, combined falls and fractures, mortality and the duration of recruitment including measuresments and case file review. These outcomes were assessed by

the recruitment rate, time to complete assessment using of the tools (i e the actual duration to compute the scores on the computer for FRAX, QFractureScores and Garvan nomogram, the calculator for BMI and the duration to perform the test for the TUGT), screening performance and the clinical discriminatory capacities of the tools.

4.1.3 Results

217/618 (35%) care home residents were enrolled between April 2015 and May 2016, and all 217 were included in the analysis. The main reason for non-enrolment was inability to obtain consent from consultees in residents unable to provide informed consent themselves. All 217 (100.0 %) were Caucasian by ethnicity and 134 (61.8%) were female. The mean age was 81.2 (12.5 SD) years. There were 94 fallers of which 10 had incident fractures.

The mean times taken to complete the risk assessment were: 1 minute for FRAX, Garvan nomogram, and BMI and 2 minutes for QFractureScores and the TUGT. These excluded the the duration needed to collect the relevant information from the case file and treatment sheet.

The sensitivity and specificity of the tools were as follows: QFractureScores 10 year fracture probability for major fracture of ≥ 20%; falls 69.1% and 36.6%, fractures 90% and 35.3%, combined falls & fractures 90% and 35.3% respectively; BMI of ≤ 20kg/m²; falls 41.5% and 73.2%, fractures 60% and 68.1%, combined falls & fractures 60% and 68.1% respectively; BMI of ≤ 25kg/m²; falls 74.5% and 43.9%, fractures 90% and 31.2%, combined falls & fractures 90% and 31.2% respectively; TUGT of ≤ 12 seconds falls 95.7% and 40%, fractures 100% and 8.2%, combined falls and fractures 100% and 8.2% respectively. The sensitivity and specificity of FRAX and Garvan nomogram were not calculated because neither tool significantly predicted falls, fractures or combined falls and fractures.

Binary logistic regression analyses were as follows: FRAX prediction of falls odds ratio (OR) 1.003 SE 0.011 (p=0.813), prediction of fractures OR 1.027, SE 0.024 (p=0.267), prediction of combined falls and fractures OR 1.027, SE 0.024 (p=0.267); QFractureScores prediction of falls OR 1.007, SE 0.005 (p=0.160), prediction of fractures OR 1.024, SE 0.011 (p=0.036), prediction of combined falls and fractures OR 1.024, SE .011 (p=0.036); Garvan nomogram prediction of falls OR 1.010, SE 0.005 (p=0.054), prediction of fractures OR 1.021, SE 0.011 (p=0.062), prediction of combined falls and fractures OR 1.021, SE 0.011 (p=0.062); BMI prediction of falls OR 0.952, SE 0.021 (p=0.015), prediction of fractures OR 0.868, SE 0.073 (p=0.024), prediction of combined falls and fractures OR 0.868, SE 0.073 (p=0.024); TUGT of ≤ 12 seconds prediction of falls OR 0.999, SE 0.000 (p=0.013), prediction of fractures OR 1.000, SE 0.001 (p=0.829), prediction of combined falls and fractures OR 1.000, SE 0.001 (p=0.829).

4.1.4 Conclusions

This pilot study was feasible mainly for the residents who possess mental capacity. Although the average times to conduct the risk assessment could be accommodated within routine work schedules, conduct of the TUGT was challenging. The screening performances of the tools were generally poor; of the fragility tools, BMI of 25kg/m² or less had the highest sensitivity for predicting falls. BMI was the only tool that significantly predicted falls, fractures and combined falls and fractures,

QFractureScores predicted fractures and combined falls and fractures, TUGT predicted falls but the associations were weak. Neither FRAX nor Garvan nomogram predicted these outcomes. A fully powered study that will include a representative sample of residents without mental capacity is feasible if the current legislation that governs consent for people without mental capacity changes but it is arguable if such a study is necessary because cognitive

impairment is common in care home residents. However, this pilot project has provided the necessary data to design a future fully powered study.

4.2 Background

In project one, I found FRAX, QFractureScores, the Garvan nomogram and BMI, were practicable for care home residents. These tools were designed to predict fractures and not falls therefore it was important to include a primary falls risk assessment tool, the Timed Up and Go Test (TUGT) which was recommended for falls assessment in the priamary care setting by the National Clinical Care Excellence (NICE) for comparison.

4.2.1 Aims of Project

The aims of this pilot study were:

1. To determine recruitment rate of care home residents for the study

2. To identify if the existing scores for fracture risk and the TUGT have relevance for care home use in the frail elderly

3. To determine if the tools are practicable (feasible)

4. To determine if clinical algorithm can be developed as most tools are for 10 year prediction risk (not relevant in a care home population)

4.3 Methodology

In order to meet aim 1:

1. The total number of participants was calculated as a proportion of the entire care home population.

2. The proportions of mentally competent and incompetent participants were calculated.

For aim 2:

1. A range of independent and dependent variables were measured
2. Then the sensitivity and specificity of the tools were estimated
3. Then the relationship between independent and dependent variables were modelled
4. Then the sample was clustered into three groups (falls, fractures, falls and fractures) and the differences between them with respect to the measures taken were explored.

For aim 3:

1. The duration for the risk assessment of each tool was determined
2. Then a telephone interview of 20 care home managers in Lincolnshire (on what they considered an easy fragility tool to use in care home residents) was conducted.

For aim 4:

1. Develop a clinical algorithm using factors which were identified as relevant from the exploratory analyses.

4.3.1 Design of the Study

This was a multicentre, prospective, observational, open cohort pilot study. An open design was used because this allowed participants to be enrolled throughout the 12 month period of study (i.e. not all participants were recruited at the same time as in a closed study). A closed cohort is one with fixed membership. Once the cohort is defined by enrolling participants and follow-up begins, no one can be added. The number of participants may decline because of death or loss to follow-up, but no additional participants are added. As a result closed cohorts always get smaller over time. Also a closed study would have been impossible to conduct by a single person because that would require many assessors working concurrently.

4.3.2 Setting

Participants were enrolled by one investigator (FI) from all 18 care homes in Boston. These care homes provide 24-hour institutional care for adults who require care for conditions such as old-age disability, dementia and learning disability. In the residential homes, the residents are generally more mobile and are less dependent on others to perform activities of daily living compared to those in the nursing homes. Nursing home residents are usually extremely frail and incapable of standing unaided, they ambulate only with assistance and most of their activities are conducted under heavy supervision. Some of the care homes in this project are registered to cater also for people who are on the end-of-life pathway.

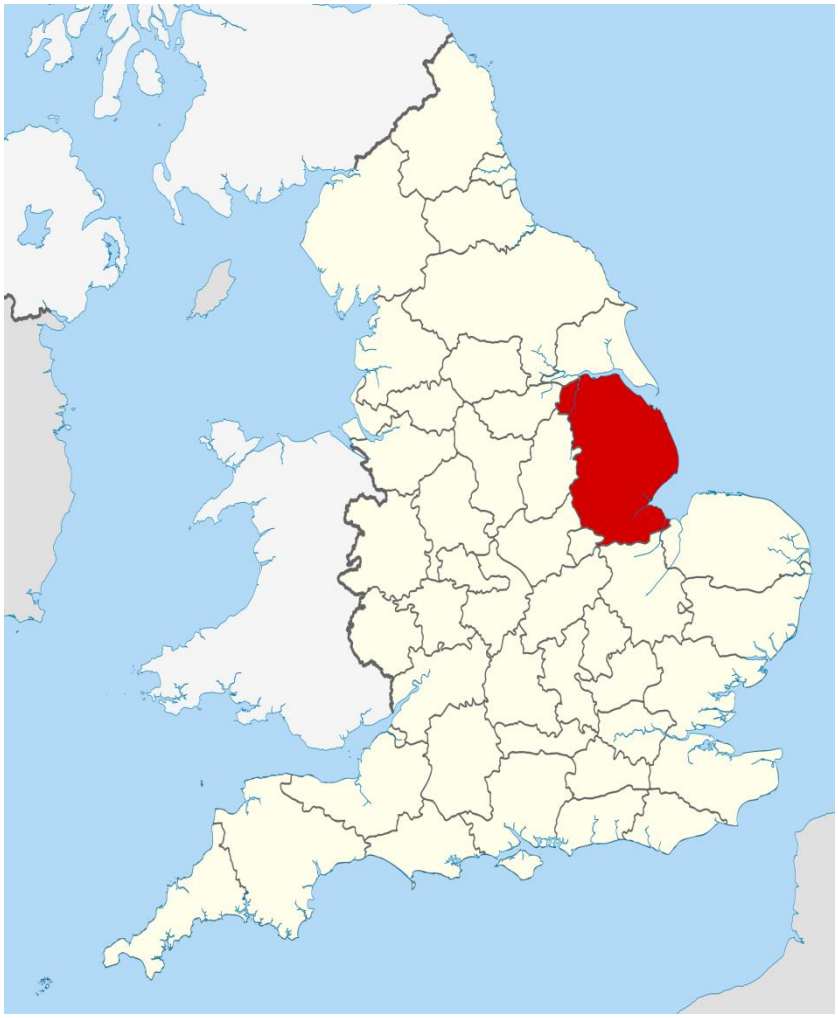
The town of Boston is situated on the East coast of England in the county of Lincolnshire, where the River Witham becomes the Haven on its short journey to the Wash (figures 4 and 5). The town is approximately 120 miles directly north of London. According to the 2001 census, there were 35,124 people residing in Boston town, of whom 48.2% were male and 51.8% were female. 23% of the resident population were of retirement age. By mid-year 2015, the population had increased to 66,900 (Office of National Statistics (ONS), 2018).

The local population is older than the national average with 21% aged above 64 years compared with 18% nationally (Office of National Statistics (ONS), 2018). In the 2011 census the Borough of Boston had a population of 64,000 with 15% of the population born outside of the UK and 11% in the European Union accession countries such as Poland and Lithuania. The non-white population made up 2.4% of the total population in 2011 (Office of National Statistics (ONS), 2018).

Pilgrim Hospital is the major provider of secondary care in Boston and immediate surrounding areas. As such, it plays a vital role in the community and serves a very large rural community with an estimated catchment population of about 400,000 which is more than the national

average of between 200,000 and 300,000. (Advisory Committee on Resource Allocation (ACRA), 2016).

Figure 4 is a map of the United Kingdom (UK) showing Lincolnshire in red, and Figure 5 is a map of part of Lincolnshire showing the location of Boston where this observational study was undertaken.



Reproduced with the kind permission of Wikipedia

Figure 4: A map of the United Kingdom (UK).

Interpretation

The county of Lincolnshire is shaded in red and situated on the East coast of England in figure 4.

Reproduced with the kind permission of Wikipedia

Figure 5: A map of part of the county of Lincolnshire showing Boston.

Interpretation

Figure 5 shows that Boston is a town and a small port in Lincolnshire on the East coast of England, approximately 100 miles north of London. It is the largest town of the wider Borough of Boston.

4.3.3 Order of Selection of Care Home Sites

To avoid bias in the selection process of the order of the 18 care homes, a randomisation sequence was computer generated thus (Random.org, 2018) (appendix P);

1. Enter the smallest value i.e. 1
2. Enter the largest value i.e. 18
3. Enter 1 for format
4. Get sequence

4.3.4 Participants

Participants were enrolled from April 5, 2015 to May 12, 2016 from the 18 care homes in Boston and number of residents in each care home at the first visit of the investigator was taken as the resident population.

4.3.5 Study Criteria

4.3.5.1 Inclusion Criteria

Residents were eligible for inclusion in the study if they were adults and provided informed written (signed) consent directly or indirectly (from a consultee).

4.3.5.2 Exclusion Criteria

Residents were excluded for the study if they were on end of life pathway, they were non-English speaking and interpreters were not available.

An anonymised screening log was kept of all potentially eligible participants including residents who were excluded (and the reason for exclusion) and residents who were not

approached or included (and the reasons for this). Appendix L shows the template of the screening log.

4.3.6 The Process of Recruitment

Recruitment of participants followed a systematic process which started with the initial contact with the care home, then obtaining consent and then finally undertaking the interview and assessments. All visits, written and emailed communications, and phone calls were conducted by a single researcher, FI.

4.3.6.1 First Visit (preparatory visit)

The researcher contacted the care home manager or deputy by phone and explained the purpose of the research and then scheduled an appointment to visit and discuss the details. The care home manager or deputy assisted in identifying potentially eligible residents and advise whether they were likely to be able to give fully informed consent, or whether a consultee may be required.

4.3.6.2 Second Visit (information giving to residents)

Prior to any contact with residents the researcher introduced himself to the care home manager or deputy. The purpose of the visit was discussed and the resident was given the information leaflet (see appendix). After this, another appointment was scheduled to respond to questions, clarify concerns and obtain consent, if the resident was willing to participate. A minimum period of 24 hours was observed for the resident to reconsider before signing the consent as recommended by Integrated Research Application System (IRAS).

4.3.6.3 Third Visit (consent taking and recruitment)

4.3.6.3.1 Residents with Mental Capacity

The researcher assessed mental capacity by asking the resident if they had read and understood the study detailed in the participant information leaflet which they had received earlier. The resident was asked to summarise what they understood of the study, what their participation involved, the potential risks and benefits of the study. If they were able to communicate these, then mental capacity was established and the resident was asked if they had any questions or needed clarification on any aspect of the study.

The resident was then asked if they would like to participate. If the answer was `yes`, then the resident was requested to sign the consent form in the presence of a witness (the original copy put in the participant`s case file, one copy was given to the resident, and the third copy was put in researcher`s file). If the answer was `no`, the researcher thanked the resident for the taking time to read the information leaflet. For the residents who signed the consent form, another appointment was scheduled to administer the questionnaire and take study measurements.

4.3.6.3.2 Residents without Mental Capacity

The Department of Health guidance (Department of Health (DOH), 2001) states that for residents who cannot give informed consent, assent should be sought, usually from a near relative. Therefore the care home manager or deputy was asked to introduce the study to consultees and obtain permission for their contact details to be forwarded to the researcher for discussion. If the consultee was happy to act on behalf of the resident and felt that the resident would be prepared to take part in the study, the consultee information leaflet and the consultee forms were posted in a stamped self-addressed envelope for return. Verbal consent via the

telephone, confirmed by an independent witness, was also accepted. When assent was obtained, the care home manager or deputy was informed and a time scheduled to conduct the assessment in the manner similar to participants with mental capacity.

4.3.6.4 Fourth Visit (Collection of Study Outcomes)

The fourth visit was undertaken at the end of 12 months for each participant. The incident books were reviewed for the study outcomes; falls, fractures, combined falls and fractures. The care home manager or nurse were asked if the participant was alive or dead.

4.3.7 Duration of the Consenting Process and Assessments

The time taken to complete the recruitment and baseline assessment of the participant was calculated from the time of first contact with the participant to the time when the assessment, measurements and case file reviews were completed. For the participants who required consultee, the duration was taken from the time the research documents were posted by mail to receiving signed consent and completion of the baseline assessment process and case file review.

4.3.8 Administration of the Questionnaire

All questionnaires were interviewer-administered to eligible residents who gave informed consent after discussions with the care manager on the fourth visit. The meeting took place in the resident`s private room with a carer in attendance for the entire duration of the visit. The resident was given options to be seated in the chair or bed and was put at ease by the care nurse. Eye glasses and hearing aids were checked to ensure they were in good working condition and then worn or fitted. With the permission of the resident, all the sound systems in the room were switched off when the questionnaire administration and assessments were undertaken.

4.3.8.1 Residents with Mental Capacity

The carer introduced the researcher who then explained the purpose of the scheduled meeting. Mental capacity was reassessed in the understanding that it can fluctuate. If it was absent, the researcher expressed gratitude to the resident and carer for their time and the resident was transferred to the pathway for participants without mental capacity described earlier. If mental capacity was present and the resident was still willing to participate, the researcher then sat on a chair about 2 feet away facing the participant and asked the questions one at a time but skipped if a similar question was asked earlier. After this, the measurements were taken by following the methods described below.

At the end, the researcher expressed gratitude to both the resident and carer for their time and proceeded to obtain more information from the participant`s casefile and drug chart. The next of kin identified as the primary care-giver in the nursing admission notes was interviewed when the resident was unable to communicate, too ill or where the required information was unclear. The General Practitioner (GP) was contacted for clarification when necessary.

4.3.8.2 Residents without Mental Capacity

The researcher was introduced to the resident by the carer. The researcher then made attempts to facilitate understanding of the reason for the meeting and to reassure the resident. Due to lack of mental capacity, prompts were repeated as necessary to reduce anxiety. After this, the researcher proceeded to take measurements by following the methods already described. Thereafter, the researcher expressed gratitude to both the resident and carer for their time. The participant`s casefiles and drug chart were then obtained for more information. Where these were not available, the next of kin or GP were contacted for clarification.

4.3.9 Measurements

The measurements required for the study were: the height, the weight, the body mass index and the Timed Up and Go Test (TUGT).

4.3.9.1 Height

For the participants who were ambulant, the height measurements were done by using wall mounted scales. For the participants who were chair or bed bound, the height were estimated by using the ulna length. Measurement was taken at the left forearm with a tape measure from the point of the elbow (olecranon process) and the midpoint of the wrist (styloid process) (Haboubi, Hudson & Pathy, 1990). If the left forearm was not accessible or deformed by previous fracture or disease, the right forearm was used instead. The measurement was initially in centimetres and then converted to meters by dividing the number obtained by 100.

4.3.9.2 Weight

For the participants who were ambulant, the weight measurement were done by sit-in electronic Seca weighing scales (which were available in all the care homes) with the participant wearing light clothes and the feet off the ground. For the participants who were bed bound, the weight was measured by using the hoists (which were available in all the care homes). All the measurements were in kilograms.

4.3.9.3 Body Mass Index

The body mass index was calculated by dividing the weight in kilograms by the height in meters squared.

4.3.9.4 Timed Up & Go Test

1. A flat stretch of space in the care home about 10 feet (3 metres) long was identified for the test.

2. The participant was asked to sit in an armchair placed so that it faced one end of the test space with their back to the chair and their arms resting on the arm rests of the chair.

3. The participant was asked to stand up from the chair then walk the distance of 10 feet (3 metres) then turn around, then walk back to the chair and then sit down again.

The procedure was timed using a stop watch. Timing began when the resident started to rise from the chair and ended when he or she returned to the chair and was seated again. The resident was given one practice trial and then three tests were taken. The mean duration in seconds of the three tests was calculated. The participants were allowed to use any walking aids and/or assisted by the care nurse if they so desired.

4.3.10 Collection of Clinical and Demographic Data

The participant characteristics were obtained from interviews, medical record review, GP and relatives. These included: age, sex, weight(kg), height(cm), body mass index(kg/m^2), smoking history, alcohol history, type of care home, history of previous fractures, parental history of osteoporosis and fractures, history of falls, glucocorticoids, rheumatoid arthritis, secondary osteoporosis, diabetes mellitus, endocrine problems, dementia, cancer, asthma, ischaemic heart disease, cardiovascular disease, chronic liver disease, chronic kidney disease, Parkinson’s disease, malabsorption, epilepsy, taking anticonvulsants, antidepressants, oestrogen only HRT, number of co-morbidities.

The 10-year fracture probability for FRAX, QFractureScores, Garvan nomogram, average duration in seconds to complete each fracture risk assessment, Charlson`s Comorbidity Index (CCI) and the duration in days to complete recruitment/assessment were computed.

4.3.11 Follow-Up

After the screening visit, each participant was followed-up for 12 months. Twelve months follow-up was chosen for 2 reasons:

1. The investigator had limited time for the study
2. There might be a low retention rate of the participants if the duration of follow-up is longer than 12 months given the high mortality rate of care home residents.

12 Monthly visits to each of the care homes were conducted by the investigator. During these visits staff and incident books were consulted to verify the number of falls, fractures and mortality. At the end of the 12 months, the number of falls, fractures and deaths were collated and cross referenced with the monthly data. If there were no incidents before a participant died, this investigator assumed that no incident had occurred. Significant study events were recorded prospectively in a field note book and reviewed monthly.Participants and their families were not consulted directly during follow-up.

4.3.12 Outcomes

The outcome measures were the recruitment rate, ease of use of the tools (assessed by the duration in minutes taken to assess each participant with the tool), screening performance of the tools, clinical outcomes (falls, fractures, combined falls and fractures, mortality), the clinical discriminatory capacities of the tools and the duration of recruitment of the participants.

4.3.12.1 Recruitment rate

The recruitment rate was determined by the number of participants as a proportion of the care home resident population.

4.3.12.2 Ease of Use

Justification

The ease of clinical use determines acceptance of the tool and it is a function of the ease of the required associated procedures, extent of demand on staff time, perceived efficiency, quality and added clinical value of speedy results and the actual reduction in time to a result for the new diagnostic test compared with the method in use. To the best of the researcher`s knowledge, only one formal rating system (US Food and Drug Administration (FDA), 2013) has been described to score ease and speed of use of diagnostic methods which are applicable to laboratory investigations therefore for this project, the duration taken to compute the risk assessment was taken as the surrogate measure of the ease of clinical use.

4.3.12.2.1 Duration of Risk Assessment

The duration of the risk assessment was defined as an uninterrupted time period (using a stop watch) beginning from the time point when the first data for the risk model were entered on to the computer to be processed until the output. If the process was interrupted, the procedure was repeated. This assessment took place in the office of this investigator using the raw data which were collected following the care home visit.

4.3.12.2.2 Interview with Care Home Managers Relating to Ease of Use

A supplementary telephone interview was conducted in 20 different randomly selected care homes in Lincolnshire to explore what the care home managers felt were the desirable features of a fragility risk assessment tool that could affect the ease of use.

4.3.12.3 Sensitivity and Specificity, Positive and Negative Predictive Values

The screening tests that were assessed were the sensitivity, the specificity, the positive predictive values (PPV) and negative predictive values (NPV). The sensitivity is how good the screening test is in identifying disease in people. The specificity is the accuracy of the screening test in correctly classifying truly non-diseased people. The positive predictive value is the probability that subjects with a positive screening test truly have the disease. The negative predictive value is the probability that subjects with a negative screening truly do not have the disease. The formula for calculating these are detailed in the statistical analysis section.

4.3.12.4 Primary Outcome

In this project prediction of falls was used as the primary measure to evaluate the performance of the fragility tools.

4.3.12.4.1 Justification for Using Falls as a Primary Measure

Fall is an indirect assessment and surrogate for fractures because it has internal validity as it is highly unlikely for participants to have non-vertebral fractures without falls. Falls are more common than fractures. Older people in care homes have increased levels of chronic illness, polypharmacy and cognition, vision, vestibular, strength and balance impairment and falls become relatively more important in this population (Hayes et al., 1993, Visentin et al., 1995).

According to the World Health Organisation (WHO), falls are the leading cause of chronic disability worldwide (Murray, Lopez, 1996). The number of hospital admissions due to an older person falling is set to rise to nearly 1000 a day in England and Wales by the end of the decade according to the data obtained by the Local Government Association (Local

Government Association (LGA), 2018). Fall-related injuries are also the leading cause of death in the over 65s and cost the NHS over £2 bn. a year and 4 million bed days (Fenton 2014).

Falls account for about 90% of hip fractures and 87% of all fractures in elderly people (Diez-Perez et al., 2007). The annual incidence of falls in care homes is reported to be 1.5 falls per person (Nurmi, Luthje, 2002) compared to fracture incidence of 70 per 1000 person years (Ytterstad, 1999). Thus preventing falls in frail older people may result in reduction of the incidence of fractures.

A fall was defined as an unexpected event in which the participant comes to rest on the ground, floor or lower surface (Lamb et al., 2005). It was not necessary for the fall to be observed to be counted as an event.

4.3.12.5 Secondary Outcomes

The secondary outcomes were: the clinical discriminatory capacity of the tools for fractures, combined falls and fractures (and falls discussed above), the number of incident falls, incident fractures, combined incident falls and fractures, the duration taken to complete risk assessments, the duration of the recruitment and assessment process (including consent and data collection) and mortality.

Justification

1. Prediction of falls and fractures: this will assess how good the fragility tools are in predicting falls and fractures in the frail elderly.
2. Number of falls: this will assist in the calculation of fall incidence.

3. Number of low trauma non-pathological fractures: this will assist to calculate fracture incidence
4. Number of falls and fractures: this will assist to define the number of fractures that result from falls.
5. Mortality: this will inform the design of larger studies in future.
6. Duration to complete the recruitment and assessment of participants: this will inform the design of larger studies in future.

Fractures were defined as break in the continuity of the bone verified by x-ray. A fragility fracture was defined as fracture sustained after low trauma. Skull fractures, facial fractures, fractures resulting from road traffic accidents and pathological fractures were excluded. While fractures did not have to be symptomatic to be included, asymptomatic fractures would not have been identified, as there was no systematic radiological screening.

Fractures in the participants were identified by the care home incident books and verified by X-ray reports or the General Practitioner (GP) records. Deaths were verified from the GP register.

4.3.13 Development of Algorithm

From the exploratory analyses of the data, some factors which could be useful in the development of a clinical algorithm were identified using backtracking process. This was reported by:

- Following a step- by- step process
- Including variables and their usage

- If there were any loops, give sub number lists
- And going back to step number if loop or condition failed

4.3.14 Data Management

The participants` anonymised data were checked for accuracy (by cross-checking the data entries) and then exported to a password protected EXCEL spreadsheet for storage. Later, they were exported to the Statistical Package for Social Scientists (SPSS) and before embarking on the data analysis, they were probed for missing values using the software.

4.3.15 Scoring of the Responses

Categorical variables were coded numerically and quantitative variables were recorded as the raw values. Appendix N shows the scoring system. Where an answer was not available, it was recorded as unknown.

4.3.16 Sample Size

A particular challenge of a pilot study is recruiting an appropriate study population. Formal sample size calculations are not required (Thabane et al., 2010). As there were no previous data, sample size calculation was based on feasibility considerations. It was considered possible to recruit 5 participants per week. Assuming a 40 week working year, this would enable the researcher to recruit 200 residents, a number adjudged by the consultant statistician to be adequate to provide a meaningful primary outcome measure. This was higher than the 24 to 50 recommended for feasibility studies (Brown, 1995, Julious, 2005).

A statistical rule of thumb is that 15 to 20 incidents are required per covariate to give good estimates of a prognostic model (Peduzzi et al., 1996). For this study, there were two

covariates (the absolute fracture risk probability score and the number of co-morbidities). Using these, it was estimated that 30 to 40 falls may occur in the 200 participants during the study duration of 12 months. However, Marshall and colleagues found an incidence of 1.6 falls per person per year in a care home population (Marshall, Johnell & Wedel, 1996). If this was true for this population, 212 falls would be expected.

4.3.17 Statistical Analysis

Categorical variables were reported as absolute numbers and percentages. Continuous variables were tested for normality and then reported either as means and standard deviations or median and interquartile range.

The sensitivities, specificities, positive predictive values (PPV) and negative predictive values (NPV) of the tools were calculated at generally accepted thresholds using standard formula (MEDCALC, 2018). The identification of the groups was facilitated using pivot tables on EXCEL spread sheet.

$$Sensitivity = \frac{number\ of\ true\ positives}{number\ of\ true\ positives\ + number\ of\ false\ positives}$$

$$Specificity = \frac{number\ of\ true\ negative}{number\ of\ true\ negative\ +\ number\ of\ false\ negative}$$

$$PPV = \frac{number\ of\ true\ positive}{number\ of\ true\ positive\ +\ number\ of\ false\ positive} = \frac{number\ of\ true\ positives}{number\ of\ positive\ calls}$$

$$N\ PV = \frac{number\ of\ true\ negatives}{number\ of\ true\ negatives\ +\ number\ of\ false\ negatives} = \frac{number\ of\ true\ negatives}{number\ of\ negative\ calls}$$

$$Crude\ incidence\ rate\ = \frac{Number\ Of\ Cases}{Population}\ x\ 100$$

PPV= Positive predictive value

NPV= Negative predictive value

Exploratory analyses were done to determine the relationship between the clinical outcomes (falls, fractures and death), the tools and the predictors. First homogeneity within groups were determined by Levene`s test before further exploration with appropriate statistical tests, parametric or non-parametric. Binary logistic regression models were then used to model the prediction of falls, fractures combined falls and fractures (dependent variables) for each tool and predictor (independent variables) (Campbell, Machin, 2000).

Odds ratios (OR) were used to measure the strength of association between dependent and independent variables - the exponentiation of the beta coefficients (Exp B) (LaMorte W.). A

value greater than 1 indicates an increase of risk by 1 unit increase of the predictor, a value of 1 indicates that there is no influence of the predictor and a value less than 1 indicates a decrease of risk by 1 unit increase of the predictor. The size of the effect of the ORs was calculated in percentages by using the formula (Gingaras C);

Percentage increase in risk = OR – 1 X 100 (if OR was greater than 1)

Percentage decrease in risk = 1- OR X 100 (if OR was less than 1)

All p-values were reported as two-tailed and values of 0.05 or less indicate statistical significance. The analyses were performed using SPSS software (version 24; SPSS Inc. Chicago, IL, USA).

4.3.18 Study Governance

The protocol, amendments, patient information sheets, informed consent forms and informed consultee forms for this study were reviewed and approved by the independent ethics committees (Health Research Authority [HRA]); the Lincolnshire Research Ethics Committee (LREC Reference; 14/EM/1225) on the 09/01/2015 (appendices A & B) and the institutional review board of the Research Governance unit; the Research and Development Department of the United Lincolnshire Hospitals Trust (ULHT Reference; 141014Ihama) on the 11/03/2015 (appendix C). A substantial amendment (addition of a consultee information sheet) was approved by the ethics committee on the 10/03/2015.

The R & D monitored the conduct of the study (by periodic visit to the office of the investigator to inpect the research documents and their storage) to ensure compliance and fidelity to the protocol and also to verify the accuracy and completeness of the data on behalf

of Keele University. Clinical oversight was done by the clinical supervisor (CR) and together with the co-supervisor (AP) offered guidance on the statistical analysis of the data and structure of the thesis.

All the participants provided informed written signed consent either directly or indirectly from consultees. This study was conducted according to the good clinical practice guidelines, applicable local laws and the ethical principles encoded in the revised Declaration of Helsinki (WMA, 2013) and standards of the International Council for Harmonisation guidelines for Good Clinical Practice (Guideline for Good Clinical Practice-ICH, 2016). The study was registered on a public database and can be viewed on the link provided (INVOLVE, 2018).

4.3.19 Confidentiality

The participants were assigned unique study codes which did not include identifiable descriptors. From the point of recruitment into the study, these codes were used for identification. The participant`s identifiable raw data were kept in a locked office (investigator`s office) in a locked cabinet for 3 years and then destroyed.

4.3.20 Definition of Terms

Definition of terms is in appendix N.

4.4 Results

4.4.1 Recruitment

All the 18 care homes in Boston participated in the study (table 26). 17 (94%) were privately owned and the other was owned by a charity. The total number of residents (at the first visit of

the investigator to each care home) was 618. The services which they offered were as follows: residential/nursing/dementia 8 (44%), residential/dementia 7 (39%), residential/nursing/ dementia/adult learning disability 1 (6%), dementia only 1 (6%), and adult learning disability only 1 (6%). Seventeen (94%) of the care homes provided dementia care, 16 (94%) of which were with residential and/ or nursing care. Each care home had varying bed capacity; the mean was 34 (minimum to maximum range 17 to 92). Twenty seven (4.4%) residents were excluded because they were on end of life pathway, 111 (18%) were excluded because although they possessed mentally capacity, they did not provide consent, 263 (42.6%) were excluded because they did not possess mental capacity and informed consent was not obtained from the consultees (figure 6).

The total number of residents that possessed mental capacity in all the 18 care homes was 258/618 (42%) of whom 147/258 (57%) provided informed consent. The total number of residents without mental capacity was 333/618 (54%) of whom consultee consent was obtained in 70/333 (21%). Thus of the 217/618 (35%) participants, 147/217 (68%) possessed mental capacity and 70/217 (32%) did not. Before this study, none of the care homes had participated in research.

Summary: A range of residents from residential homes, nursing homes, dementia care homes and institutions that offer services for adults with mental disability participated in the study.

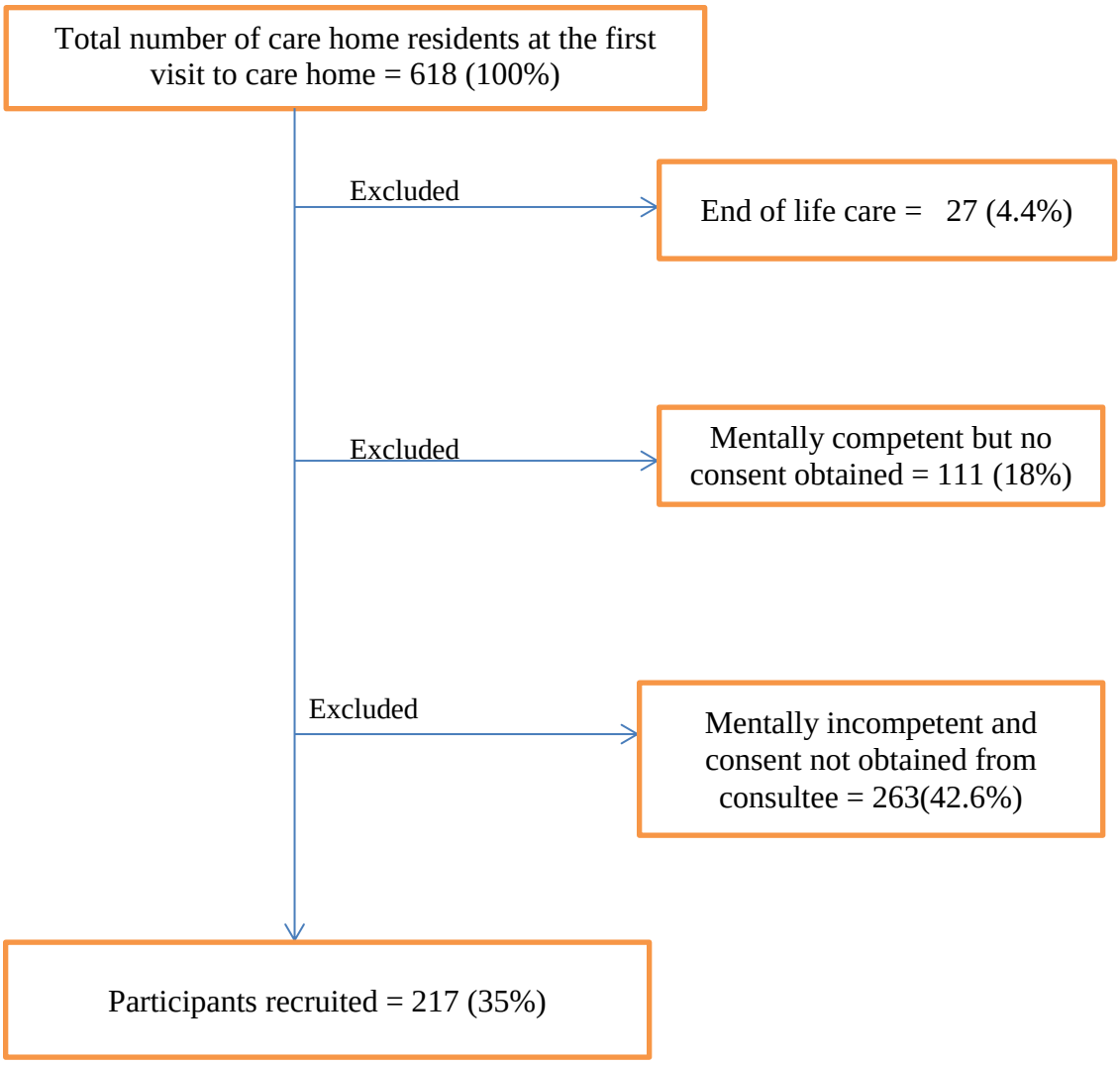


Figure 6: Flow diagram showing the recruitment process of the participants from the 18 care homes

Interpretation

Figure 6 shows that the total number of care home residents at the first visit of the investigator to all 18 care homes was 618 (100%). Of this, 27 (4%) were excluded because they were on end of life care pathway, 111 (18%) were excluded because although they had mental capacity, they declined consent and 263 (42.6%) were excluded because they lacked mental capacity and consent could not be obtained from consultees. Informed written consent was obtained from 35% (217/618) of the residents.

Table 26: Recruitment and mental capacity of residents in each of the 18 care homes

No	Type of care home	Number of residents at first visit	Number of residents excluded by care home manager n (%)	Number of residents with mental capacity n (%)		Number of residents without mental capacity n (%)		Number of residents consenting & assenting n (%)	Care home previously involved in research	
				Consent	Not consenting	Assenting	Not assenting		Yes (%)	No (%)
1	RH/dementia (SC)	39	3(7.6)	8(28.6)	14(71.4)	12(80)	3(20)	18(46.1)		No
2	RH/dementia (RCH)	27	0(0)	0(0)	5(100)	3(13)	20(87)	3(11.1)		No
3	RH/dementia (TM)	25	1(4)	7(70)	3(30)	9(64.3)	5(35.7)	16(64)		No
4	RH/dementia (FH)	25	0(0)	7(77.8)	2(22.2)	6(31.3)	11(68.8)	12(48)		No
5	RH/NH/dementia (WG)	19	6(31.6)	5(55.6)	4(44.4)	2(20)	8(80)	7(36.8)		No
6	RH/NH/dementia (ME)	34	2(5.9)	8(57.1)	6(42.9)	8(40)	12(60)	16(47.1)		No
7	RH/NH/dementia (WF)	27	0(0)	9(81.8)	2(18.2)	2(12.5)	14(87.5)	11(40.7)		No
8	RH/NH/dementia (HC)	92	2(2.2)	29(61.7)	18(38.3)	7(15.5)	38(84.4)	34(37)		No
9	Adult learning disability (A)	17	0(0)	9(90)	1(10)	0(0)	7(100)	9(52.9)		No
10	RH/NH/adult learning disability/dementia (V)	30	1(3.3)	6(100)	0(0)	4(16.7)	20(83.3)	10(33.3)		No
11	RH/dementia (OR)	35	0(0)	10(66.7)	5(33.3)	12(60)	8(40)	22(62.9)		No
12	RH/NH/dementia (W)	35	4(11.4)	11(78.6)	3(21.4)	0(0)	21(100)	11(31.4)		No
13	RH/NH/dementia (G)	37	2(5.4)	12(54.5)	10(45.5)	3(7.1)	14(73.3)	13(35.1)		No
14	RH/dementia (TMGH)	22	0(0)	3(33.3)	6(66.6)	0(0)	8(100)	3(17.6)		No
15	RH/NH/dementia (EL)	41	2(4.9)	8(38.1)	13(61.9)	3(10)	18(90)	10(24.4)		No
16	Dementia (SJ)	35	4(14.3)	0(0)	0(0)	4(10)	27(90)	3(10)		No
17	RH/dementia (GRH)	38	0(0)	10(58.8)	7(41.2)	0(0)	21(100)	10(26.3)		No
18	RH/NH/dementia (WLC)	40	0(0)	5(29.4)	12(70.6)	5(26.3)	8(73.7)	10(27.8)		No
Total number		618	27 (4.4)	147(57)	111(43)	70(22.1)	263(77.9)	217(35.6)		No

RH=residential home

NH=nursing home

The initials represent the names of the care homes

Interpretation

Table 26 shows that of the 18 care homes, 89% (16/18) offered RH care, 50% (9/18) offered NH care, 94% (17/18) offered dementia care and 11% (2/18) offered care for adult learning disability. The services were combined in the majority 89% (16/18) and single in 11% (2/18). None of the care homes had participated in research before now.

4.4.2 Baseline Characteristics of the Participants

From the 5th of April 2015 to the 12th of May 2016, a total of 217 residents were enrolled from the 18 care homes. The GPs and the next of kin were contacted 24 and 17 times respectively to clarify the presence or absence of comorbidities in the participants. Questions asked were guided by the questionannire. The baseline characteristics are summarized in table 27. The mean age was 81.2 years (SD 12.5), 134 (61.8%) were females and all 217 (100%) participants were Caucasian. The mean weight was 69.2 kilograms (SD 21.8) [mean of 62.1 kg (SD 21.6) for females and mean of 69.7 kg (SD 21.2) for males], mean height was 167.9 centimeters (SD 8) [mean of 164.8 cm (SD 6.2) for females and mean of 172.7cm (SD 8.1) for males]. Nine (4.2%) participants were current smokers, 5 (2.3%) took 3 or more units of alcohol daily and the majority (177 [81%]) were living in a residential home.

The comorbidities were as follows: dementia 70 (32%), IHD/stroke/TIA 53 (24.4%), type 2 diabetes mellitus 40 (18.4%), epilepsy/taking anticonvulsants 30 (13.8%), cancer 27 (12.4%), chronic kidney disease 18 (8.3%), asthma/COPD 17 (7.8%), Parkinson`s disease 10 (4.6%), chronic liver disease 4 (1.8%), malabsorption 4 (1.8%), secondary osteoporosis 3 (1.4%), other endocrine problems 3 (1.4%), type 1 diabetes mellitus 2 (0.9%) and rheumatoid arthritis 1 (0.5%). The majority (84.8%) of the participants had one or more comorbidities. Seventy (32.3%) took antidepressants, 30 (13.8%) antiepileptic medications but it was unclear if these were also for pain relief, 7 (3.2%) oral glucocorticoids) and 2 (0.9%) estrogen only HRT. The majority of the participants had history of falls (163 [75%]) and the frequencies were: 1 fall 52 (24%), 2 falls 94 (43.3%). 82 (37.8%) had prevalent fractures as follows: 1 fracture 64 (29.5%), 2 fractures 14 (6.5%), 3 or more fractures 12 (5.5%). 18 (8.3%) participants had parental history of fractures. The mean 12-months Charlson Comorbidity Index (CCI) was 30.7% (SD 20.8).

Summary: The demography and clinical characteristics of the participants show that they were mostly frail elderly Caucasian females. The majority did not smoke or take alcohol in excess.

Most of the participants were in residential care. About two-thirds of the participants had fallen in the past and over 40% had sustained fractures. The participants had different comorbidities and the majority had multmorbidities. The participants had a mean CCI of 30.6% which indicates that they were not at imminent risk of death in 12 months.

Table 27A: Baseline characteristics of the participants

Age	Mean, (SD)
Age of the participants in years,	81.2 (12.5)
Sex	n (%)
Male	83 (38.2)
Female	134 (61.8)
Ethnic group	n (%)
Caucasian	217(100)
Others	0 (0)
Physical characteristics	Mean (SD)
Mean weight of both sexes in kg	69.2 (21.8)
Mean weight of females	62.1 (21.6)
Mean weight of males	69.7 (21.2)
Mean height of both sexes in cm.	167.9 (8)
Mean height of females	164.9 (6.2)
Mean height of males	172 (8.1)
Social history	n (%)
Alcohol ≥ 3 units/day	5 (2.3)
Smoking	9 (4.2)
Type of accommodation	n (%)
Residential	177 (8)
Nursing	40 (19)
Falls in the previous 12 months (in and out of care home)	n (%)
Number of falls =0	71 (32.7)
Number of falls=1	52 (24)
Number of falls=2	94 (43.3)
Number of falls=≥3	0 (0)
Prevalent fractures	n(%)
Number of prevalent fractures=0	117 (58.5)
Number of prevalent fractures=1	64 (29.5)
Number of prevalent fractures=2	14 (6.5)
Number of prevalent fractures=≥3	12 (5.5)
Other comorbidities	n (%)
Rheumatoid arthritis	1 (0.5)
Secondary osteoporosis	3 (1.4)
Type 1 diabetes mellitus	2 (0.9)
Type 2 diabetes mellitus	40 (18.4)
Other endocrine problems	3 (0.9)
Dementia	68 (31.3)
Cancer	27 (12.4)
Asthma/COPD	17 (7.8)
IHD/Stroke/TIA	53 (24.4)
Chronic liver disease	4 (1.8)
Chronic kidney disease	18 (8.3)
Parkinson`s disease	10(4.6)
Malabsorption	4 (1.8)
Epilepsy/anticonvulsants	30 (13.8)

Table 27B: Baseline characteristics of the participants (continued)

Medications	n(%)
Oral corticosteroids	7 (3.2)
Taking oestrogen only HRT	2 (0.9)
Taking antidepressant	70 (32.3)
Parental history of any osteoporotic fracture	n (%)
Number of Participants with Parental history of fractures	18 (8.3)
Number of comorbidities	n(%)
Number of comorbidities=0	1 (0.5)
Number of comorbidities=1	32 (14.7)
Number of comorbidities= ≥2	164 (84.7)
12 month Charlson Comorbidity Index	Mean (SD)
Score on the Charlson Comorbidity Index	30.7 (20.8)

N.B: 36 participants were on Adcal D3 (combination of calcium and vitamin D) but none was on any other osteoporotic medication.

Interpretation

Tables 27A and 27B show that most of the participants were elderly female Caucasians. There were differences in the mean weights and heights between the males and females. The male participants were taller and heavier than the females. The majority of the participants did not smoke or take alcohol in excess and most of them were in residential setting.

63% (136/217) had past history of falls and they were multiple in 43% (94/217). 37.8% (82/217) had prior fractures and they were single in about 30% (64/217).Nearly all the (99.6%[216/217]) participants had comorbidities and the majority had multimorbities.

4.4.2.1 Missing Data

There was no missing data at base line or follow-up.

4.4.3 Outcomes

In this section the assessment of the outcome measures of the study are reported in the following order: the ease of use of the tools, the screening performances of the tools, the clinical discriminatory capacity of the tools, and finally a summary of the important results.

4.4.3.1 Ease of use of tool (duration of risk assessment)

The mean duration to complete fragility fracture risk assessments were as follows: FRAX 1 minute, QFractureScores 2 minutes, Garvan nomogram 1minute, BMI 1minute, and TUGT 2 minutes (table 28)

Summary: Risk assessment with FRAX, QFractureScores, Garvan nomogram and BMI were not time consuming and can be accommodated within clinical schedules of care home staff.

Table 28: The duration of risk assessment for each of the tools

Tool	Duration of assessment in mins.
FRAX	1
QFractureScores	2
Garvan nomogram	1
Body mass index	1
TUGT†	2

Timed Up & Go Test (TUGT). † Ninety-three (43%) participants could not perform the TUGT and 83 (38%) needed a walking aid.

Interpretation: Table 28 shows that the duration of assessment was longest for QFractureScores and TUGT and lowest for FRAX, Garvan nomogram and BMI. The short duration suggest that assessments with any of these tools were not time consuming.

4.4.3.2 Interview of Care Home Managers

The telephone interview survey of the 20 different randomly selected care home managers (table 29) showed that the majority of respondents felt that the duration of 5 minutes or less would be acceptable but 20% did not regard the duration as an issue. All the respondents advised that a simple tool which is of tick box style and devoid of medical jargons would be helpful. Just under half felt that a web based tool would be discouraging.

Table 29: Telephone survey of 20 care home managers on the important features in fragility tool that influence ease of use

Qualities of a useable tool suggested by 20 care home managers	Responses
Duration of assessment in minutes	n (%)
≤ 5	6 (30)
≥10 -15	5 (25)
≥16 -20	2 (10)
≥20 -25	0 (0)
≥26 - 30	3 (15)
Unlimited duration	4 (20)
Simplicity of tool (tick box style, easy to read and understand)	n(%)
Number of managers that suggested simplicity improves use of tool	20 (100)
Web-based assessment is a disadvantage	n (%)
Number of managers who felt web-based tool is a disadvantage	9 (45)

Interpretation

Table 29 shows that the majority of the care home managers felt that the assessment duration of 5 minutes or less would be good and all of them felt that the tool should be simple. 45% felt a web-based tool would be discouraging to use, this suggests that the majority (55%) did not consider this to be a problem.

.

4.4.3.3 Screening Performances of the Tools

The sensitivity, specificity, positive predictive value and negative predictive values of the tools are presented in table 30. FRAX and Garvan nomogram were excluded because neither tool demonstrated statistically significant association for the prediction of falls, fractures combined falls and fractures.

For BMI, the range of normality is between 20 kg/m² and 25 kg/m² (UK Metric Association, 2013). For FRAX, QFractureScores and Garvan nomogram, a 10-year fracture probability estimate of 20% or above for major osteoporotic fracture is recommended (Dawson-Hughes et al., 2008). Individuals with a 10-year estimated risk of major osteoporotic fracture between 10% and 20% are at moderate fracture risk, whereas individuals with an estimated risk of at least 20% have a high risk for fracture (Viswanathan et al 2018). For the TUGT, people who take longer than 12 seconds to complete the TUGT have high risk of falls (Bischoff et al., 2003b).

Table 30 show the actual scores and table 31 the summary of the screening performances of the tools.

For falls assessment, TUGT showed the highest level of sensitivity and QFractureScores the lowest, QFractureScores showed the highest level of specificity and TUGT showed the lowest, BMI of 20kg/m² and below showed the best positive predictive value and TUGT showed the worst, TUGT showed the highest negative predictive value and QFractureScores the lowest.

For fracture assessment: TUGT showed the highest level of sensitivity and QFractureScores the lowest; QFractureScores showed the highest level of specificity and TUGT the lowest, QFractureScores showed the highest level of positive predictive value and TUGT the lowest, TUGT showed the highest negative predictive value and BMI of 20 kg/m² and less the lowest.

For combined falls and fracture assessment the performances of the tools were similar to the performances for fractures.

Summary: The interpretation of the screening results was based on the recommendations of the Royal College of Physicians (The Royal College of Physicians of London and The British Geriatrics Society, 1992) which states: ` When screening, sensitivity (avoiding false negatives) may be more important than specificity (avoiding false positives) because opportunities for

clarifying the status of the false positives patients will arise but the false negative patients is lost to further scrutiny`. For the PPV and NPV values, these are dependent on the prevalence of the disease in the population of interest (Lalkhen, McCluskey, 2008) and because falls are more common than fractures they were used as the outcome for this evaluation.

TUGT had the highest sensitivity for falls and of the fragility fracture tools, BMI of 25kg/m² had the highest.

Table 30: Screening performance of the tools

Tools	Sensitivity (%)	Specificity (%)	PPV value (%)	NPV (%)
Body Mass Index of ≤20kg/m²				
Falls	41.5	73.2	54.1	62.1
Fractures	60	68.1	8.3	95.2
Falls & fractures	60	68.1	8.3	95.2
of ≤25kg/m²				
Falls	74.5	43.9	50.4	76.2
Fractures	90	31.2	6.5	98.7
Falls & fractures	90	31.2	6.5	98.7
QFractureScores of ≥ 20% 10 y probability for major fractures				
Falls	69.1	36.6	45.5	60.8
Fractures	90	35.3	6.3	98.6
Falls & fractures	90	35.3	6.3	98.6
QFractureScores of ≥ 20% 1 y probability for major fractures				
Falls	8	86	48.5	36.6
Fractures	30	85.5	9.1	96.2
Falls & fractures	30	85.5	9.1	96.2
TUGT of ≤ 12 s				
Falls	95.7	40	45	95
Fractures	100	8.2	5	100
Falls & fractures	100	8.2	5	100

Positive predictive value (PPV), Negative predictive value (NPV)

Interpretation

The rational for this interpretation is based on the study which classified mammograms as good tests for detecting breast cancer with sensitivity of ≥70% (Stephanie 2014).

Table 30 shows that the sensitivity for the prediction of falls was poor for BMI of ≤ 20kg/m² and QFractureScores fracture probability of 1-year but good for BMI of 25kg/m² and TUGT. For fractures and falls & fractures combined, the sensitivity was good only for BMI of 25kg/m², Qfracturescores of 10-year fracture probability and the TUGT.

The specificity for falls and falls & fractures combined was good only with BMI of ≤20kg/m² and QFractureScores fracture probability of 1-year. The positive predictive values for the tools for any outcome were poor but the negative predictive values were good with BMI, QFractureScores and TUGT for fracture and falls & fracture combined and only with TUGT for falls.

Table 31: The summary of the screening performance of the tools for falls, fractures, falls and fractures

Outcome	Best sensitivity	Worst sensitivity	Best specificity	Worst specificity	Best PPV	Worst PPV	Best NPV	Worst NPV
Falls	TUGT	QFrac.	QFrac.	TUGT	BMI≤20	TUGT	TUGT	QFrac.
Fractures	TUGT	QFrac.	QFrac.	TUGT	QFrac.	TUGT	TUGT	BMI ≤20
Falls & fractures	TUGT	QFrac.	QFrac.	TUGT	QFrac.	TUGT	TUGT	BMI ≤20

QFrac. = QFractureScores
BMI ≤ 20 = BMI of 20kg/m² and less
PPV= positive predictive value
NPV=negative predictive value

Interpretation

Table 31 shows that the tool with the best sensitivity for any of the outcome was TUGT and the tool with the worst sensitivity was QFractureScores. QFractureScores had the best specificity and TUGT the worst specificity for any outcome. The best PPV tool for falls was BMI ≤ 20kg/m² and QFractureScores for fractures and combined falls & fractures. The worst tool for the PPV tool was TUGT for any outcome. The best tool for the NPV for any outcome was TUGT and the worst tool for NPV for falls was QFractureScores and for fractures and falls & fracture combined, BMI ≤20kg/m².

The Royal College of Physicians recommend that for screening, sensitivity (avoiding false negatives) may be more important than specificity (avoiding false positives) because opportunities for clarifying the status of false positive will arise but the false negative patient is lost to further scrutiny (RCP 1992).

4.4.4.1 Clinical Discriminatory Capacity of the Tools

4.4.4.1.1 10 year Risk of Major Osteoporotic Fractures and Mean BMI and TUGT Scores of the Participants

Table 32 shows the mean (SD) 10-year risk of major osteoporotic fracture for FRAX, QFractureScores and Garvan nomogram and the mean BMI and TUGT. The 10-year absolute probabilities of major osteoporotic fractures of the tools were: FRAX 19.5% (SD 12, 95% CI 17.9 - 21.1), QFractureScores 35.8% (SD 26.5, 95% CI 32.2 - 39.3) and Garvan nomogram 42.1% (SD 27.8, 95% CI 38.4 - 45.9). The mean BMI was 24.3 kg/m² (SD 7.2, 95% CI 23.3 - 25.2) and the mean time for the TUGT was 33.8 seconds (SD 23.4, 95%CI 29.6 - 37.9).

Summary: The mean 10-year absolute risk of major osteoporotic fractures estimates of the participants for FRAX, QFractureScores and Garvan nomogram were different. FRAX predicted a 19.5% risk while QFractureScores and Garvan nomogram predicted about twice the risk. For the fragility tools, a 10-year fracture probability estimate of 20% or above for major osteoporotic fracture is recommended for treatment following guidelines (Dawson-Hughes et al., 2008). Thus both QFractureScores and Garvan nomogram indicate that the participants are at high risk of major osteoporotic fractures and for appropriate residents, pharmacological treatment should be offered. However the scores between the fragility tools are not interchangeable. The medications recommended by NICE (2016) are: bisphosphosnates (alendronic acid, ibandronic acid, risedronate and zoledronic acid) and nonbisphonates (raloxifene, denosumab, teriparatide, calcitriol and hormone replacement therapy [HRT]). HRT is not relevant for care home residents.

The mean BMI of participants was within the normal range of 20 to 25 kg/m² (Hellec, Campbell-Scherer & Allan, 2015) and 55 (25%) of the participants were below the normal range. The mean TUGT was over two-times the normal for community dwelling older people i.e. 12 seconds.

However it was within the range of 12.7 to 50.1 seconds for institutionalised women (Bischoff et al., 2003a).

Table 32: Results of the fragility risk assessment in this pilot study

Test	Result
10-year probability of any osteoporotic fracture with FRAX, mean(SD)	19.5 (12)
10-year probability of any osteoporotic fracture with QFractureScores, mean (SD)	35.8(26.5)
10-year probability of any osteoporotic fracture with Garvan nomogram, mean(SD)	42.1 (27.8)
BMI kg/m², mean (SD)†	24.3 (7.2)
BMI less than 20 kg/m², n (%)	55 (25)
Timed Up and Go Test, mean (SD) in seconds	33.8 (23.4)

† The body-mass index is the weight in kilograms divided by the square of the height in metres.

Interpretation

Table 32 shows that the scores of the 5 tools were different. For 10-year fracture probability, QfractureScores had the highest and FRAX the lowest. The mean BMI of the participants was within the normal range but 25% were below normal. The mean TUGT duration was about 2.8 times normal (normal is ≤12 seconds).

4.4.4.1.2 Logistic Regression Models of the Tools

Table 33 shows the odds ratios (OR) of the binary logistic regression models of the tools.

The odds ratios for the prediction of falls were as follows: FRAX 1.003, standard errors (SE) 0.011 (p=0.813); QFractureScores 1.007, SE 0.005 (p=0.160), Garvan nomogram, 1.010, SE 0.005 (p=0.054), TUGT 0.999, SE 0.000 (p=0.013), and BMI 0.952, SE 0.021 (p=0.015). The effect size for a unit increase of each tool for the prediction of falls was: FRAX 0.3 times more, QFractureScores 0.7 times more, Garvan nomogram 1.01 times more, TUGT 1.001 times less, BMI, 1.1 times less.

For fractures the ORs were as follows: FRAX 1.027, SE 0.024 (p=0.267), QFractureScores 1.024, SE0.011 (p=0.036), Garvan nomogram 1.021, SE 0.011 (p=0.062), BMI 0.868 (p=0.024) and TUGT 1.000 (p=0.829). The effect size for a unit increase of each tool were: FRAX 1.027 times more, QFractureScores 1.024 times more, Garvan nomogram 1.021 times more, BMI 1.2

times less, TUGT no effect. The same ORs and effect sizes were obtained for combined falls and fractures as for fractures for all the tools.

Summary

Of the four tools, only BMI predicted falls, fractures and combined falls and fractures. A unit increase of BMI resulted in statistically significant decrease of falls risk, fracture and combined falls and fracture risk of 4.8% 13.2% and 13.2% respectively.

A unit increase in QFractureScores resulted in a non-significant increase of falls risk, significant increase of fracture risk and combined falls and fracture risk of 0.7%, 2.4% and 2.4% respectively. Practically, these were not relevant.

A unit increase of FRAX resulted in a non-significant increase of falls, fracture and combined falls and fracture risk of 0.3%, 2.7% and 2.1% respectively.

A unit increase of Garvan nomogram resulted in non-significant increase of falls, fracture and combine falls and fracture risk of 1%, 2.1% and 2.1% respectively.

A unit increase in TUGT resulted in a significant increase of falls risk of 0.1% but no effect on fracture and combined falls and fracture risk. Practically, this was not relevant.

The associations of the tools with the clinical outcomes falls, fractures, combined falls and fractures were weak although statistically significant in some cases. The screening performance of FRAX and Garvan nomogram were not calculated because they did not show significant association for falls, fractures and combined falls and fractures.

Table 33: Odds ratio and Standard errors of the binary logistic models

Tools	**OR, SE for prediction of falls (p)**	**OR, SE for prediction of fractures (p)**	**OR, SE for prediction of combined falls & fractures (p)**
FRAX	1.003,0.011 (0.813)	1.027,0.024 (0.267)	1.027,0.024 (0.267)
QFractureScores	1.007,0.005 (0.160)	**1.024,0.011 (0.036)**	**1.024, 0.011 (0.036)**
Garvan nomogram	1.010,0.005 (0.054)	1.021,0.011 (0.062)	1.021, 0.011 (0.062)
BMI	**0.952,0.021 (0.015)**	**0.868,0.073 (0.024)**	**0.868, 0.073 (0.036)**
TUGT	**0.999,0.000 (0.013)**	1.000,0.001 (0.829)	1.000, 0.001 (0.829)

Statistically significant values $p \leq 0.05$
OR = Odds ratio
SE = Standard error
p= level of statistical significance
Statistically significant odds ratios are given in bold

Interpretation

Table 33 shows that of the tools, only BMI was a predictor of falls, fractures and combined falls & fractures. TUGT was a predictor of falls and QFracturescores was a predictor of fractures and combined falls & fractures.

4.4.5 Summary of the results

This pilot study was feasible but the majority of the participants possessed mental capacity and this was not representative of the care home resident population, the majority of whom did not have mental capacity. The tools were easy to use as per the duration to complete the risk assessment but there were logistic problems particularly with the participants who did not possess mental capacity. The sensitivity, specificity, positive predictive values, and negative predictive values were generally poor. Of the tools, BMI of 25 kg/m² was the best predictor of falls, fractures and combined falls and fractures and the impact was more with fractures than falls. All the participants were Caucasians.

4.4.6 Field Notes

These were the field notes during the recruitment and follow-up of the participants:

1. The TUGT was performed in a public area in one care home; this led to two instances of interruption; one from a passing member of the public and the other by a wandering resident.

2. All the care home documentations were paper-based and there were variations between care homes, Zermansky et al observed the same (Zermansky et al., 2007). GP letters and care plans were often missing. However, there was consistency in the documentation of resident's contact details, medicine records and accident books which contained details of falls and other incidents.

3. On six occasions, the data collection from the drug charts were appropriately interrupted by drug rounds.

4. One care home manager mailed information sheets to the next of kin/guardian of all residents in the care home regardless of mental capacity.

5. A care home manager excluded some residents who were bed bound but not classified as end of life because she felt they were unlikely to experience falls.

6. The recruitment process was delayed in two care homes because the information sheets were given to the residents for less than 24 hours before consent was due to be obtained.

7. Care home staff were often diligent and supportive as they claimed research was a new experience. One deputy care home manager remarked `I am happy we have been included in this study which may have a positive impact on the care we give to our care home residents. More of this please'.

8. Falls were recorded in an incident book in 17 out of 18 care homes, this facilitated data collection. The care home without an incident book documented falls within the residents` individual care plans; this made accurate and reliable identification of falls more challenging.

4.5 Discussion

The key findings from this observational study were: .the study included a wide range of residents from residential homes, nursing homes, dementia care homes and institutions that offer services for adults with mental disability. Just over a third of care home residents were recruited. Most of the participants in the study had mental capacity which did not represent the care home population, most of whom lack mental capacity. Thus the study was feasible mainly for care home residents who had mental capacity. The duration of the risk assessments were short and can be accommodated within nursing care schedules but the TUGT posed logistic problems particularly in some participants who lacked mental capacity. The screening performances of the tools were generally poor but TUGT, a tool designed primarily for falls assessment had good sensitivity. BMI was the only tool that showed significant association with falls, fractures and combined falls and fractures but the associations were weak. QFractureScores had significant

association with fractures and combined falls and fractures and the TUGT had significant association with falls and like BMI the associations were weak. Both FRAX and Garvan nomogram did not show significant association with these outcomes. All the participants were Caucasians. The participants were generally frail but the mean Charlson`s Comorbidity Index was 30.7% which suggests that the majority were not at imminent risk of dying within 12 months. The mean CCI of the 54 of the 217 participants (24%) who died was 36%. Falls are common in care home residents but most of them were not complicated by fractures.

The discussion is presented in the order in which the results were reported: baseline characteristics of the participants, primary feasibility, ease of clinical use, screening performance, clinical discriminatory capacity of the tools, exploratory analysis of the outcomes and finally recommendation for clinical practice.

4.5.1 Participant Characteristics

The sociodemographic characteristics of the participants in this study show that they were frail; the majority were females, mean age 81.2 years, (maximum to minimum age range 36 to 103 years). The relatively younger participants were recruited from a facility that caters exclusively for people with learning disability. All the participants were Caucasians, thus the findings may not be applicable to other ethnic groups. Most of the participants had multi-morbidities. The commonest diseases were dementia, diabetes mellitus, cancer, cardiovascular diseases, chronic kidney disease, epilepsy and asthma/chronic pulmonary disease.

These characteristics are broadly similar to the characteristics of the care home residents in the large BUPA multinational survey in the UK, Australia, New Zealand and Spain (Lievesley, Crosby, 2011).

All the participants in this research were Caucasians. This is because Boston is in a semirural location and the immigrant population is small. According to the Office of National Census, the non-white population made up only 2.4% of the total population in 2011 compared with the national non-white population of 14 % and 30.2% in London (Office of National Statistics (ONS), 2018). Cultural and religious practices may also have contributed.

It is not known what the effects of Brexit on migration will be and there are arguments on either side (Begum, 2018). The majority of participants were in residential care in comparison to the BUPA multinational survey where nearly three quarters were in nursing homes (Lievesley, Crosby, 2011). This is probably because they were less frail and or there were fewer facilities that cater for nursing home residents in Boston.

4.5.2 Recruitment of the Participants

The study included a wide range of residents from residential homes, nursing homes, dementia care homes and institutions that offer services for adults with mental disability. Just over a third of care home residents were recruited. Most of the participants in the study had mental capacity which does not represent the care home population thus the data is skewed in favour of residents who possess mental capacity.

The majority of residents in the 18 care homes in this study lacked mental capacity and assent was obtained in 21%. This may have been due to the dearth of face to face contact with consultees as the participation rate increased when this researcher managed to meet with the next of kin or guardian face to face. Zermansky and colleagues obtained higher assent rate of 41% (Zermansky et al., 2007). Consent was 57% in residents who possessed mental capacity compared to 42% by Zermansky et al and the overall consent/assent was 35% compared to 42% (1163/2779) by Zermansky and colleagues.

This might have been because they had a dedicated research nurse and this researcher did not. Unfortunately, the other available publications (Nijs et al., 2006, Fossey et al., 2006, Winblad et al., 2006, Law et al., 2006) in care home research did not state consent/assent rates. The recruitment is worryingly low especially for the residents without mental capacity who constitute the higher proportion of care home residents. The proportion of the participants who were excluded from this study because they were on end of life care pathway was 4.4% compared to 27% in a study by Hall and colleagues (Hall, Longhurst & Higginson, 2009).

There are three plausible explanations for this; first, there is a dearth of palliative care services in Lincolnshire. A recent local mortality report for the United Lincolnshire Hospital Trust showed that the Trust is currently 10% below the national average for palliative care coding for mortalities (United Lincolnshire Hospitals NHS Trust (ULHT), 2018). Second there may be resistance to changing the established clinical practice code of identifying people who should be on end of life care pathway. This was highlighted in a recent report of the Trust`s Mortality Review Action Group (United Lincolnshire Hospitals NHS Trust (ULHT), 2017). Finally it may reflect the study population.

4.5.3 Ease of Clinical Use

The duration that was taken to undertake the risk assessment were 1 minute each for FRAX, QFractureScores, Garvan nomogram and 2 minutes each for QFractureScores and TUGT. These can be accommodated within clinical practice schedules. There are no publications for duration of risk assessment tools therefore comparisons could not be made. Experience and speed in using these tools are achieved with practice. Assessments for FRAX, QFractureScores and Garvan nomogram are web-based therefore require computers. Computers are readily available in most

developed countries but availability does not necessarily translate to use because many practitioners may not interrupt their schedules to use the computer.

One experiment found that providers who are well versed in osteoporosis care were unlikely to access a web-based fracture risk tool. Only 1 in 20 providers who referred patients for bone densitometry testing responded to a mailed invitation to access a tool like FRAX (Watts, Ettinger & LeBoff, 2009). This is likely to change with the introduction of the Patient Electronic Healthcare Record System which mandates all GPs to go online for patient management. The TUGT poses logistic problems in the frail elderly resident particularly in the cognitively impaired. Conducting it requires adequate space, stop-watch and focused commitment which could be challenging.

4.5.4 Clinical Discriminatory Capacity

The odds ratios for the prediction of the outcomes of the tools indicate that for a unit increase in the score, there was 0.3% non-significant increase in fall risk, 2.7% non-significant increase in fracture and combined falls and fracture risk for FRAX, 0.7% non-significant increase in falls risk, 2.4% significant increase in fracture and combined falls and fracture risk for QFractureScores; 1% non-significant increase in falls risk, 2.1% non-significant increase in fracture and combined falls and fracture risk for Garvan nomogram; 4.8% significant reduction in falls risk, 13.2% significant reduction in fracture and combined falls and fracture risk for BMI; 0.1% significant reduction in falls risk and no change in fracture and combined falls and fracture risk for TUGT.

The results show that there were differences in the performances of the tools. FRAX, QFractureScores and Garvan nomogram were not good at predicting falls within the one year of follow-up. Although there were statistically significant differences for the prediction of fractures

and combined falls and fractures for FRAX, Garvan nomogram and QFractureScores, the effect sizes differed only a little, therefore for practical purposes, none of them was effective at predicting fractures and combined falls and fractures in this cohort. TUGT, the tool recommended by National Institute for Care Excellence (NICE) for falls risk assessment predicted falls but again the effect size was minimal; therefore it was not useful as falls risk tool in this cohort.

This finding emphasises the limitations of p-values in interpreting research data. A recent Nature commentary (Diong, 2016) highlighted a statement by the American Statistical Association on the principles to guide the use of p-values for interpretation of research findings out of concern for the lack of understanding of p values and what they imply. Specifically the 6 principles of the statement are:

1. P values can indicate how incompatible the data are with a specified statistical model;
2. P values do not measure the probability that the studied hypothesis is true, or the probability that the data were produced by random chance;
3. Scientific conclusions and business or policy decisions should not be based only on whether a p value passes a specific threshold;
4. Proper inference requires full reporting and transparency;
5. A p value, or statistical significance, does not measure the size of an effect or the importance of a result;
6. By itself, a p-value does not provide a good measure of evidence regarding a model or hypothesis.

BMI predicted falls, fractures, combined falls and fractures with the highest odds ratios but the associations were weak. The effects were more on fractures than falls. The influence of BMI on

fractures is largely through the BMD. This was shown in a large population-based prospective meta-analysis which was cited earlier (De Laet et al., 2005).

The underlying mechanisms by which low BMI causes falls and fractures are conjectural but might include greater liability to falls (Willig, Luukinen & Jalovaara, 2003), nutritional deficiencies of protein and amino acids, vitamins A, C, D, and E as well as minerals such as iron, selenium and zinc (Bischoff et al., 2003a, Wootton et al., 1979, Cespedes, 2017). Low BMI also results in compromised immune system with increased propensity to falls and fractures because of infections, lethargy, insomnia (Cespedes, 2017) and the decreased padding over the greater trochanter (Nilsson, 1970). The effects of some unmeasurable factors such as reduced mobility which result in secondary osteoporosis has also been suggested (Frost, 1997). There are also the effects of inflammatory secondary to low BMI.

The skeletal and the muscular organ systems are tightly intertwined: the strongest mechanical forces applied to bones are those created by muscle contractions that condition bone density, strength, and microarchitecture. Not surprisingly, decrease in muscle strength leads to lower bone strength. Ageing *per se* and the reduced gonadal hormone levels seen in ageing are responsible for the increase in catabolic pro-inflammatory cytokines such as IL-1, IL-6 and tumour necrosis factor (TNF-a) which are partly regulated by anabolic hormones. Low BMI is also associated with elevated levels of these cytokines (Takele et al., 2016) which have detrimental effects on both the muscle and the bones.

In the muscle the cytokines result in reduced muscle mass and increased muscle weakness (sarcopenia) (Bischoff et al., 2003a, Bischoff et al., 2003b) by causing muscle breakdown, the molecular basis is linked to the ubiquitin-proteasome system and the muscle fibre actin and myosin proteolysis (Glass, 2010). Sarcopenia is considered one of the hallmarks of the aging process. It is characterised by the loss of fast-twitch type 11 fibres and loss of motor-neurons

both of which are important factors involved in the onset of fall (Cederholm, Cruz-Jentoft & Maggi, 2013).

In the bone the cytokines are partly responsible for the differentiation of osteoclast precursors into activated osteoclasts via the RANKl/RANK/OPG pathway that result in osteoporosis (Boyce, Xing, 2007). Cathepsin K, a protease with specific action on bone collagen and expressed by osteoclasts has also been implicated in the process. Thus the combined effect of sarcopenia and osteoporosis i.e. the hazardous duet (Crepaldi, Maggi, 2005) contribute to the increased risk of falls and fractures especially in the frail older person.

Body mass index (BMI) is a measure of weight adjusted for height and it is calculated as weight in kilograms divided by the square height in metres (kg/m^2). Obtaining accurate weight and height measurements in the elderly can be challenging due to the changes in body physique and decline in mobility. Weight can be assessed with sit-in weighing scales or by hoist in bed bound residents. Height can be measured either with wall-mounted scales for ambulant residents or ulna length and demispan in those who cannot stand (BAPEN, 2018). For the residents in whom conventional measurements cannot be done, BMI estimates can be obtained by the mid-upper arm circumference (MUAC) (BAPEN, 2018). BMI assessment is simple, non-invasive, and inexpensive and within the repertoire of most care home nurses and BMI nomograms are widely available. Where there is access to proper equipment, BMI can be calculated with reasonable accuracy.

Besides falls and fracture assessment, measurement of BMI has other health benefits. It is a surrogate measure for body fat and a high BMI has been shown to predict future morbidity and mortality (Abdelaal, Le-Roux & Docherty, 2017). Thus, it has been used to track weight status in individuals and populations. Its use has resulted in an increased availability of published data that

allow health professionals to make comparisons across time, regions and population sub-groups. It is debated that different reference standards should be used for specific sub-groups. There is robust evidence that at any given BMI, some health risks such as diabetes mellitus are higher in some ethnic groups than others (Deurenberg-Yap et al., 2000). In the current study, all the participants were Caucasians therefore BMI could not be compared between ethnic groups.

The use of BMI for risk assessment has some limitations. It does not take into account the weight from fat, bone or lean body mass. People with large amount of muscle mass such as athletes may have high BMI and be perfectly healthy. Conversely, BMI can underestimate health risk in people who are within the normal reference range but are not healthy (Cespedes, 2017). Also, it is not a good measure of weight in short or tall people. For example, it may underestimate the true values in people with vertebral collapse (Trefethen, 2013). With age, body fat increases and muscle mass decreases (Rothman, 2008) therefore BMI may not correspond to the proportional changes in body fat or mass. Finally, BMI does not correct for sex differences in age related decline in muscle mass.

FRAX and Garvan nomogram were not predictors of any of the outcomes. QFractureScores predicted fractures but not falls which is consistent with the fact that it is a fragility tool. BMI is a common predictor in the three fragility models. A plausible explanation for the differences observed was that many of the predictors in the models were not essential and therefore diluted the association of BMI towards the null. An attempt was made to obtain the weightings of the predictors for FRAX from the WHO headquarters in Switzerland but the researcher was informed it is classified information. TUGT was a predictor of falls but not of fractures consistent with the fact that TUGT is a falls risk tool. Although the mean duration of TUGT was statistically significant, the effect size was small which may be because the derivation cohort of the TUGT was younger (mean age 79.1 years) compared to this cohort (mean age 81.2 years).

There were no publications that compared the performance of fragility risk tools in care home residents but some were available for community dwelling older people. A study compared FRAX, Garvan nomogram, age plus prior fracture using the GLOW cohort (Sambrook et al., 2011). The AUC for hip fracture were 0.78, 0.76, 0.76 respectively and 0.61, 0.64 for major osteoporotic fractures for FRAX and Garvan nomogram. Another study compared FRAX (New Zealand) and Garvan nomogram in participants who were enrolled in a 5-year randomised control trial of calcium supplementation (Bolland et al., 2011). For hip fracture, the AUC for FRAX incorporating BMD was 0.70 (95% CI 0.64-0.77), FRAX without BMD 0.69 (95% CI 0.63-0.76), and 0.67 (95% CI 0.60-0.75) for Garvan nomogram. For major osteoporotic fractures, the AUC were between 0.60 and 0.64 for Garvan nomogram and FRAX plus BMD. Neither FRAX nor Garvan nomogram demonstrated better discrimination compared to the Kanis risk algorithm which uses age and BMD alone in the assessment of fracture risk (Kanis et al., 2001).

Henry and colleagues (2011) compared FRAX (UK and USA) and Garvan nomogram in 600 post-menopausal Australian women; for major osteoporotic fracture without BMD (AUC 0.66) and with BMD (AUC 0.67-0.70) were comparable (Henry et al., 2011). Cummins and colleagues (2011) also showed that the AUCs of QFractureScores and FRAX were comparable in a group of 246 postmenopausal women aged 50-85 years from six centres in Ireland and the UK, the AUCs were: 0.632 vs 0.710 for hip fractures and 0.668 vs 0.665 for major osteoporotic fractures respectively (Cummins et al., 2011).

4.5.5 Screening Performance of the Tools

The screening performance showed that generally, the fragility risk tools had poor sensitivities and specificities. Screening tests assist to identify accurately diseased and non-diseased individuals; there is rarely a clean distinction between “normal and “abnormal” but 100% is desirable. The sensitivity of a clinical test refers to how accurately the screening test is in

identifying disease in people who truly have the disease. The specificity focuses on the accuracy of the screening test classifying truly non-diseased people (Felson, 2018). Sensitivity and specificity focus on the efficacy of the screening tool for a population and not the individual per se. The RCP (1992) recommends that when screening, sensitivity (avoiding false negatives) may be more important than specificity (avoiding false positives) because opportunities for clarifying the status of false positive patients will arise but the false negative is lost to further scrutiny.

The predictive values take the test results a step further to the individual level. Thus the PPV is the probability that subjects with a positive screening test truly have the disease and the NPV is the probability that subjects with a negative screening test truly do not have the disease. Unlike sensitivity and specificity, the PPV and NPV are dependent on the prevalence of the disease. A common condition will result in a high PPV and low NPV whereas an uncommon condition will result in a low PPV and a high NPV. Thus in daily practice, the clinician and patient will be more interested in the predictive values (Altman, Bland, 1994).

Of the fragility tools, BMI of 25kg/m² or less had the highest sensitivity of 74.5%. Compared to the fragility tools, the TUGT had the highest sensitivity of 95.7% for falls, but specificity was poor at 40%. This was not surprising because TUGT is primarily a falls risk assessment tool. Sensitivity of 70% and above is regarded as good. Mammograms are an example of a test that generally has a high sensitivity (70 – 80%) (Stephanie 2014)

4.5.6 Conclusions

This pilot study has added to the knowledge base in falls and fragility risk assessment in care home residents. It has provided important process, resource, management and scientific data to guide the design of a future powered study. The complex fragility tools are not useful for risk assessment in care home residents and the simpler tools are not only cost saving but more

practical and effective. The tools were generally easy to use but their sensitivity and specificity were poor.

Of the four fragility risk assessment tools, Body Mass Index (BMI) was the best predictor of falls, fractures and combined falls and fractures although the associations were weak. QFractureScores predicted fractures and combined falls and fractures but neither FRAX nor Garvan nomogram predicted any of the outcomes and the Timed Up and Go Test predicted falls only. This preliminary evidence requires confirmation in a future definitive adequately powered study that incorporates a representative sample of residents without mental capacity.

Chapter 5 Exploratory analysis of the data of the Observational Study and Clinical Algorithym

5.1 Abstract

5.1.1 Background

A general review of the data of the observational study showed that there were differences in the clinical outcomes in the 18 care homes and three subgroups of participants were identified. The aim of the exploratory analyses was to identify the factors which may be useful for the development of a clinical algorithm.

5.1.2 Methodology

The methodology of the observational study has been described in chapter four. The three subgroups of participants identified were:

Group 1: the participants who did not fall and did not sustain incident fractures

Group 2: the participants who had falls but did not sustain incident fractures

Group 3: the participants who had falls and sustained incident fractures

5.1.3 Results

The fall incidence in the residents was 2.7 per resident per year and 1.5 per participant per year and incident fractures were 0.17 per resident and 0.05 per participant. There were variable numbers of falls and fractures in the care homes. Of the 10 incident fractures, 40% occurred in the participants who had dementia and all incident fractures resulted from falls. There was a reduction in the number of fallers following institutionalisation 165 vs. 94 but fractures were more 88 vs. 103

The covariates that showed significant association with falls were: age OR 1.025 (p=0.030), Parkinson`s disease OR (p=0.017), prior history of falls OR 1.949 (p=0.014), body weight OR

0.982 (p=0.008), BMI OR 0.952 (p=0.015), alcohol use OR 0.000 (p=0.016). For fractures and combined falls and fracture the significant associations were: age OR 1.025 (p=0.030), BMI OR 0.886 (p=0.024), body weight OR 0.952 (p=0.019). When the Bonferroni correction was applied the only covariate that was different between the groups was the body weight.

There were significant differences between subgroups. The differences were: age. no falls, no fracture group vs falls, no fracture group (p=0.017), no fall, no fracture group vs fall & fracture group (p=0.046); body weight no fall, no fracture group vs fall, no fracture group (p=0.0170, no fall, no fracture group vs fall & fracture group (p=0.014); Parkinson`s disease no fall, no fracture group vs fall, no fracture group (p=0.025): QFractureScores no fall, no fracture group vs fall & fracture group (p=0.020); Garvan nomogram no fall, no fracture group vs fall & fracture group (p=0.025); BMI no fall, no fracture group vs no fall, no fracture group (p=0.042), no fall, no fracture group vs fall & fracture group (p=0.021); TUGT no fall, no fracture group vs fall, no fracture group (p=0.002). However when the Bonferroni correction was applied, the only tool that differentiated fallers from non-fallers was the TUGT.

5.1.4 Conclusions

Falls were common in the residents and participants but fractures, less so. All the incident fractures resulted from falls. Despite the small representation of participants who lack mental capacity, 40% of the incident fractures were observed in this group, thus dementia is a strong risk factor for fractures in this cohort. Body weight and body mass index predicted falls, fractures, falls and fractures combined. There were some demographic differences between fallers and non-fallers but there were no differences between fallers who sustain fractures and those who did not. However, when Bonferroni correction was applied, the only predictors that were significantly different between the groups were body weight and the TUGT but as the numbers of the participants in subgroups were small and not equal, the findings may be spurious.

5.2 Background

A general review of the data of the observational study in chapter four showed that there were variations in the number of clinical outcomes between the 18 care homes. Also three subgroups of the participants were identified. These were: group 1, the participants who did not fall and did not sustain incident fractures; group 2, the participants who had falls but did not sustain incident fractures; group 3, the participants who had falls and sustained incident fractures. The aim of the exploratory analyses was to identify the factors which may be useful for the development of a clinical algorithm.

5.3 Methodology

The methodology of the observational study has been described in chapter four. The clinical outcomes in each care home were obtained from the study database and tabulated. The participants were divided into three subgroups:

Group 1: the participants who did not fall and did not sustain fractures

Group 2: the participants who had falls but did not sustain incident fractures

Group 3: the participants who had falls and sustained incident fractures.

5.3.1 Statistical Analysis

The comparison between groups was done using appropriate statistical methods. To compare all three groups simultaneously (Bonferroni correction), the desired alpha value ($\alpha = 0.05$) was divided by the number of groups (i.e. 3) to obtain the p value (Bland, Peacock, 2000) i.e. 0.017. Box and whisker plots were plotted where appropriate

5.4 Results

5.4.1 Falls and Fractures in Care Home Residents and Participants

Table 34 shows the total number of falls and fractures in care homes residents and the participants.

5.4.1.1 Residents

There were 1671 falls in all 18 care homes with population of 618 residents. The fall incidence was 2.7 per resident per year (1671/618). The total number of fractures in all the 18 care home residents was 103, that is, fracture incidence of 0.17 fractures per year (103/618). The proportion of falls resulting in fractures was 6.2% (103/1671 x 100).

5.4.1.2 Participants

The total number of falls and fractures in the 217 participants (35% of care home population) were 325 and 10 respectively that is fall incidence of 1.5 per participant per year and fracture incidence of 0.05 per participant per year respectively. This equates to 3.1% (10/325 x 100) of fractures complicating the falls.

Ninety four (42%) out of the 217 participants in the study had a fall; that is classified as fallers. Ten (5%) participants in the study had both falls and a fracture; that is every participant who had an incident fracture also had a fall.

Summary: There was a high incidence of falls (1.5 per annum) in participants, but only few resulted in fractures (3.1%).There were higher incidence of falls (2.7 per annum) in all residents (including those not enrolled in the study) and a higher proportion of these resulted in fractures (6.2%). The data show higher incidence of falls and fracture in an unselected sample of all care

home residents (about 50% more compared to the participants) therefore the data for the participants is skewed. This was due to the disproportionate representation of residents without mental capacity because of the difficulties encountered with consent.

Falls were common in this population with average annual incidence of 1.5 falls per participant and 2.7 falls per resident. Fall incidence in nursing care facilities are reported to be about three times that in the community, equating to rates of 1.5 falls per bed per year (Luukinen 1994, Rubenstein 1994) or 1.4 falls per person per year (Nurmi 2002). The Center for Disease Control in the USA reported an incidence rate of 2.6 falls per person per year (Rubenstein et al 1990). Thus these data compare with previous studies. Within the 12 month follow-up period, fractures were infrequent in the participants, affecting only 5% of participants but they were more common in the care home residents (17%) and all the fragility fractures resulted from falls.

Table 34: Comparison of clinical outcomes in the participants and the residents.

Participants in this study	**Result**
Total number of participants in this study	217
Number of fallers	94
Total number of falls in participants over 12 months	325
Number of fractures in participants	10
Fall incidence per participant per year of study	1.5
Fracture incidence per participant per year of study	0.05
Proportion of falls resulting in fractures in the participants	3.1%
Duration in days taken to consent and baseline assessment and review Median Interquartile range (IQR) Minimum to maximum	 10 10 1 - 299
Number of participants who died during 12 months of follow-up (%)	54 (25)
Mean Charlson comorbidity index of all participants (SD)	30.6 (20.7)
Mean Charlson mortality index of participants who died (SD)	36 (21.1)
All residents of the 18 care homes	Result
Total number of care home residents	618
Total number of falls in care home residents	1,671
Total number of fallers	Not available†
Total number of fractures in care home residents	103
Fall incidence per resident per year of study	2.7
Fracture incidence per resident per year of study	0.2
Proportion of falls resulting in fractures in the care home residents	6.2%

†; no falls was available in 2 care homes

Interpretation

Table 34 shows that the incidence of falls in the participants was 1.5 per participant per year and 0.05 per participant per year for fractures. The proportion of fractures that complicated falls in the participants was 3.1%. For the residents, the fall incidence and fracture complication rates were approximately double at 2.7 per resident per year and 6.2% respectively; the fracture incidence was 0.2 per resident per year. This suggests that the resident population had a higher proportion of people who were susceptible to falls and fractures e.g people with dementia. The duration for recruiting participants was considerable and the mortality was high.

5.4.2 Number of Falls in Each of the 18 Care Homes in All Residents and Participants

The aim was to explore variations in the distribution of falls amongst the care homes and to determine whther falls in participants were representative of falls in the whole care home population. .

Table 35 shows the numbers of falls in each care home during the study period. The table shows that falls occurred in most of the care homes and the numbers were variable in both the residents and the participants. The crude falls incidence rate was highest in two facilities, ME and SJ. Both of them catered for patients with dementia but the latter was exclusively for dementia. The lowest was in A, a facility for adults with learning disability. All (100%) the facilities conducted routine falls risk assessment on the residents of which 14(78%) used the facility`s own risk tool and the remaining 4(22%) used generic tools.

Summary: Falls occurred in most of the care homes. The crude falls incidence was particularly high in a facility exclusively for dementia care and low for adults with learning disability. The residents in the latter home were much younger. All care homes conducted routine falls risk assessments, but most of them used the facility`s falls risk assessment tool which were different in each care home**.**

Table 35: Falls in each Care Home during the study period

No	Care homes	Total number of falls in 12 months in all residents n=618	Total number of falls in participants in 12 months n=217	Falls incidence /100 residents	Routine falls risk assessment Y/N	Type of falls risk tool Used in care home
1	**RH/dementia (SC)**	59	6	151	Y	Company
2	**RH/dementia (RCH)**	67	2	248	Y	Company
3	**RH/dementia (TM)**	96	9	384	Y	Company
4	**RH/dementia (FH)**	63	1	352	Y	Generic
5	**RH/NH/dementia (WG)**	10	0	53	Y	Company
6	**RH/NH/dementia (ME)**	250	85	735	Y	Company
7	**RH/NH/dementia (WF)**	93	7	344	Y	Company
8	**RH/NH/dementia (HC)**	262	86	284	Y	Generic
9	**Adult learning disability (A)**	9	2	53	Y	Generic
10	**RH/NH/dementia (VC)**	171	33	570	Y	Company
11	**RH/dementia (OR)**	53	20	151	Y	Company
12	**RH/NH/dementia (W)**	113	22	323	Y	Company
13	**RH/NH/dementia (G)**	66	7	178	Y	Company
14	**RH/dementia (TMGH)**	40	13	182	Y	Generic
15	**RH/NH/dementia (EL)**	79	19	193	Y	Company
16	**Dementia (SJ)**	240	1	727	Y	Company
17	**RH/dementia (GRH)**	NA	6	NA	Y	Company
18	**RH/NH/dementia (WLC)**	NA	6	NA	Y	Company
	Total	1,671*	325		18	

Y= yes
N=no
The initials represent the names of the care home
RH= residential home
NH= nursing home
Company= facility`s own falls risk assessment tool
Generic= common falls risk assessment tool
NA= not available (no falls log was available)

Interpretation

Table 35 shows that there were 1,671 falls in the 618 residents excluding two care homes in which falls incidents were not available and there were 325 falls in the 217 paraticipants. All the care home residents including the participants had incident falls. The highest incident occurred in a facility that cared exclusively for residents with dementia. All the care homes conducted falls assessment on residents routinely and the majority used the facility`s falls risk assessment tool

5.4.3 Classification of Care Home by Fallers (1 or more falls) and Fractures (1 or more fractures)

Table 36 shows the fallers with prevalent and incident fractures in the care homes. During the 12 months follow-up, 94 participants (43%) were classified as fallers of which 10 (11%) had incident fractures. One hundred and sixty five (76%) were classified as fallers with 88 (53%) prevalent fractures. Seventy-one (43%) participants who were classified as fallers did not fall following institutionalisation and there was a reduction of fractures by 88%.

There were 103 incident fractures in all the residents. Fifteen (83%) care homes recorded incident fractures but there were variations in the numbers. The incidence rate was highest in WLC and zero in three care homes. There were 10 incident fractures in the participants of which 3 (33%) occurred in a facility that provided residential and dementia services (SC). The care home with the highest number of fractures was also the most challenging home for this researcher: it was more difficult to arrange appointments and there were several cancellations.

Summary: Prevalent falls and fractures were common in the cohort but there was a reduction in falls following admission to the care homes (165 vs 94). However incident fractures increased (103 vs 88). This suggests that although there were fewer fallers, falls resulted in more fractures. This may be related to reduced bone strength due to the relative immobility of the residents secondary to frailty and vitamin D deficiency. One review from the electronic records of 265,195 participants in the UK found an increased incidence of fractures at all sites was strongly associated with advancing frailty. (Ravindrarajah et al.,2017).

Vitamin D deficiency is common in care home residents and it increases the risk of falls and fractures (Chapuy et al., 1992). Another explanation is undernutrition which is common in care home residents. Undernutrition particularly protein malnutrition contributes to the occurrence of osteoporotic fracture by lowering bone mass and altering muscle strength (Rizzoli, Bonjour

1999). At least a third of care home residents are undernourished (Stephenson 2015). Finally, the fall mechanics that result in fragility fractures may be more common in care home residents. Incident fractures occurred in most care home residents, but only about 10% of these occurred in the participants. There was no documented history of falls in three residents who had prevalent fractures in care home A.

Table 36: Fallers with and without fractures in each care home

Care homes	No of fallers in participants during 12 months of study *n,(%)	No of fallers in participants 12 months prior to study ☨* n,(%)	Participants during 12 months of study (n)	Participants with incident fractures *n,(%)	Participant swith prior fractures *n,(%)	Residents with incident fractures *n, (%)
RH/dementia (SC)	7 (18)	14 (36)	6	3 (8)	9 (23)	9 (1.5)
RH/dementia (RCH)_	2 (7.4)	3 (11)	2	0 (0)	1 (4)	4 (0.6)
RH/dementia (TM)	9 (36)	15 (60)	9	1(4)	11(44)	2 (0.3)
RH/dementia (FH)	2 (8)	8 (32)	1	0 (0)	3 (12)	0 (0)
RH/NH/dementia (WG)	0 (0)	7(37)	10	2 (11)	2 (11)	1 (0.2)
RH/NH/dementia (ME)	6 (18)	13 (38)	85	1(3)	5 (15)	11 (1.8)
RH/NH/dementia (WF)	7 (26)	8(30)	7	0 (0)	3 (11)	0 (0)
RH/NH/dementia(HC)	18 (20)	23 (25)	86	0 (0)	7 (8)	12 (1.9)
Adult disability (A)	2 (12)	0(0)	2	0 (0)	3 (18)	7 (1.1)
RH/NH/ADD (VC)	8 (32)	8 (32)	33	0 (0)	3	7 (1.1)
RH/dementia (OR)	8 (23)	17(49)	20	2 (6)	12 (34)	7 (1.1)
RH/NH/dementia (W)	6 (17)	7(20)	22	0 (0)	7 (20)	4 (0.6)
RH/NH/dementia (G)	5 (14)	10(37)	7	1 (3)	4 (11)	9 (1.5)
RH/dementia (TMGH)	3 (14)	2(9)	13	0 (0)	1(5)	5 (0.8)
RH/NH/dementia (EL)	1 (2)	9(22)	19	0 (0)	4 (10)	0 (0)
Dementia (SJ)	3 (9)	3(9)	1	0 (0)	0 (0)	2 (0.3)
RH/dementia (GRH)	1 (3)	9(24)	6	0 (0)	9 (24)	12 (1.9)
RH/NH/dementia (WLC)	6 (15)	6 (15)	6	0 (0)	4 (10)	17 (2.8)
Total	94	165	325	10	88	103

*As a percentage of the care home population on recruitment; ☨ 12 months prior to the study (past history of falls). RH= residential home, NH= nursing home, ADD= adult learning disability/dementia. The initials represent the names of the care homes

Interpretation

Table 36 shows that there was a reduction in the number of fallers following institutionalisation (165 vs. 94) but there were increase in the numbers of fractures (88 vs 103).

5.4.4 Association of the Covariates in the Tools with Falls, Fractures, Combined Falls & Fractures

The prediction of falls, fractures and combined falls and fractures is shown in table 37. The statistically significant associations were, for falls: Parkinson`s disease OR 5.628, p=0.017, history of falls OR 1.949, p=0.041, age OR 1.025, p=0.030, body weight OR 0.982, p=0.008, body mass index OR 0.952, p=0.015, alcohol OR 0.000, p=0.016; for fractures and combined falls and fractures: age OR 1.072, p=0.041, body weight OR 0.952, p=0.019 and body mass index OR 0.868, p=0.024.

Summary: For falls, Parkinson`s disease, history of falls, age, body weight, body mass index and alcohol use were the significant predictors. The effect size for a unit increase of the predictor were, for falls: Parkinson`s disease (5.6 more), history of falls (2 times more), age (1.025 times more), BMI (1.1 times less), body weight (1.01 less), history of alcohol (the effect size could not be determined).

For fractures, body weight and body mass index were the significant predictors. The effect size for a unit increase of the predictor was BMI (1.2 times less), body weight (1.1 less). Similar ORs were obtained for combined falls and fractures as for fractures. For the three outcomes, body weight and body mass index were the only significant predictors but the associations were weak. The effect sizes were higher for fractures, combined falls and fractures than for falls.

Table 37: Odds ratios of the binary logistic models of the predictors and outcome

Predictors	**Unadjusted OR for the prediction of falls (p)**	**Unadjusted OR for the prediction of fractures (p)**	**Unadjusted OR for the prediction of combined falls and fractures (p)**
Age	**1.025** (**.030**)	**1.072 (.041**)	**1.072 (.041**)
Sex	1.176 (.564)	0.680 (.577)	0.680 9.577)
Body weight	**0.982 (.008)**	**0.952(.019)**	**0.952 (.019)**
Body height	0.981(.254)	0.987(.745)	0.987 (.745)
Body mass index	**0.952 (.015)**	**0.868 (.024)**	**0.868 (.024)**
Previous fractures	1.218 (.484)	2.586 (.146)	2.586 (.146)
Parental fractures	0.764 (.550)	1.242(.846)	1.242 (.846)
Current smoking	0.819 (.691)	2.984 (.233)	2.984 (.233)
Alcohol	**0.000(.016)**	0.000 (.490)	0.000 (.490)
Glucocorticoids	0.513 (.423)	0.000 (.412)	0.000 (.412)
Rheumatoid arthritis	0.764(.195**)**	0.000 (.758)	0.000 (.758)
Secondary Osteoporosis	2.652 (.411)	0.000 (.593)	0.000 (.593)
Diabetes	0.786 (.181)	0.677 (.425)	0.677 (.425)
Type of care home	0.653 (.236)	0.479 (.481)	0.479 (.481)
History of falls	**1.949(.041)**	3.097 (.223)	3.097 (.223)
Dementia	0.880 (.667)	1.490 (.553)	1.490 (.553)
Cancer	1.481 (.341)	0.774 (.805)	0.774 (.805)
Asthma	0.694 (.487)	3.200 (.208)	3.200 (.208)
Cardiovascular illness	0.907 (.760)	2.150 (.265)	2.150 (.265)
Chronic liver disease	4.022 (.194)	7.556(.151)	7.556 (.151)
Chronic kidney disease	1.051 (.920)	0.000 (.183)	0.000 (.183)
Parkinson`s disease	**5.628 (.017)**	2.444(.465)	2.444(.465)
Malabsorption	1.315 (.786)	0.000 (.537)	0.000 (.663)
Endocrine problems	1.312 (.849)	0.000 (.663)	0.000 (.663)
Epilepsy	1.170 (.691)	0.682 (.708)	0.682 (.708)
Taking antidepressants	0.892 (.698)	0.511 (.376)	0.511 (.663)
Taking oestrogen HRT	0.000(.131)	0.000 (.663)	0.000 (.663)

p= level of statistical significance. Significant odds ratios are given in bold. HRT: hormone replacement therapy.

Interpretation

Table 37 shows that the predictors that demonstrated statistically significant associations with falls were age, body weight, BMI, alcohol consumption, prior history of falls and Parkinson`s disease. Of these, Parkinson`s disease had the highest odds ratio. For fractures and combined falls & fractures; they were age, body weight and BMI. Body weight and BMI were the only predictors that had statistically significant association with all three outcomes.

5.4.5 Comparison of the Subgroups of Participants

Table 38 shows the comparison of the three subgroups of participants (Group 1: No falls or fractures, Group 2: Falls but no fractures, Group 3: Falls and fractures). It is divided into 4 sections, (A) demographic characteristics, (B) fragility fracture risk factors, (C) number of comorbidities, and (D) fagility fracture risk assessment scores.

Comparison of demographic characteristics

Demographic characteristics for each of the three groups are shown in table 38 A. The mean ages of the groups ranged from 78 to 88 years. Fallers were significantly older than non-fallers. Patients who fell and fractured were non-significantly older than those with falls alone. Most were female (58-70%), all were Caucasians, and the majority (lived in residential settings (79-90%), with no significant diffences between gourps for any of these. When the three groups were compared simultaneously using the Bonferrani correction, there were no differences between the groups.

Comparison of risk factors for fragility fractures

Risk factors for fragility fractures for each of the three groups are shown in table 38 B. Fallers had significantly lower body weight compared with non-fallers (mean.65.4 vs 72.8 kg, p=0.017). Participants with falls and fratures had even lower weight (mean 55.5 kg). This was statistically significant in comparison with those who neither fell nor fractured, but not in comparison with fallers. There was a significantly higher incidence of Parkinson's disease in fallers than in non fallers (8.3 vs 1.6%, p=0.025). There was no significant difference in any of the other risk factors for fragility fractures between the three groups. When the three groups were compared simultaneously using the Bonferrani correction (p=0.017), the only statistically significant risk factor was body weight (p=0.017, 0.014).

Comparison of comorbidities for fragility fractures

Number of comorbidities for each group are shown in table 38C. They ranged from 0 to 10 and over. The majority (99.5% [21/217]) of the participants had multimorbidities (2 or more long term health conditions) and there were no significant differences between the groups.

Comparison of the scores for the tools

The mean scores of the tools are shown in table 38D. There were no differences between groups with FRAX and Garvan nomogram. There were statistical diffences in the QFractureScores between the no fall no fracture and the combined fall and fracture groups (53.8 vs 33.5, p= 0.020). There were statistical differences in the BMI between no fall no fracture and the fall no fracture groups (25.3 vs 23.2, p=0.042 and the no fall no fracture and the combined fall and fracture groups (25.3 vs 20, p=0.021). There was statistical diffence in TUGT between no fall no fracture and fall no fracture groups (40.9 vs 27.3, p=0.002). When the three groups were compared simultaneously, the only statistically significant tool was the TUGT (p=0.002).

.

Table 38 A: Demographic and clinical characteristics of the three subgroups and their comparison: demographic characteristics

Variable	Statistical method	(Group 1) No falls or fractures	(Group 2) Falls & no fracture	(Group 3) Falls & fractures	Comparison Groups 1&2 p value	Comparison Groups 1&3 p value	Comparison Groups 2&3 p value
Age (y), mean(SD)	FET	79.5(13.3)	82.9 (11.3)	88.1(17.2)	**0.053**	**0.046**	0.161
Sex, female ,n (%)	FET	78 (63.6)	49 (58.3)	7 (70)	0.471	1.000	0.735
Ethnicity: Caucasian, n (%)	NA	123 (100)	84 (100)	10 (100)	NA	NA	NA
Setting: Residential, n (%)	FET	97 (78.9)	71 (84.5)	9 (90)	0.367	0.400	1.000

Significant p-values are given in bold.

Interpretation

Table 38A shows that the age range of the participants was from 79.5 to 88.1 years. Those who had no fall or fractures were the youngest and the participants who fell and fractured were the oldest; those who fell but had no fracture were in between. There were statistically significant differences in the mean ages between the groups. In all three groups, females were in the majority. All the participants were Caucasians and the majority of the participants in each group were cared for in residential settings.

Table 38 B: Demographic and clinical characteristics of the three subgroups and their comparison: demographic characteristics: fragility fracture risk factors

Variable	Statistical method	(Group 1) No falls or fractures	(Group 2) Falls & no fracture	(Group 3) Falls & fractures	Comparison Groups 1&2 p value	Comparison Groups 1&3 p value	Comparison Groups 2&3 p value
Current smoking n, (%)	FET	11 (8.9)	5 (6)	2 (20)	0.598	0.253	0.160
Alcohol≥ 3 units/day, n (%)	FET	5 (4.1)	0 (0)	0 (0)	0.082	1.000	--
Weight (kg) mean(SD)	STT	72.8 (21.7)	65.4 (21.8)	55.5 (10.1)	**0.017**	**0.014**	0.160
Height (cm) mean (SD)	STT	168.3 (8.1)	167 (7.8)	167 (8.4)	0.225	0.602	0.093
Prior fall, n (%)	FET	86 (69.9)	68 (81)	9 (90)	0.078	0.280	0.683
Prior fracture, n (%)	FET	44 (35.8)	32 (38.1)	6 (60)	0.770	0.176	0.306
Parental fracture, n (%)	FET	8 (6.5)	7 (8.3)	1 (10)	0.786	0.516	1.000
Secondary osteoporosis,n (%)	FET	1 (0.8)	2 (2.4)	0 (0)	0.567	1.000	1.000
Diabetes mellitus, n (%)	PCS	28 (22.7)	13 (15.5)	1 (10)	0.280	0.631	1.000
Dementia,n (%)	FET	40 (32.5)	24 (28.6)	4 (40)	0.646	0.730	0.478
Cancer,n (%)	FET	13 (10.6)	13 (15.5)	1 (10)	0.393	1.000	1.000
Asthma/COPD,n (%)	FET	11(8.9)	4 (4.8)	2 (20)	0.290	0.253	0.122
Cardiovascular disease,n (%)	FET	31 (25.2)	18 (21.4)	4 (40)	0.618	0.454	0.236
Chronic liver disease,n (%)	FET	1 (0.8)	2 (2.4)	1 (10)	0.567	0.145	0.289
Chronic kidney disease,n (%)	FET	10 (8.1)	8 (9.5)	0 (0)	0.727	0.348	0.392
Parkinson`s disease,n (%)	FET	2 (1.6)	7 (8.3)	1 (10)	**0.025**	0.210	1.000
Malabsorption,n (%)	FET	2 (1.6)	2 (2.4)	0 (0)	1.000	1.000	1.000
Other endocrine disease,n (%)	FET	1 (0.8)	1 (1.2)	0 (0)	1.000	1.000	1.000
Epilepsy,n (%)	FET	16 (13)	13 (15.5)	1 (10)	0.685	1.000	1.000
Oral steroids,n (%)	FET	5 (4.1)	2 (2.4)	0 (0)	0.703	1.000	1.000
Antidepressant,n (%)	FET	41 (33.3)	27 (32.1)	2 (20)	0.881	0.499	0.719
HRT,n (%)	FET	2 (1.6)	0 (0)	0 (0)	0.515	1.000	1.000

Significant p-values are given in bold.

Interpretation: Table 38B shows that the only significant risk factors between the groups were body weight and the presence of Parkinson`s disease. The participant who had no fall or fractures had the highest weight followed by the participants who fell but had no fracture and the participants who had combined falls and fractures had the lowest weight. Parkinson`s disease was commonest in the participants who fell but had no fractures.

Table 38 C: Demographic and clinical characteristics of the three subgroups and their comparison: comorbidities

	Statistical method	**(Group 1) No falls or fractures n (%)**	**(Group 2) Falls & no fracture n (%)**	**(Group 3) Falls & fractures n (%)**	**Comparison Groups 1&2 p value**	**Comparison Groups 1&3 p value**	**Comparison Groups 2&3 p value**
No of comorbidities							
0		1 (0.8)	0 (0)	0 (0)			
1		17 (13.8)	14 (16.7)	1 (10)			
2		29 (23.6)	16 (19)	4 (40)			
3		24 (19.5)	20 (23.8)	2 (20)			
4		23 (18.7)	14 (16.7)	0 (0)			
5	PCS	17 (13.8)	8 (9.5)	0 (20)	0.782	0.924	0.734
6		8 (6.5)	8 (9.5)	0 (10)			
7		1 (0.8)	2 (2.4)	0 (0)			
8		2 (1.6)	1 (1.2)	0 (0)			
9		1 (0.8)	0 (0)	0 (0)			
≥ 10		0 (0)	1 (1.2)	0 (0)			
Charlson comorbidity score mean (SD)	STT	30 (19.1)	31.3 (23.2)	33.1 (20.7)	0.655	0.624	0.817

Interpretation: Table 38C shows that multimorbidity (presence of 2 or more long-term health conditions) was present in all three groups but there were no statistical differences between groups. The range of the mean Charlson Comorbidity Index was from 30 to 33.1 and there were no statistical differences between the groups.

Table 38 D: Demographic and clinical characteristics of the three subgroups and their comparison: Fagility fracture risk assessment scores

No of comorbidities	**Statistical method**	**(Group 1) No falls or fractures n (%)**	**(Group 2) Falls & no fracture n (%)**	**(Group 3) Falls & fractures n (%)**	**Comparison Groups 1&2 p value**	**Comparison Groups 1&3 p value**	**Comparison Groups 2&3 p value**
FRAX score mean (SD)	STT	19.1 (12.3)	19.6 (10.8)	23 (17.5)	0.754	0.280	0.305
BMI mean (SD)	STT	25.3 (7.1)	23.2 (7.3)	20.0 (3.4)	**0.042**	**0.021**	0.170
QFractureScores mean (SD)	STT	33.5 (25.8)	36.9 (26.4)	53.8 (30.1)	0.357	**0.020**	0.063
Garvan nomogram score mean (SD)	STT	38.3 (27.3)	45.8 (27.8)	58.7 (27.2)	0.055	**0.025**	0.169
TUGT mean (SD)	STT	27.3 (15.8)	40.9 (28.8)	32.7 (14.4)	**0.002**	0.398	0.463

Significant p-values are given in bold

Interpretation

Table 38D shows that the mean scores of the participants in the groups were different. The scores for FRAX and Garvan nomogram were not statistically different. The mean BMI were statistically different; no fall no fracture group had the highest weight and the combined falls and fracture the lowest. The mean QFractureScores was statistically different; the combined fall and fracture group had higher scores compared to no fall no fracture group. The mean TUGT duration was statistically different between the fall no fracture group and the no fall no fracture group.

n= number
NA= Not applicable
HRT= Hormone replacement therapy
SD= Standard deviation
TUGT=Timed Up &Go Test.
STT=Student`s t-test
FET=Fisher’s Exact Test
PCS=Pearson Chi Square

5.4.6 Distribution of BMI in the Subgroups of Participants

The rationale was to explore the distribution of BMI in the three groups.

The box and plot chart of BMI is shown in figure 7. `No falls and no fracture` chart represents the distribution of the participants in group 1. The minimum BMI was 14 kg/m² and the maximum was 42 kg/m². The lower quartile was 20 kg/m² and the upper quartile was 29 kg/m². The interquartile range was 9. The median was 24 kg/m² and there were four outliers above the upper quartile. These observations were classified as outliers because they were outside the `1.5 X IQR rule` (Khan Academy, 2018).

`Fall but no fracture` chart represents the distribution of BMI in the participants in group two. The minimum BMI was 13 kg/m² and the maximum was 38 kg/m². The lower quartile was 17.8 kg/m² and the upper quartile was 26.6 kg/m². The interquartile range was 8.8. The median was 21.2 kg/m² and there was one outlier above the upper quartile (Khan Academy, 2018).

`Fall and fracture` chart represents the distribution of BMI in group three. The minimum BMI was 14 kg/m² and the maximum was 25.4 kg/m². The lower quartile was 18 kg/m² and the upper quartile was 23.3 kg/m². The interquartile range was 5.3. The median was 19.9 kg/m² and there were no outliers.

Summary

The distributions of the participants in group one shows that the majority of the participants were either normal or overweight, a few were underweight, obese and morbidly obese. The median was at the upper half of the normal range (20-25 kg/m²). There were four outliers and these participants were morbidly obese. In group two, the majority of the participants were underweight, normal and overweight, a few were underweight and obese. The median was at

the lower half of the normal range. There was one outlier and this participant was morbidly obese. The majority of the participants in group three were in the lower half of the normal range, a few were underweight. The median was below the normal range.

The majority of the participants in groups one and two were more dispersed around the median compared to group three where they were more compact. Thus, the majority of the participants in group one appeared to be well nourished, those in group three were malnourished and those in group two were in-between if BMI is used as surrogate for assessing nutritional status.

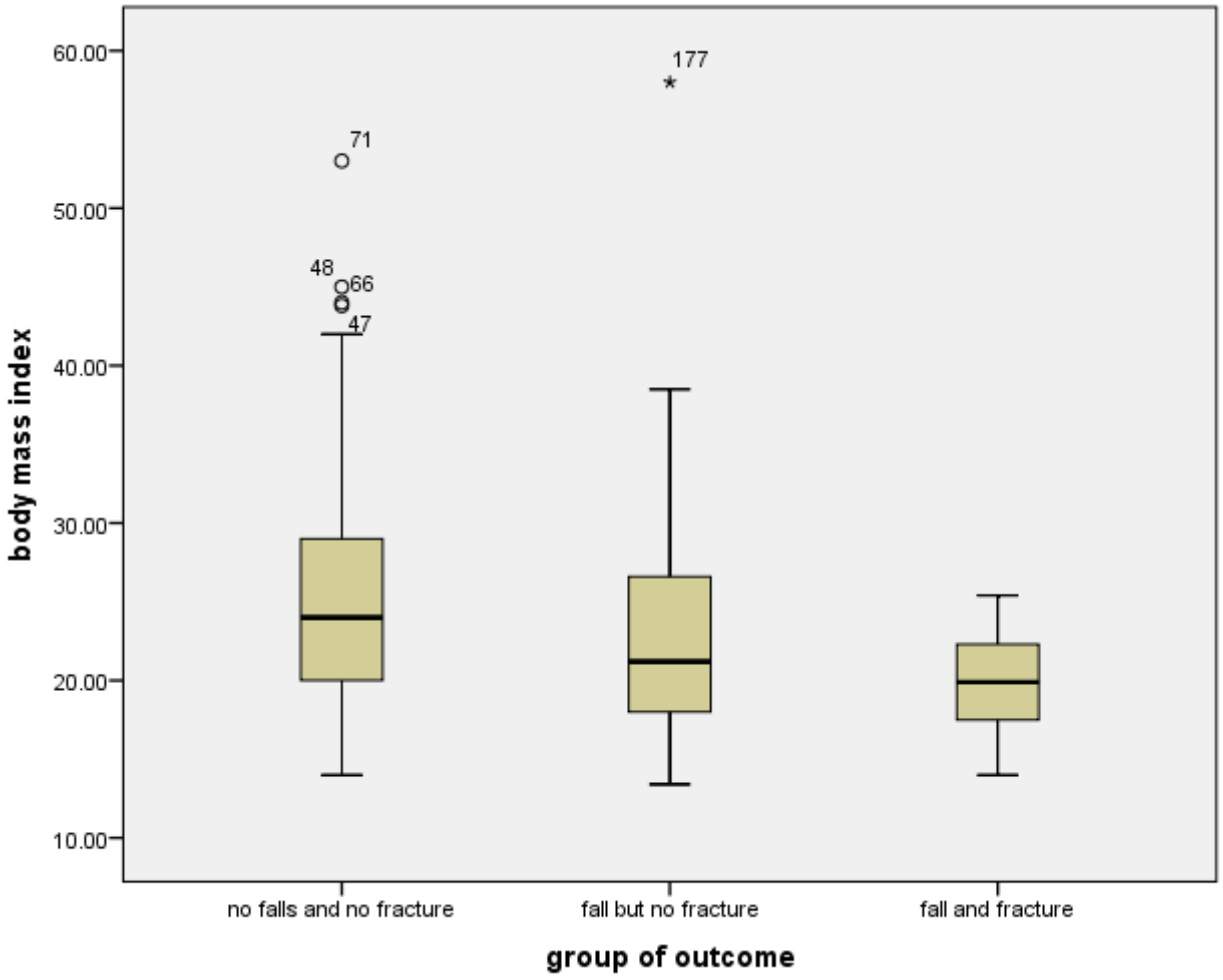


Figure 7: Box plot of the BMI of the three subgroups

Interpretation

Figure 7 shows that the distribution of BMI in the three subgroups was different. The median of the no fall no fracture group was the highest, the interquartile range was also the highest. The combined falls & fracture group had the lowest median and interquartile range. This suggests that the combined fall & fracture group was the most frail and least nourished of the three. No fall, no fracture group had 4 outliers, fall no fracture group had 1 outlier and combined fall & fracture had no outlier.

5.4.7 Mortality

Fifty- four participants (25%) died during the 12 months of follow-up.

Interpretation: The mortality of the participant was high when compared to community dwelling older people. It was not clear if the deaths were related to incident fractures.

5.4.8 Charlson Co-morbidity Index (CCI)

The mean Charlson Comorbidity Index was 30.6% (SD 20.7) for all the participants and 36% (SD 21.1) in those who died. For the participants who died, the statistics of using a CCI threshold of ≥ 36% were as follows;

1st quartile 28%

2nd quartile (median) 26%

3rd quartile 54%

Interquartile range 26

Minimum – maximum range 12 – 85 %

Sensitivity = 29 %

Specificity 77%

CCI prediction of outcome (alive/dead) R^2 (coefficient of determination)]= 0.021 (p=0.034) (normal range 0 – 1)

When the CCI threshold was increased to ≥ 85%, the sensitivity and specificity for prediction of death were 30 and 77 % respectively

Summary: During the 12 months of study, the mean Charlson Comorbidity Index did not indicate high risk of death in the participants. The mean score was higher in those who died. However the sensitivity was not good. At higher CCI of 85% the sensitivity and specificity did not change remarkably.

5.4.9 Duration of Recruitment

The median duration for recruitment including information giving, consent, and baseline assessment was 10 days (minimum to maximum range 1 - 299). The longest recruitment duration of 299 days was a lone outlier which was caused by the late return of the consultee form.

Summary: The recruitment process was very time consuming with long periods of time between identifying a patient and obtaining consent**.** The recruitment duration for each participant was considerable.

5.5 Discussion

The main findings from the exploratory analyses are:

- Falls were common in the care home residents but fractures were less common.
- All the fractures in the participants resulted from falls.
- Falls and fractures were commonest in the facilities that catered for the participants with dementia. 40% of the fractures occurred in the participants with dementia.
- There was reduction in falls following institutionalisation but fractures increased.
- The significant predictors of falls were: Parkinson's disease (OR 5.628), history of prior falls (OR 1.949), age (OR 1.025), BMI (OR 0.952), body weight (OR 0.982) and alcohol use (OR 0.000).
- The significant predictors of fractures, falls and fractures combined were: age (OR 1.072), body weight (OR 0.952) and BMI (OR 0.868).
- The Bonferroni correction showed that the significant differences between the three subgroups were the body weight and the TUGT.

- The mortality of the participants was considerable, 25% died in the 12 months of follow-up.
- The recruitment duration for each participant was considerable, the median was 10 days.

The discussion that follows will compare these findings with published articles.

5.5.1 Falls and Fractures in the Residents and Participants

The results show that the incidence of falls and fractures in care homes in Boston were 2.7 and 0.2 per resident year respectively. Given that the falls data was not obtained from two care homes, the overall incidences were probably higher. The corresponding incidences were 1.5 falls and 0.05 fractures per participant per year.

Previous studies have shown that falls are common in the elderly population. About 30% experience a fall annually, this risk increases after the age of 75 with 50% of elderly people over the age of 80 years having at least one fall every year. Fall incidence in care home facilities are reported to be about three times that in the community, equating to 1.5 falls/per bed per year (Luukinen et al., 1994, Rubenstein, Josephson & Robbins, 1994) or 1.4 falls per person per year (Nurmi, Luthje, 2002). The Centers for Disease Control reported a higher incidence of 2.6 per person per year (Centers for Disease Control and Prevention, 2012). The results from this study are comparable to the CDC and higher than the earlier studies. This may be related to differences in research methodologies or an increasing propensity to fall in an ageing population (Tinetti, Williams, 1997, Downton, Andrews, 1991).

There were ten incident fractures in the participants and all of them resulted from falls which shows that falls are important causes of fractures. This is consistent with previous publications

that over 90% of hip fractures and over 87% of all fractures in older people result from falls (Grisso et al., 1991, Melton, 1993). Various incidences of fractures in care homes have been reported. Ytterstad reported 70 per 1000 person years (Ytterstad, 1999) while Kane reported 35 per 1000 person years for all long bone fractures (Kane, Burns & Goodwin, 1995). These incidences could not be compared with data from this pilot study because of the different metrics of reporting.

There were at least 1,671 incident falls but only 103 incident fractures in the residents that is, a complication rate of 6%; in the participants there were 325 falls and only 10 incident fractures that is, a complication rate of 3%. This shows that in this cohort, fractures were uncommon complication of falls. Previous publications have reported that only about 5% of falls result in fractures (Tinetti, Speechley & Ginter, 1988, Campbell et al., 1981, Lord, Mclean & Stathers, 1992), although a systematic review showed that the complication rate was higher at between 10 and 20% (Sterke et al., 2008).

5.5.2 Incidence of Falls and Fractures in each Care Home

The results show that incident falls occurred in most of the care homes which offered combined services. The crude incidence rates were variable but they were particularly high in a care home that catered exclusively for residents with dementia. The Alzheimer's Society report that people with dementia are four to five times more likely to fall than older people who do not have cognitive impairment (Alzheimer Society Manitoba, 2014). Van Dijk and colleagues (1993) reported 1,343 falls over a 2-year period in 240 patients with dementia (Vandijk et al., 1993). Another study found that dementia participants experienced nearly 8 times more incident falls than controls (Allan et al., 2009).

There were reductions in falls following admission to the care homes. There are some plausible explanations for this. First, falls assessments were undertaken on the participants during admission and appropriate personalized care was instituted (Department of Health, 2001). Second, falls and fractures were the reasons for the admission to the care home therefore some of the participants received one to one care and were therefore less likely to fall. The publicity given to risk assessments since the establishment of the Care Quality Commission (CQC) in 2009 followed by the personalised care makes the second proposition more likely. Although this hypothesis is speculative, it is supported by a publication that falls prevention programmes which were introduced to new entrants in 300 nursing homes in Germany reduced the incidence of falls and fractures (Rapp et al., 2008).

Since 2003, given the well recognised association of vitamin D and musculoskeletal health and the high prevalence of calcium and vitamin D deficiency in care home residents and the reduction of hip fracture rates following supplementation (Chapuy et al., 1992), I wrote to all GPs in North Lincolnshire to prescribe calcium and vitamin D for care home residents, if appropriate. Since April 2015, low level prevention of falls has formed part of Lincolnshire`s Wellbeing Service (Lincolnshire County Council 2015). The Wellbeing Service provides a range of interventions and community based support to promote confidence in living independently. Preventing and reducing the incidence of falls is a key challenge for organisations and is a top priority of Commissioners, Providers and Voluntary Services in Lincolnshire. For example the North East Lincolnshire Falls Prevention Collaborative was formed in 2005 to address the issue of falls in this area. They are a group of specially trained community volunteers who provide advice and information on how to prevent and reduce falls amongst the elderly working alongside health professionals, police, local authorities and local organisations.(Leary 2005).

Although all the care homes in this study undertook falls risk assessment, 72% used their own risk tool, and 27% used generic falls tools. In other words there was no uniformity in the types of tool which were used. The falls risk assessment tools currently used for the elderly do not show sufficiently high predictive validity for differentiating high and low risk fall risk (Park, 2017) and it was noticeable that no care home used the TUGT or the 180 degree turn tests which are recommended by NICE (NICE, 2013).

The standard of documentation in the care homes was inconsistent in this study. Oygard et al also observed that there were significant differences between the nursing homes in how frequently an injury report form was completed (Oygard et al., 2017). The causes for the variations may be related to education, experience of the care home staff, poor labour force, pragmatism of falls risk tool and the fear of litigation or negligence. Accurate documentation is important for data analysis and implementation of preventive strategies.

Accurate and timely documentation ensure that people who are at increased risk are identified and appropriate interventions implemented. It is recommended that this risk assessment is carried out for all patients over the age of 65 years. This should take place no later than 24 hours after admission, or after the first meeting with the patient. Fall assessment must be conducted by a nurse or healthcare worker and be re-assessed if the patient`s general level of fitness changes or if the patient has a fall, or at least once a year for any long-stay patient.

5.5.3 Association of the Covariates in the Tools with the Outcomes

Binary logistic regression analyses showed that for falls, Parkinson`s disease (OR 5.625, p=0.017), history of prior falls (OR 1.949, p=0.041), age (OR 1.025, p=0.030), body mass index (OR 0.952, p=0.015), body weight (OR 0.982, p=0.008) and history of alcohol use (OR 0.000, p=0.016) were the predictors, for fractures and combined falls and fractures, age (OR

1.072, p=0.041) body weight (OR 0.952, p=0.019) and BMI (OR 0.865, p=0.024) were the predictors. Body weight and BMI were the only predictors for all the three outcomes but the effect size were small.

A systematic review and meta-analysis of falls risk factors in nursing home residents and hospitals found the strongest associations were: history of falls (OR 3.06), walking aid use (OR 2.08) and moderate disability (OR 2.08) for the nursing home cohort (Deandrea et al., 2013). In a prospective study of 18,855 care home residents in 272 nursing homes, Kiely et al also found that the most important predictor was a history of falls (Kiely et al., 1998). They found that residents with a fall history were three times more likely to fall during the follow-up period than residents without such a history. The other independent risk factors that they found were: wandering behaviour, use of a cane or walker, deterioration in activities of daily living performance, age greater than 87 years, unsteady gait, independence in performing transfers, not requiring a wheelchair and male gender. The definition of what constitute a care home was not clear from the publications. The participants in this pilot study were partly from residential homes (81%) and partly from nursing homes (19%). Nursing home residents are generally frailer and more dependent and the type of care is strongly related to functional impairment particularly mobility (Fried, Guralnik, 1997).

For fractures, a systematic review and meta-analysis of fracture risk factors in care home residents identified prior fractures, female gender, low BMI, older age, low BMD, glucocorticoid use, rheumatoid arthritis, cognitive impairment, mobility and history of falls (Khatib et al., 2014). There were few incident fractures in this study during the relatively short duration of 12 months which may explain the differences. Before a new treatment for osteoporosis can be approved, the European Medicine Agency (EMA) recommends that

placebo-controlled trials be conducted for a minimum period of 2 years (European Medicines Agency (EMA), 2006).

5.5.4 Comparison of the Groups

The significant differences between fallers and non-fallers were: older age, low body weight, BMI, alcohol use and Parkinson`s disease.

The participants who had falls were significantly older (mean age 82.9 years) than those who did not (mean age 79.5 years). Older age has been identified as a risk factor for falls in many studies. The proportion of falls in people who are 75 years and older has been reported to be between 32 and 42 % in community dwelling people (Downton, Andrews, 1991, Tinetti, Speechley & Ginter, 1988). Both Luukinen et al and Rubenstein et al reported falls incidence rate of 1.5 falls per bed per year (Luukinen et al., 1994, Rubenstein, Josephson & Robbins, 1994) or 1.4 falls per person per year in care home residents (Nurmi, Luthje, 2002). Kiely et al reported a threshold of 87 years and older as a falls risk factor in nursing home residents (Kiely et al., 1998) but a systematic review and meta-analysis did not (Deandrea et al., 2013). The differences may be due to inconsistences in research methodologies and the different definitions of what constitute a fall. It was not 2005 until that a universal definition was adopted (Lamb SE et al 2005).

Low body weight and body mass index were significantly associated with falls in this study but the associations were weak. No fall no fracture group had BMI of between 20 and 28 kg/m², fall no fracture group , 19 to 26 kg/m² and fall & fracture group between 18 and 22 kg/m². But this data did not give clarity to the exact thresholds at which falls occur. There was a dearth of publication for comparison. One study in a cohort of 1377 community-dwelling

people in Northern Taiwan did not show that body weight and body mass index were significant risk factors for falls (Lin, Liao & Pu, 2011). However, the mean age of the participants in that study was 74.9 ± 6.8 years, of which 48.9% were females.

Parkinson`s disease was more common in the participants who fell compared to those that did not (8.3% vs 1.6%, p= 0.025). A large study which compared the fall incidence of 28,280 Parkinson`s disease patients with 28,280 matched non-Parkinson`s patients, found an overall adjusted incidence rate ratio was 2.05 (95% CI 1.88 - 2.24) (Kalilani et al., 2016). A systematic review and meta-analysis also found that Parkinson`s disease had a strong association with falls (OR 2.7; 2.8) (Deandrea et al., 2010). Parkinson`s disease captures some of the causes of falls such as gait and balance abnormalities (Youn et al., 2017, Kerr et al., 2010, Bloem et al., 2004) but the frequency of falls declines in the late stages because of the patient`s immobility (Bloem, van Vugt & Beckley, 1999).

For fractures, the significant differences between those who sustained fractures and those who did not were age, body weight and BMI. The mean age of the participants in the fracture group was 88 years. Many studies have shown that increasing age is associated with higher fracture risk (Kanis et al., 2001, Hui, Slemenda & Johnston, 1998). Old age is associated with lower BMD in both sexes and all races. Age has a particularly strong relationship with hip fracture risk. From the known relationship there is approximately a 4-fold increase in hip fracture risk between the age of 55 and 85 years in women because of the age-related decrease in BMD. In practice, the incidence in many countries is much higher than this (Kanis et al., 2001). Using DEXA scan at the femoral neck to predict hip fracture risk, at 50 years, the 10-year hip fracture probability is approximately 2% in women but at the age of 80 years, it is 12% for the same T-score. This indicates that age has some other effects on fracture risk independently of BMD.

However, one study of 1414 ambulant women in residential homes in Yorkshire, England found that the mean age of participants who sustained hip fracture was not significantly different from those that did not (85.3 years vs 83.9 years, p=0.07) but the mean broad band ultrasonic attenuation (BUA, a non-invasive radiation free assessment of skeletal structures) index and score for cognisance for the group that had incident fractures were significantly lower compared to women who did not (Porter et al., 1990). The participants who sustained fractures were significantly more mobile. Generally, residents who are more mobile by default expose themselves to more risky situations that result in falls. This explanation is supported by Chandler et al who reported independence in transfer to be a significant predictor of osteoporotic fractures in female nursing home residents (Chandler et al., 2000).

In this pilot study, the participants who had falls or combined falls and fractures had significantly lower body weight compared to the participants who did not fall (mean 65.4 and 55.5kg vs 72.8kg, p=0.011, 0.009) respectively and similar differences were observed for BMI (23.2 and 20 kg/m² vs 25.3 kg/m², p=0.042, 0.021). There were no statistical differences in mean height between the groups (167cm, 167 vs 168.4 cm p= 0.504, 0.891) suggesting that the differences in body weight were responsible for the differences observed.

Low body weight or low BMI is a reported risk factor for fractures whereas high BMI appears to be protective (Cummings, Black, 1995, Honkanen et al., 2000, Joakimsen et al., 1998, Turner, Faile & Tomlinson, 1999, van der Voort, Geusens & Dinant, 2001). But one meta-analysis showed that being underweight had no significant effect on the risk of fracture in men (RR; 0.89, 95% CI; 0.53-1.49, p=0.658) and women (RR; 0.98, 95% CI: 0.79-1.20, p=0.816) in BMD-adjusted studies. However, when the results were not adjusted for BMD, being underweight increased the risk of fracture in men (RR: 1.89, 95%CI 1.18-3.15, p=0.009) and women (RR: 1.51, 95%CI 1.35-1.68; p=<0.001) (Xiang et al., 2017).

It is reported that in all age groups, low BMI is associated with all fragility fractures especially hip fractures but the risk ratio is not linear being markedly higher at lower BMI particularly of ≤20kg/m². By contrast between BMI of 25 and 35kg/m², the differences in the risk ratio are small. A study from Japan found that both underweight and overweight/obesity are risk factors for fractures at different sites. It was reported that underweight was associated with increased incidence of femoral neck and long bone fractures while overweight/obesity were associated with vertebral fractures (Tanaka et al., 2013). In many studies, BMI was chosen rather than weight to explore the association with fracture risk because of the variation in the average weight and height in different populations which is reduced by adjusting weight for height; also BMI is as good a predictor of fractures in most studies of hip fractures (Johnell et al., 1995, Kanis et al., 1999).

There were differences in the mean scores of FRAX, QFractureScores and Garvan nomogram. QFractureScores and Garvan nomogram were predictors of fractures not of falls and FRAX was not a predictor of any of the outcomes. The possible explanations for the differences have been discussed earlier. The TUGT scores were significantly different between no fall no fracture and fall no fracture groups (p=0.002) but not in no fall no fracture and fall & fracture groups (p=0.398) and 2 and 3 (p=0.463). This suggests that the TUGT was good at identifying fallers and non-fallers only. The mean duration for the test was 33.8 seconds which is much higher than the recommended threshold of 12 seconds (Bischoff et al., 2003) Ninety three (42.9%) participants could not undertake the test and of those who did, 83(38%) performed it with the assistance of walking aids. This indicates that the majority of the participants had significant problems with mobility.

A systematic review of falls risk assessment tools showed there is a lack of evidence regarding which assessment tool is most predictive of falls and therefore most useful (National Institute

for Health and Clinical Excellence (NICE), 2014). The National Institute for Health and Care Excellence (NICE) however suggested that the TUGT (Podsiadlo, Richardson, 1991) and the Turn 180˚ (Kobayashi, Usuda, 2016) are useful in primary care settings as no special equipment is required (NICE, 2013). It is recommended that the Turn 180˚ should not be used in patients who require a walking aid to turn and are not able to fully weight bear and who cannot follow instructions (National Institute for Health and Clinical Excellence (NICE), 2014). Therefore this model will not be useful for care home residents because most of them require assistance with mobility.

5.5.4.1 Fall Mechanics and Fractures

In this study, it was observed that there were no differences in characteristics between the fall no fracture group and the fall & fracture. What then determines the risk of fractures in people who fall? Cummings and Nevitt have propounded a hypothesis of how a fall could cause a fracture (Cummings, Nevitt, 1989). This was tested in two case-control studies: one was in the community (Nevitt et al 1993), the other was in a nursing home (Hayes et al., 1993) but much of the findings related to hip fractures in Caucasian women.

Bones break when the force applied to it exceeds its strength. Falls are the most common types of force involved in fractures. 80% of non-spine fractures are attributed to falls (Nevitt, Cummings, 1992b) but only 5% of falls in the elderly result in fractures of which 1% are hip fractures (Cummings, Nevitt, 1989, Nevitt, Cummings, 1992a, Tinetti, 1986). These suggest that the fall mechanics are important in the genesis of fractures. They postulated that for a fracture to occur, the faller must be orientated so that the point of impact is or is near the hip and that the protective responses (such as the strength of an outstretched hand) and shock

absorbers must also fail to reduce the energy to a level less than that required to break the proximal femur.

Falling onto the side of the leg or buttock near the greater trochanter was 20 to 30 times more likely to cause a hip fracture than falling onto other parts of the body. Falls that occur while turning were associated with hip fractures (Cummings-Vaughn, Gammack, 2011). One study in care home residents found an increased risk of hip fractures with falls to the side (OR 3.9, 1.3-11), low hip BMD (OR 1.8, 1.03-3.0) and impaired mobility (OR 6.4, 1.9-21.0) (Greenspan et al., 1998). Among women who landed near the greater trochanter during a fall, those who landed on outstretched hands or broke the energy of the fall by grabbing or hitting an object before hitting the floor had about a third risk of fracturing the hip compared with women who did not (Nevitt et al., 1993a). The reduced muscle strength and impaired reflexes in older people reduce the effectiveness of automatic protective responses that are necessary to break the energy of impact.

The energy of impact is the product of velocity and mass of an object. This implies that taller and heavier fallers would have greater risk of fracture. A fall from a standing height generates about 400 to 500 joules which is about 10 times the energy required to fracture the proximal femur of an elderly woman (Hayes et al., 1993, Hayes, Piazza & Zysset, 1991). The velocity of the impact depends on the height of the fall which means that the risk of hip fracture would increase as the distance from the greater trochanter to the floor increases.

Hayes and colleagures (1993) reported that each 9 centimetre increase in a person`s height would increase the risk of fracture by about 50%. Of people who fell on the hip, taller women had greater risk of fracture (1.5 fold increase in the odds ratio for a fracture for each SD increase in height i.e. 6 centimetres). To support this observation, a large prospective study

among middle aged women found that taller women (1.7 meters) had a much greater risk of hip fracture than shorter women (1.55 meters) (Meyer, Tverdal & Falch, 1993). This increased risk may also be accentuated by the longer hip axis in taller people (Faulkner et al., 1993). The mass of an object is the other determinant of the energy of impact.

In one community based study, there was a non-significant trend towards greater fracture risk among obese women who fell onto the hip after adjusting for other predictors of hip fracture (Nevitt et al., 1993b). Conversely larger body mass may be protective because it is accompanied by more padding of the greater trochanter thereby reducing fracture risk from trauma. Robinovitch et al estimated that a three-fold increase in trochanteric soft tissue in women reduces the fall impact force at the bone by about one-third (Robinovitch, Hayes & Mcmahon, 1991). Some studies have shown that wearing protective pads over the greater trochanter dramatically reduced the risk of hip fracture in nursing home residents (Lauritzen, Petersen & Lund, 1993, Parker, Gillespie & Gillespie, 2000).

The risk of fracture is also dependent on the amount and rate of energy that is transmitted to the bone by the texture of the surface of impact. Falling on a soft surface is less likely to cause a fracture than on a hard surface such as concrete. Nevitt and colleagues observed that after adjusting for the other predictors of hip fractures, women who fell on a hard surface were three times more likely to suffer hip fracture than those who landed on a soft surface; 11% of people who fell on hard surfaces sustained fractures (Nevitt et al., 1993a). This finding has implication for the kind of flooring that should be used in care homes.

Van Schooten et al observed that frequent fallers had a lower risk of injury per fall and they suggested that the circumstances of falls and the development of adaptive protective responses are possible explanations (van Schooten et al., 2017). In essence, the factors that determine

fractures from falls are: the energy generated by the fall, the protective responses which mitigate the potential energy and any factors that help to absorb the energy before it is delivered to the skeleton.

Bone strength provides the last resistance to fracture. There is an inverse relationship between the bone density (strength of bone) and the risk of fracture (Nevitt et al., 1993a). Bone strength is dependent on the geometry, mass and qualitative factors such as trabecular integrity and amount of fatigue fractures present. In this study the effect of BMI was more on fractures than falls (ORs 0.868 vs 0.952). The plausible explanation is the disproportionate reduction of bone strength because of the reduced mechanical loading from low BMI due to reduced mobility and multi-morbidities.

There is limited research on the mechanics of other types of fragility fractures. Almost all wrist fractures resulted from fall onto an outstretched hand (Nevitt et al., 1993a). Falling backwards or obliquely forward, landing on the hand and putting out the hand to break a fall are associated with increased fracture of the distal forearm (Nevitt et al., 1993a, Palvanen, Kannus & Parkkari, 2000). Falling obliquely forward or sideways, landing on a hard surface and especially on the shoulder is associated with 90% to 97% of proximal humerus fractures (Palvanen, Kannus & Parkkari, 2000, Keegan et al., 2004). Although most vertebral fractures are considered to be atraumatic, it is believed that common activities (lifting and bending) and body habitus (upper body weight and kyphosis) can substantially influence the forces applied to the vertebral body (Hayes, Piazza & Zysset, 1991).

Thus, the number of falls, type of fall and the strength of the bone appear to be the important determinants of fractures but these were not validated in this pilot study because that was not the aim.

5.5.5 Mortality

Fifty-four (24%) participants died during the 12 months of follow-up. This is comparable to the results of Shah and colleagues who found 12 month mortality of 26.2% of 2,558 residents (Shah et al., 2013). A large BUPA survey of 11,565 residents reported that half died by 462 days, around 27% lived for more than three years, with the longest stayer living for over 20 years. Residents had a 55% chance of living for the first year after admission, which increased to nearly 70% for the second year before falling back over subsequent years (Forder, Fernandez, 2011).

This data shows that care home residents have reduced life span and therefore relatively short window of opportunity for intervention. Thus, a prognostic model that accesses conditions in this cohort for over 2 years is unlikely to be useful clinically as most of the participants may be dead. Treatment decisions are often based on prognosis and the Charlson Comorbidity Index (CCI) score may be useful for this purpose. The mean scores for all the participants were 30.6% and 36% in those who died but there are no published data for comparison.

5.5.6 Duration for Recruitment

The median duration for the recruitment of each participant was 10 days, and for one participant who required Consultee consent, it was 299 days. There are no publications for comparison of the optimum duration for recruitment. Walters and colleagues observed that recruitment of participants was often slower or more difficult than expected and many trials fail to reach the planned sample size within the originally envisaged trial time scale (Walters et al., 2017). A long duration can have substantial impact on the number of participants who can be recruited, the numbers of investigators and therefore the feasibility of the study.

5.5.7 Strengths and Weaknesses of the Study

Strengths and weaknesses discussed below relate to the observational study (chapters 4 and 5).

5.5.7.1 Strengths

1. To my knowledge, this is the first study to evaluate the performances of four fragility risk assessment tools exclusively in care home residents simultaneously. The methodology was rigorous and it followed international guidelines.
2. The follow-up duration of 12 months is a strength given the relatively short life expectancy of care home residents. FRAX, Garvan nomogram estimate fracture probability in 10 years by which time many of the care home residents may be dead. QFractureScores assesses fracture probability annually for 10 years; in this context it is an advantage for care home residents.
3. The sample size of 217 participants was large for a feasibility study. Isaac and Hill suggested 10 to 30 participants for pilot studies (Isaac, Michael B, 1995, Hill, 1998); Julious and van Belle suggested 12 (Julious, 2005, van Belle, 2002), Treece and Treece suggested 10% of the project sample size (Treece, Treece, 1982). Therefore given the relatively large number of participants in this project, the data could be pooled into subsequent powered studies if type 1 and type 2 errors are controlled for.
4. All the 18 care homes in Boston participated in this study which included both sexes and residents of residential and nursing homes, therefore the results have the potential for greater generalisability.
5. There were no missing data therefore the inferences from the project are valid.

5.5.7.2 Weaknesses

1. Many residents who did not possess mental capacity and were at high risk of falling did not provide informed consent through Consultees therefore only a few (32%) of

them were recruited. More incident falls and fractures may have been recorded if a higher proportion of them had been recruited. For example of the 10 incident fractures, 4 (40%) occurred in this subgroup and given that the majority (54%) of the care home residents lacked mental capacity, the data are skewed. A possible solution to mitigate this limitation would be to improve staff education, to encourage people to develop interest in care home research and for the Government to set up schemes to achieve this. In addition, the Government could consider including in the Lasting Power of Attorney (LPA) application the question 'If you are admitted to a care home in the future, would you be willing to participate in research`? Research regulatory bodies such as the Health Research Authority (HRA) could modify some of the rules that govern participation in care home research without compromising the standards that breach research ethics. For example, the care manager could be authorised to be a proxy decision maker if the ethics committee considers the proposal to be non-invasive. Also, the waiver of consent adapted by the USA should be considered (Wichman, Sandler, 1997). This guidance recommends public consultation. In this regard, the theme for discussion should be waiver for observational studies. A futher method to facilitate research participation is to initiate the discussion with the next of kin at the point of admission to the care home. If it is felt that the resident would be willing to participate in future research, then the authority to consent could be delegated to the care home managers.

2. The study was not powered for any analysis therefore the inferences made may not be valid. Determining the optimal sample size for a study assures an adequate power to detect statistical significance and avoid making type 1 and type 11 errors (Jones, Carley & Harrison, 2004). A type 1 error is when the null hypothesis is incorrectly rejected and a type 11 error is when the alternative hypothesis is incorrectly accepted.

Using too many participants in a study is expensive and exposes more number of subjects to procedures. Similarly if a study is underpowered, it will be statistically inconclusive. Sample size is a function of three factors: the significance level, power and magnitude of the differences (effect size) (McCrum-Gardner, 2010). This study does provide data to inform fully powered studies.

3. While the study duration of 12 months may be considered a strength for study of falls (because it limits recall errors), paradoxically it is a weakness for a study on fragility fractures because of the relatively short duration which limits the number of incident fractures. Before a new treatment for osteoporosis can be approved, the European Medicine Agency (EMA) recommends that placebo-controlled trials be conducted for a minimum period of 2 years for studies when the primary outcome is BMD and 3 years when the principal criterion for efficacy is a demonstration of a clinically significant reduction in the number of patients with vertebral fractures (Committee for Proprietary Medicinal Product (CPMP), 2002).

4. There might have been misclassification bias because spine fractures could have been missed as X-rays of the spine were not done before or during the study. Approximately two-thirds of vertebral fractures are not associated with fracture-related back pain (Cooper et al., 1992, Kotowicz et al., 1994).

5. There might have been under-reporting of falls by care home staff because they were missed or due to malpractice. Nursing malpractice is a growing area (Boockvar, Lachs, 2002). The fear of malpractice litigation together with the importance placed on family anxieties may result in underreporting of incidents. It is more difficult to under report non-spine fractures because they are more obvious.

6. Despite explicit explanation of the exclusion criteria for this study (i.e. residents on end of life care and residents who are non-English speaking and interpreters are not available), some care home managers contacted only residents whom they felt could participate. Thus the selection of participants was not random and the inferences from the project may not be generalizable.

7. Interrater reliability of the individual components of the questionnaire and assessments were not done. This may have introduced experimenter bias in the scores of the tools.

Despite these limitations, this project has provided data for the development of an algorithm for fracture assessment for care home residents. This will be discussed in the next chapter.

5.5.8 Conclusions

The exploratory analyses showed that the fall incidence in this cohort was high and compares with published data. Incident fractures were not so common which also support epidemiological studies that most falls do not result in fractures and that most fractures result from falls. There were variations in the numbers of falls and fractures in the care homes. This indicates that the type of facility and residents has an influence on the occurrence of these incidents. There was reductions in falls but not fractures following institutionalisation.

The predictors that were significantly associated with falls, fractures, combined falls and fractures were older age, low body weight, low body mass index, history of alcohol use, history of prior falls and history of Parkinson`s disease. Although dementia did not feature as a significant predictor, it was interesting to note that of the 10 incident fractures, 40% occurred

in the participants with dementia despite the small representation of this group which suggest that it is an important risk factor for fractures.

The subgroup comparisons showed that the significant differences between the fallers and non-fallers were: fallers were older, had lower body weight, took more alcohol and had history of Parkinson`s disease compared to the non-fallers. For fractures, those who sustained incident fractures were older and had significantly lower body weight compared to those who did not have fractures.

The scores on the tools were different; the participants who had falls had longer TUGT and lower BMI compared to the participants who did not fall. Also the participants who had fallen and sustained fractures had lower BMI, higher QFractureScores and Garvan nomogram scores compared to those who did not fall but there were no significant differences in TUGT between the groups. There were no differences in the fallers who sustain fractures and those who did not.

The mortality of the participants was high given that 25% died during the 12 months of follow-up: the mean CCI index was higher in this group compared to the mean for all the participants.

Chapter 6 Discussion, Conclusions and Future Research

6.1 Introduction

Many tools exist for the assessment of fragility fracture risk in older persons but these were developed from community-based older people and it is not known if they can be used for care home residents. The overarching aim of this project was to identify fracture risk assessment tools which are practicable in care home residents and to determine which is most suitable for use in this population. This was addressed by a systematic literature review of fragility fracture risk assessment tools, development and testing of a questionnaire containing the predictors of fragility fractures, and conducting a pilot study compare the tools identified.

The systematic literature review identified thirty-three fragility tools of which four were practicable for care home residents. These were FRAX, QFractureScores, Garvan nomogram and BMI. Testing of the questionnaire developed from the tools in consultation with care home staff and residents led to refinements including increases in font size and addition of a consultee information sheet. The majority of the participants in the observational study had full mental capacity, which was not representative of the care home resident population as a whole, thus the data was skewed. The key finding was that all four fragility tools had poor screening performance. BMI was the best predictor of falls, fractures and combined falls and fractures but the associations were weak. QFractureScores was a predictor of falls and combined falls and fractures. Neither FRAX nor Garvan nomogram were predictors of these outcomes. Of the 10 incident fractures, 40% were observed in participants who had dementia despite the small representation of this group, thus dementia is a strong risk factor for fractures in this cohort.

The narrative that follows will summarise and discuss the findings of each results chapter, develop an algorithm for screening fracture risk in care home residents, discuss strengths and weaknesses and explore potential avenues for future research.

6.2. The Systematic Literature Review

The systematic literature review identified thirty-three tools, the majority of which were not externally validated. Four of these tools were potentially practicable for use in care home residents. These were FRAX, QFractureScores, Garvan nomogram and BMI. Two systematic reviews of fragility risk tools also identified these tools and noted that only few models were externally validated (Nayak et al., 2014, Rubin et al., 2013). FRAX, QFractureScores and Garvan nomogram estimate fracture risk over a period of between 5 and 10 years although QFractureScores has provision for annualised risk. BMI has not been calibrated.

The absolute risk of fracture depends upon the age and life expectancy as well as the current relative risk. Most care home residents are over 85 years and they have an average life expectancy of two and a half years (National Institute for Health Research (NIHR), 2016). This may limit the use of many existing tools in the target population. While the WHO and the International Osteoporosis Foundation recommend that fracture risk should be expressed as a probability over a 10 year interval (Kanis, 2002), such time frames are too long for care home residents. The observational study conducted as part of this thesis showed that 25% of participants died within a year, thus confirming the need to ensure that fracture assessment tools are reliable in such a frail population.

The methods and the duration of assessment with each tool are likely to affect uptake in clinical practice. Some of the tools, such as FRAX, QFractureScores and Garvan nomogram

are web-based and can only be assessed through the internet, therefore require computers which may not be readily available. However FRAX also has a paper-based version. A previous study has shown that providers who are well versed in osteoporosis care were unlikely to access a web-based fracture risk tool, only 1 in 20 providers who referred patients for bone densitometry testing responded to a mailed invitation to access a tool quite similar to FRAX (Watts, Ettinger & LeBoff, 2009). This is likely to change with the introduction of the Patient Electronic System. The fracture assessment process should be simple enough to be accommodated within routine work schedules.

6.3 The Consultation Visit

Conducting research in care homes is challenging, therefore it was essential to undertake consultation visits in preparation for the observational study although this was not required by the Ethics committee and the Research and Development Department of the ULHT. The aim of the consultation visits was to determine the acceptability of the research documents and make adjustments if necessary. Involving care home staff and residents early in the development of the study also ensured that a baseline of knowledge and understanding could be established for future dialogue.

The feedback came in the form of both detailed comments and minor corrections to the draft text. Some aspects in the research documents were confirmed as acceptable and other sections refined as a result of the feedback obtained. The changes made included increases of font size, avoidance of open questions, deletion of duplicate questions and development of separate information sheets for participants and consultees. Suggestions came from consultation participants with in-depth knowledge and experience of care home procedures such as managers, deputy managers, nurses, care assistants and residents. The feedback helped to

further the understanding of various aspects of care home daily routines, future vision, appreciation and expectations.

The consultation led to an increased awareness of the importance of the research amongst care home staff, and the feedback provided invaluable insights that ensured that the research documents were practicable and could be easily implemented in the observational study. This confirms reports of earlier consultation studies which found the exercise useful in developing the protocol and exploring ethical issues (Koops, Lindley, 2002, Ali, Roffe & Crome, 2006).

6.4. The Prospective Observational Cohort Study

The aims of the pilot study were to evaluate the feasibility of a fully powered study, to identify if the existing scores for fracture risk have relevance for care home use in the frail elderly, ease of use and of the Timed Up and Go Test (TUGT).

All the eighteen care homes in Boston participated, making the study representative of local care homes. However, only 217 (35%) participants were recruited out of 618 residents in these homes, with the main reason for non-recruitment being the inability to obtain informed consent in residents who lacked capacity. This was a major issue affecting recruitment, as 54% of the care home population lacked mental capacity, and it was difficult to contact consultees. Of the participants only 32% lacked mental capacity, thus the participants were not representative of the care home population.

The tools were generally easy to use with average duration of each risk assessment of between 1 and 2 minutes; this can be accommodated within routine work schedules. However,

assessment with the TUGT posed logistic problems, particularly with participants who did not have mental capacity.

Care home residents are a high risk group for fragility fractures, and it is important that the tool for this cohort has good screening performance. The sensitivity and specificity of the tools were generally poor, BMI had acceptable scores and the TUGT had high sensitivity for the prediction of falls, but the specificity was low. There were no published data for comparison.

The clinical discriminatory capacity of the tools showed that the complex models (FRAX, QFractureScores, Garvan nomogram and TUGT) were not as good as the much simpler BMI. This was consistent with the results of Rubin and colleagues (Rubin et al., 2013). Of the five tools, BMI was the best predictor of falls, fractures and combined falls and fractures, QFractureScores predicted fractures and combined falls and fractures but neither FRAX nor Garvan nomogram predicted these outcomes. The TUGT is a dedicated falls risk assessment tool and predicted falls, as expected, but the association was only weak.

It is interesting to note that, while BMI is an aspect of each of the three specific fracture risk assessment tools, it was a better predictor on its own than as part of the tools. This is a very useful finding for clinical practice, as BMI is easy to assess, and available for all care home residents, making routine screening for fracture risk a simple procedure, which can be introduced at no cost. One meta-analysis of fracture risk in 1,734 care home participants also found that the risk of fracture increased with decreasing BMI (HR 0.94, 95% CI = 0.90-0.98) (Khatib et al., 2014).

As the participants in this observational study were not representative of residents without mental capacity, it is unclear whether the findings also apply to patients with cognitive

problems. However, while there were only 10 fractures in 217 study participants, 4 occurred in patients with dementia. Dementia is included as a predictor only in the QFractureScores, which in itself was not useful for fracture prediction. The reasons for this are unclear, but the effect of dementia may have been diluted by other factors or, as in this study, insufficient numbers of participants with dementia were included in the development of the tool. This information was not available in the original paper describing the tool (Hippisley-Cox, Coupland, 2009). The observational study in this thesis showed that 40% of patients with fractures had dementia, suggesting that dementia may indeed be an important predictor for fractures.

A systematic review and meta-analysis of 13 prospective cohort studies also identified cognitive impairment as risk factor of fractures in long term care (Khatib et al., 2014). Conversely, a meta-analysis of 24 studies in nursing homes and hospitals did not specifically identify dementia as a risk factor for falls in care home residents (Deandrea et al., 2013). These two reviews are not directly comparable, as one examined fractures and the other falls. The observational study here is small, and might therefore overestimate the risk in the subgroup with dementia. However, an increased risk in residents with dementia is plausible, and should be confirmed in a future fully powered study.

6.5 Exploratory Analyses and Clinical Algorithm

The main findings from the exploratory analyses were:

The time it took to recruit each participant was considerable, with a median of 10 days.

Falls were common in the care home residents but fractures were less common.

All fractures in the participants resulted from falls.

There was a marked reduction in the number of fallers following institutionalisation.

Falls and fractures were commonest in facilities that catered for the participants with dementia.

Mortality of the participants in this study was high, 25% died in the 12 months of follow-up.

40% of the fractures occurred in the participants with dementia.

Significant predictors of falls were Parkinson's disease (OR 5.6), history of prior falls (OR 1.9), age (OR 1.025), body weight (OR 0.982) and BMI (OR 0.982), while alcohol use appeared protective (OR 0.000), but numbers were small.

The only predictors of fractures were: age (OR 1.072), body weight (OR 0.952) and BMI (OR 0.868).

Significant predictors of fractures, falls and fractures combined were the same as for fractures alone.

When participants were divided into three subgroups (no falls or fractures, falls only, and combined falls and fractures) comparison of basic demographics, comorbidities and scores on the fragility fracture assessment tools showed no significant differences for any of the 34 variables compared (table 37) other than body weight and TUGT after application of the Bonferroni correction. Body weight was significantly lower in the participants with combined falls & fractures than in those with no events, and TUGT was significantly longer in participants who had falls. As the three subgroups are relatively small and not equal in size, statistical analysis is likely to result in spurious results. While of some interest for hypothesis generation, they are not usable for the development of a predictive model.

The fall and fracture incidence obtained in this observational study is comparable with published data in older people (Luukinen et al., 1994, Rubenstein, Josephson & Robbins, 1994, Nurmi, Luthje, 2002, Centers for Disease Control and Prevention, 2012). A substantial

number of the incident fractures that occurred in the participants of this study occurred in those who lacked mental capacity (40%). One systematic review cited earlier found that cognitive impairment was associated with an increase in the risk of fragility fractures (Khatib et al., 2014). A systematic review on the risk factors for falls cited earlier found that history of falls, walking aid use and moderate disability had the strongest association (Deandrea et al., 2013). These two studies are not directly comparable, as the outcomes are fractures in one, and fall in the other.

My take on the findings of Deandrea et al (2013) is that cognitive impairment was not excluded as a risk factor for fractures given its known association with the risk factors which they identified. Residents with dementia who constitute high proportions of care home residents are very difficult to recruit.

The group comparisons using the Bonferroni correction showed that body weight and TUGT were the significant factors. Many studies have used BMI to explore fracture risk because of the variation in average weight and height in different populations which is mitigated by adjusting the weight for height and also in studies on hip fractures, BMI was as good a predictor as body weight (Johnell et al., 1995, Kanis et al., 1999). In this study there were no statistically significant differences between the heights of the participants therefore BMI could be used instead of the body weight.

The TUGT showed high sensitivity for falls prediction but it is not pragmatic and the reasons are discussed in section 6.6.2. Mortality of care home residents in the study here was high (25%), as in other studies in care home populations (Shah et al., 2013, Forder, Fernandez, 2011). This means that a tool which assesses fracture risk on a short term basis is desirable.

6.6 Implications of the Findings of this Study for Clinical Practice and Future Directions

6.6.1 Screening for Fragility Fractures

This study shows that there are several well established fragility fractures risk assessment tools, but that only BMI is useful for screening in a care home population. The study also showed that recruitment of a representative care home population is difficult, as individuals with dementia are underrepresented, because they are unable to give informed consent. As it is also difficult to obtain consent from consultees in this group, a representative prospective study may not be possible. However, care home residents are at high risk of fractures, and risk assessment is important to allow treatment of individuals at highest risk. The results of this study give an indication of the population most at risk, and may be used to develop a screening algorithm. The choice of suggested indicators, based on this work, is discussed below.

BMI was the strongest predictor of falls and fragility fractures in the care home population studied. A BMI of 19.9 kg/m² was the median for participants who had incident falls and fractures and a BMI of 21.2 kg/m² was the median for participants who had incident falls but no fractures. Therefore a BMI of 21.2 kg/m² or below was taken as a cut-off to define high risk of falls and fractures. The proportion of participants in the study here who had BMI of 21.2 kg/m² and would reach the cut off was about 32%. This is comparable to the published data for the wider older population (Inelmen et al., 2003, Ray, Laur & Golubic, 2014, Tamura et al., 2013, Russell, Elia, 2011).

The suggested cut off of a BMI of 21.2 kg/m² is consistent with, but a bit higher than the cut off identified by an earlier meta-analysis. De Laet and colleagues found that the risk ratio for fractures was markedly higher at the lower values of BMI, particularly with a BMI of 20 kg/m² and less. A BMI of 20kg/m² or lower was associated with nearly 2-fold increase in risk

ratio (RR = 1.95) when compared with a BMI of 25 kg/m². Between a BMI of 25 and 35 kg/m², the differences in risk ratio were smaller. A BMI of 30kg/m² when compared with a BMI of 25kg/m² was associated with a 17% reduction in hip fracture risk (RR =0.83) (De Laet et al., 2005).

Although the participants were not representative of residents with dementia, because it was only possible to get consent from few individuals in this resident group, 40% of the incident fractures observed was in participants with dementia. Also the incidence of falls and fractures was over 10 times higher in residents not included in the study than in the participants with lack of capacity being the main reason for non-enrolment. This suggests that dementia is an important predictor of falls and fractures in this cohort.

While this should ideally be confirmed in a prospective study, it is very common in care home residents and it is easy to assess compared to the other risk factors identified and I would therefore recommend it as an important risk factor to be included in an algorithm for fracture risk assessment in care homes. Estimating BMI is easy and nomograms for calculation are widely available, indeed it is already been assessed routinely in many care homes both during admission and follow up and including the history of dementia in the screening process is likely to increase the pick-up rate.

This study also identified a high mortality of 25% in the care home population enrolled. While it is important to prevent fractures in individuals with a reasonable prognosis, such treatment would be futile in residents with only a few months to live. It is therefore reasonable to include a predictor of mortality into the screening algorithm. The Charlson Co-morbidity Index (CCI) is a validated predictor of mortality and was included in this study. The mean CCI for

participants who died before 1 year was 36%. A cut-off of 36% and above was therefore used as threshold for non-intervention. There were no publications available for comparison.

A screening algorithm to identify care home residents who should be considered for preventative treatment was then designed based on BMI, presence of dementia and the CCI (Figure 8).

If the BMI is 21.2 kg/m² or less or the resident has dementia or both, the CCI should be assessed. If it is below 36%, the resident should be offered treatment following recommended guidelines (NOGG 2018 NICE 2016, SIGN 2015). This algorithm has been designed based on the results obtained from the analysis. Although it was a pilot study, the size (217) of the participants was large. Obtaining representative sample of residents without mental capacity for a fully powered study may not be feasible given the ethical requirement for recruitment of residents without mental capacity. This algorithm is practicable and attracts no cost, therefore I would recommend it to manage appropriate residents along the recommended guidelines.

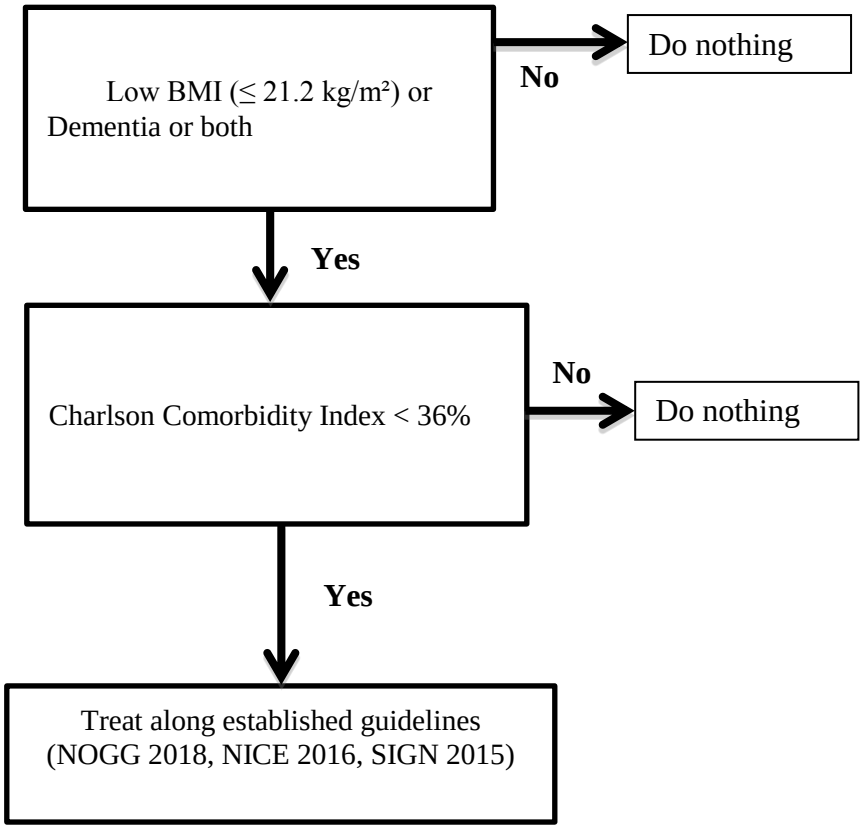


Figure 8: Algorithm for the management of fragility fractures in care home residents

Interpretation
Figure 8 shows that only three variables were used in the design. Low BMI and dementia or both are used in the identification of people at high risk of falls and fractures. The Charlson Comorbidity Index is then used for the selection of people for treatment following established guidelines.

A range of pharmaceutical interventions has been shown to be effective in reducing fracture risk in postmenopausal women with osteoporosis (Crandall et al 2014). Recommendations concerning the major interventions are based on high levels of evidence (Evidence level 1a and 1b) and the grade of these recommendations is summarised in table 39 (NOGG 2017).

Table 39. Anti-fracture efficacy of approved treatments for postmenopausal women with osteoporosis when given with calcium and vitamin D.

Intervention	Vertebral fracture	Non-vertebral fracture	Hip fracture
Alendronate	A	A	A
Ibandronate	A	A*	NAE
Risedronate	A	A	A
Zoledronic acid	A	A	A
Calcitriol	A	NAE	NAE
Denosumab	A	A	A
HRT	A	A	A
Raloxifene	A	NAE	NAE
Teriparatide	A	A	NAE

Source: NOGG 2017
A: grade A recommendation
NAE: not adequately evaluated
*in subsets of patients only (post-hoc analysis)
HRT: hormone replacement therapy

HRT and raloxifene are not useful for care home residents because the majority of them aretoo old.

Pharmacological intervention should be supplemented with lifestyle and dietary measures. The National Institute for Health and Care Excellence (2016) recommends calcium and vitamin D intake as follows:

- If the person`s calcium intake is adequate (700mg/day), prescribe 10 micrograms (400 international units) of vitamin D (without calcium) for people not exposed to much sunlight.
- If calcium intake is inadequate: prescribe 10 micrograms (400 international units of vitamin D with at least 1000 mg of calcium daily; prescribe 20 micrograms (800 international units) of vitamin D with at least 1000 mg of calcium daily for elderly people who are housebound or living in a nursing home.

These interventions should be supplemented with regular weight-bearing exercises which are tailored according to needs and abilities of the individual patient. Smoking and alcohol intake

of 3 or more units daily are associated with increase in fracture risk and should be avoided (Kanis et al 2005a, Kanis et al 2005b)

6.6.2 Screening for Falls

My results suggest that screening for falls is possible in care home residents. The majority of the participants were able to complete the tests. The duration of the assessment was between 1 and 2 minutes. NICE (National Institute for Health and Care Excellence, 2014) recommends using either the TUGT (Podsiadlo, Richardson, 1991) or Turn 180º (Simpson et al., 2002) as falls risk assessment tool in primary care setting. The TUGT poses logistic problems particularly for the care home residents who lack mental capacity. In this observational study, 93 (43%) could not perform the TUGT but there were no published data for comparison. The TUGT requires adequate space, stop watch and the undivided attention of the assessor. The Turn 180º, another test suggested by NICE, is simple to perform but it cannot be used in older people who use walking aids, who are not able to fully weight bear and who cannot follow instructions. In this study, 83 (38%) participants needed walking aids and 70 (32%) could not follow instructions because of dementia. Thus both the TUGT and Turn 180º are not pragmatic assessment tools for this cohort. Furthermore, while TUGT predicted falls in this population, the predictive value was poor with an odds ratio of 0.99 for falls in participants with lower TUGT times. Given these data TUG T cannot be considered an effective screening tool for day to day practice in this frail cohort.

Fall prevention through multidisciplinary assessment and intervention has the strongest evidence base with data supporting this approach both in primary and secondary prevention. Risk assessment and falls prevention (multifactorial) reduces falls by 24% (NHS RightCare

2019). The Prevention of Falls in the Elderly Trial (PROFET) has shown the benefits of assessing older people presenting to the Accident and Emergency Department with a fall (Close et al 1999). These assessments allow the implementation of person-specific interventions, designed to reduce the chances of a fall. Such interventions have been identified as a higher value intervention in the NHS RightCare pathway. It includes strength and balance training for those at low to moderate risk of falls, multi-factorial intervention for those at higher risk of falls and life course approach to lifestyle risk factors including smoking cessation, reduced use of alcohol and exercise (NHS RightCare 2019).

6.7 The Need for Research in Care Home Residents and the Challenges

This project shows that the majority of fracture risk assessment tools developed in the community are not useful in care home residents. This emphasizes the need for research in this vulnerable cohort. Establishing effective assessments and interventions in this population is particularly important in view of the increasing number of older people worldwide which means that a greater number are likely to be managed in long term care facilities. Care home residents are usually frail and physically and mentally challenged due to multi-morbidities. Many residents are female, in their mid-eighties and with an average life expectancy of between two and three years in residential care and one and two years in nursing homes (Bebbington, Darton & Netten, 2001, Froggatt, Davies, 2009). Therefore, the results of research in the relatively healthy community dwelling older persons should not be extrapolated to care home residents (Katz, Karuza & Counsell, 1995, Katz, 2011).

Three systematic reviews have highlighted the need for exclusive research in this setting (Cartwright, 2002, Froggatt et al., 2006, Oliver, Porock & Zweig, 2005). However, research in this population poses a number of ethical and methodological challenges. These include equity

of participant selection, informed consent, confidentiality, risk/benefit considerations, and preservation of the resident's rights and dignity (Maas et al., 2002, Addington-Hall, 2002, Pleschberger, 2007).

The difficulties which were encountered in this study were:

- Consent
- Dementia
- Mortality
- Gaining access
- Staff too busy to accommodate research into work schedules
- Families not always available

Only 35% of the entire local care home population were recruited. Zermansky and colleagues reported a recruitment rate of 41%, but it was unclear from the publication what the proportions of mentally competent and incompetent participants in the study were (Zermansky et al., 2007). Most of the participants in this observational study were assessed between 14:30 h and 17:00 h, but Hall and colleagues found that it was best not to interview residents after lunch, as they may too tired and lethargic (Hall, Longhurst & Higginson, 2009). In this study I did not formally monitor tiredness, but had no problems conducting interviews in the early afternoon.

Undertaking research in a care home is challenging but important. It requires resilience, good communication, anticipatory skills, planning, seizing opportunities and a good knowledge of who, when and how people can be approached. The importance of research in care homes is recognized by the National Institute for Health Research, who funded the Enabling Research in Care Homes (ENRICH) Programme to support research in this challenging environment

(NIHR 2012). . It is co-ordinated through the office of the National Institute for Health Research in the Office of the National Director for Dementia Research. This programme started in 2012 but none of the care homes in Boston participated.

The ENRICH project is a relatively new initiative with the overarching aim of to encourage research in care home residents. It is currently active in England, Scotland and Wales. Other networks are being established in parts of the USA and Australia, modelled around ENRICH. This network brings together care home staff, residents and researchers to facilitate the design and delivery of research. Hopefully, this will lead to improvement in the quality of life, treatment and care for all residents. Getting involved in research can potentially lead to benefits to care home residents and staff and can provide stimulation as residents take part in new activities or have someone new to talk to, give back control to residents, allowing them to feel like they are contributing to the future, stimulate residents to take an increased interest in their own health and well being, lead to professional development opportunities, enable care home staff to learn of new developments which can contribute to their business and marketing plans, encourage researchers and funders to address issues that are of interest to care home such as symptom management, or end-of-life-care, improve contact between care homes and other local health and care services, and, lastly, provide an effective voice for residents, families and staff whose views may have been previously unheard. In the short term, the network provides opportunities for care homes and residents to become involved in local and national studies. In the long term, it will help researchers understand the challenges and solutions around increasing research activity in care homes and identify better ways of working with existing care home systems to ease study delivery. Such support would have helped overcome some of the problems with recruitment identified in this study.

6.8 Strengths and Weaknesses of the Study

6.8.1 Strengths

- The first assessment of these tools in a care home population
- Preparation with consultation visit
- Single assessor allowed consistency
- High completion rate and few drop outs

6.8.2 Weaknesses

- Only conducted in Lincolnshire therefore the results may not be representative of the UK, Europe or the rest of the world
- All the participants were Caucasians; therefore the results may not be applicable to other ethnic groups.
- Skewed population with under-representation of individuals who lacked competence to consent.
- Only one reviewer, therefore it is unclear whether the same results would be seen by another person. However, all of the tests conducted were objective, and it is unlikely that this would have affected the results.
- The study duration was only 1 year and the fracture rates would have been higher with longer follow-up. However, in a population with 25% mortality this time frame might be considered appropriate.
- The algorithm designed has not been field-tested for efficacy and clinical effectiveness.

6.9 Recommendations for Future Research

1. The results of this project suggest that BMI and the presence of dementia are strong predictors of fragility fractures in a care home population. This should be confirmed in a large fully powered study.

2. The study also highlighted the difficulty of obtaining consent in residents lacking competence and the adverse impact on representation of the results.

3. The possibility of widening the criteria for consultee consent could be explored to include the care home manager, deputy or senior nurse on duty. It is also possible to obtain assent for future research during admission if it is observational. Applicants for the Lasting Power of Attorney (LPA) should be asked to state their wish about participation in future research.

4. Using different research methods, BMI and the presence or absence of dementia, as well as comorbidities which are available from General Practice registries, as are fractures, it may be possible to conduct such research from existing primary care databases.

5. The algorithm designed should be tested in future fully powered studies to include representative samples of other ethnic groups and residents who lack mental capacity.

6.10 Conclusions

Only 4 out of 33 fragility fracture assessment tools identified in the systematic review were potentially suitable in a care home population. Of these, only BMI was shown to have acceptable discriminatory and screening performance. A major problem with the conduct of

the study was obtaining consent form mentally incompetent individuals. This resulted in underrepresentation of this group. This was particularly important as 40% of participants who had fractures suffered from dementia, suggesting this as another important predictor of fractures. The results of this study indicate that combining low BMI and dementia as a screening tool could be reliable and easy to implement in a care home population. This should be assessed formally in a larger, representative and fully powered study.

6.11 Funding Source and Conflict of Interest Declaration

This thesis was entirely self-funded therefore there is no conflict of interest to declare.

References

Abdelaal, M., Le-Roux, C. & Docherty, N. 2017, "Morbidity and mortality associated with obesity", *Annals of Translational Medicine,* vol. 5, no. 7, p. 161.

Adebajo, A.O. 1989 Dietary calcium, physical activity, and risk of hip fracture. *British Medical Journal,* vol.299, pp.1165

Aboderin, I. 2004, "Intergenerational family support and old age economic security in Ghana" in *Living longer: ageing, development and social protection*, ed. P. Lloyd-Sherlock, Zed Books, London.

Abrahamsen, B., Vestergaard, P., 2010. Declining incidence of hip fracture and the extent of use of anti-osteoporotic therapy in Denmark 1997-2006. *Osteoporosis International*, vol.21 pp. 373-380.

Access Economics Pty Limited 2001, *The Burden of Brittle Bones: Costing Osteoporosis in Australia*, Access Economics Pty Limited, Australia.

Addington-Hall, J. 2002, "Research sensitivities to palliative care patients", *European Journal of Cancer Care,* vol. 11, no. 3, pp. 220-224.

Advisory Committee on Resource Allocation (ACRA) 2016, *Costs of unavoidable smallness due to remoteness*, Allocations Project Team, London.

Ahlborg, H.G., Johnell, O., Jarvinen, T.L.N. & Karlsson, M.K. 2004, "Prevalence of low bone mass in women - Secular trends over 30 years", *Journal of Bone and Mineral Research,* vol. 19, pp. S49-S49.

Ahmed, L.A., Nguyen, N.D., Bjornerem, A., Joakimsen, R.M., Jorgensen, L., Stormer, J., Bliuc, D., Center, J.R., Eisman, J.A., Nguyen, T.V. & Emaus, N. 2014, "External Validation of the Garvan Nomograms for Predicting Absolute Fracture Risk: The Tromso Study", *Plos One,* vol. 9, no. 9, pp. e107695.

Albrand, G., Munoz, F., Sornay-Rendu, E., DuBoeuf, F. & Delmas, P.D. 2003, "Independent predictors of all osteoporosis-related fractures in healthy postmenopausal women: the OFELY study", *Bone,* vol. 32, no. 1, pp. 78-85.

Ali, K., Roffe, C. & Crome, P. 2006, "What Patients Want: Consumer Involvement in the Design of a Randomised Controlled Trial of Routine Oxygen Supplementation After Acute Stroke", *Stroke,* vol. 37, pp. 865-871.

Allan, L.M., Ballard, C.G., Rowan, E.N. & Kenny, R.A. 2009, "Incidence and Prediction of Falls in Dementia: A Prospective Study in Older People", *Plos One,* vol. 4, no. 5, pp. e5521.

Altman, D.G. & Bland, J.M. 1994, "Diagnostic-Tests-2 - Predictive Values .4." *British Medical Journal,* vol. 309, no. 6947, pp. 102-102.

Alzeihmer`s Society 2013, *Record numbers of people with dementia in care homes*, Alzheimer's Society, London.

Alzheimer Society Manitoba 2014, *Reducing Risk of Falls for People with Dementia*. Available: alzheimer.mb.ca [2018, April/Friday].

Amboni, M., Barone, P. & Hausdorff, J.M. 2013, "Cognitive Contributions to Gait and Falls: Evidence and Implications", *Movement Disorders*, vol. 28, no. 11, pp. 1520-1533.

Andrich, S., Haastert, B., & Neuhaus, E. 2015. Epidemiology of pelvic fractures in Germany : considerably high incidence rates among older people. *PloS One* ; 10 e0139078

Ankjaer Jensen, A. & Johnell, O. 1996, "Prevention of osteoporosis: Cost-effectiveness of different pharmaceutical treatments", *Osteoporosis International*, vol. 6, no. 4, pp. 265-275.

National Osteoporosis Foundation (NOF) 1993,*Consensus development conference; Diagnosis, prophylaxis and treatment of osteoporosis*, American Journal of Medicine, USA.

Anonymous. 2003,"[Osteoporosis--prevention, diagnosis and treatment. A systematic literature review. SBU conclusions and summary]. [Swedish] Osteoporos--prevention, diagnostik och behandling. En systematisk litteraturoversikt. SBUs slutsatser och sammanfattning", *Lakartidningen*, vol. 100, no. 45, pp. 3590-5.

Appleby, J, Devin, N., Parkin, D., 2007. "NICEs cost effectiveness threshold" (http://www.bmj.com/content/335/7616/358). *British Medical Journal*,vol. 335 issue 7616, pp. 358- 359.

Arthritis Research UK 2015, *Arthritis Research UK*, Arthritis Research UK, Chesterfield, UK.

Aspray, T.J., Abdy, S., Stevenson, P., Rawlings, D. & Francis, R.M. 2006, "Osteoporosis in care homes -- high fracture risk with low bone mineral density measurements in EMI care... British Geriatrics Society: Abstracts of papers presented at the Spring Scientific Meeting, 6-7 April 2006", *Age & Ageing*, vol. 35, pp. i45-NaN.

Aspray, T.J., Prentice, A., Cole, T.J., Sawo, Y., Reeve, J. & Francis, R.M. 1996, "Low bone mineral content is common but osteoporotic fractures are rare in elderly rural Gambian women", *Journal of Bone and Mineral Research*, vol. 11, no. 7, pp. 1019-1025.

Atkinson, E, Achenbach, S, Crenshaw, J, Kaufman, K & Khosla, S., 2015, Can FRAX predict falls in older women? *Journal of Bone and Mineral Research*, vol. 30

Baker, S.G. & Pinsky, P.F. 2001, "A proposed design and analysis for comparing digital and analogue mammography: Special receiver operating characteristic methods for cancer screening", *Journal of the American Statistical Association*, vol. 96, no. 454, pp. 421-428.

Baker, T.L. 1994, *Doing Social Research*, 2nd ed., McGraw-Hill Inc., New York.

Bakker, A.B., Le Blanc, P.M. & Schaufeli, W.B. 2005, "Burnout contagion among intensive care nurses", *Journal of Advanced Nursing*, vol. 51, no. 3, pp. 276-287.

BAPEN 2018, *Malnutrition Universal Screening Tool (MUST).Estimating height from ulna length: instructions and tables*. Available: https://www.bapen.org.uk/pdf/must_full.pdf [2018, April/Wednesday].

Barr, R.J., Adebajo, A., Fraser, W.D., Halsey, J.P., Kelsey, C., Stewart, A. & Reid, D.M. 2005, "Can peripheral DXA measurements be used to predict fractures in elderly women living in the community?", *Osteoporosis International,* vol. 16, no. 10, pp. 1177-83.

Barrett-Connor, E., Siris, E.S., Wehren, L.E., Miller, P.D., Abbott, T.A., Berger, M.L., Santora, A.C. & Sherwood, L.M. 2005, "Osteoporosis and fracture risk in women of different ethnic groups", *Journal of Bone and Mineral Research,* vol. 20, no. 2, pp. 185-194.

Baum, M. 1993, "New approach for recruitment into randomised controlled trials." *Lancet,* vol. 341, pp. 812-813.

Bebbington, A., Darton, R. & Netten, A. 2001, *Care Homes for Older People: Volume 2. Admissions, Needs and Outcomes. The 1995/96 National Longitudinal Survey of Publicly-Funded Admissions.*, Personal Social services Research Unit (PSSRU), Canterbury, UK.

Bedene, A, Mencej Bedrac, S, Jese, L, Marc, J & Vrtacnik, P, 2016, MIR-148a the epigenetic regulator of bone homeostasis is increased in plasma of osteoporotic postmenopausal women, *Wiener Klinische Wochenschrift*, vol. 128, pp 519- 526.

Begum, N. 2018, *Minority ethnic attitudes and the 2016 EU referendum*, E.

Berard, A. Bravo, G. & Gauthier, P. 1997, "Meta-analysis of the effectiveness of physical activity for the prevention of bone loss in postmenopausal women", *Osteoporosis International,* vol. 7, no. 4, pp. 331-337.

Bertram, M., Norman, R., Kemp, L. & Vos, T. 2011, "Review of the long-term disability associated with hip fractures", *Injury Prevention,* vol. 17, no. 6, pp. 365-370.

Berry, S.D; Kiel, D.P; & Colón-Emeric 2019. Hip Fractures in Older Adults in 2019. *Journal of the American Medical Association*, doi:10.1001/jama.2019.5453

Bhat, A.K. & Dhruvarajan, R. 2001, "Ageing in India: drifting intergenerational relations, challenges and options", *Ageing and Society,* vol. 21, pp. 621-640.

Biesheuvel, C.J. Vergouwe, Y. Oudega, R., Hoes, A.W., Grobbee, D.E. & Moons, K.G. 2008, "Advantages of the nested case-control design in diagnostic research", *BMC Medical Research Methodology,* vol. 8, pp. 48.

Bischoff, H.A., Stahelin, H.B., Dick, W., Akos, R., Knecht, M., Salis, C., Nebiker, M., Theiler, R., Pfeifer, M., Begerow, B., Lew, R.A. & Conzelmann, M. 2003a, "Effects of Vitamin D and Calcium supplementation on falls: A randomized controlled trial", *Journal of Bone and Mineral Research,* vol. 18, no. 2, pp. 343-351.

Black, D., Arden, N., Palermo, L., Pearson, J., Cummings, S. & Study Osteoporotic Fractures Res Grp 1999, "Prevalent vertebral deformities predict hip fractures and new vertebral

deformities but not wrist fractures", *Journal of Bone and Mineral Research,* vol. 14, no. 5, pp. 821-828.

Black, D.M., Cummings, S.R. & Melton, L.J. 1992, "Appendicular Bone-Mineral and a Woman`s Lifetime Risk of Hip Fracture", *Journal of Bone and Mineral Research,* vol. 7, no. 6, pp. 639-646.

Black, D.M., Cummings, S.R., Karpf, D.B., Cauley, J.A., Thompson, D.E., Nevitt, M.C., Bauer, D.C., Genant, H.K., Haskell, W.L., Marcus, R., Ott, S.M., Torner, J.C., Quandt, S.A., Reiss, T.F. & Ensrud, K.E. 1996, "Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures", *Lancet,* vol. 348, no. 9041, pp. 1535-1541.

Black, D.M., Steinbuch, M., Palermo, L., Dargent-Molina, P., Lindsay, R., Hoseyni, M.S. & Johnell, O. 2001a, "An assessment tool for predicting fracture risk in postmenopausal women", *Osteoporosis International,* vol. 12, no. 7, pp. 519-28.

Blake, A.J., Morgan, K., Bendall, M.J., Dallosso, H., Ebrahim, S.B.J., Arie, T.H.D., Fentem, P.H. & Bassey, E.J. 1988, "Falls by Elderly People at Home - Prevalence and Associated Factors", *Age and Ageing,* vol. 17, no. 6, pp. 365-372.

Bland, M. & Peacock, J. 2000, *An introduction to Medical Statistics,* 3rd ed., Oxford University Press, Oxford, United Kingdom.

Blattenberger, G. & Lad, F. 1985, "Separating the Brier Score into Calibration and Refinement Components - a Graphical Exposition", *American Statistician,* vol. 39, no. 1, pp. 26-32.

Bliuc, D., Nguyen, D.N., Milch, V.E., Nguyen, T.V., Eisman, J.A. & Center, J.R. 2009, "Mortality Risk Associated With Low-Trauma Osteoporotic Fracture and Subsequent Fracture in Men and Women", *JAMA-Journal of the American Medical Association,* vol. 301, no. 5, pp. 513-521.

Bloem, B., van Vugt, P. & Beckley, J. 1999, "Balance and falls in Parkinson`s disease", *Gait Disorders*.

Bloem, B.R., Hausdorff, J.A., Visser, J.E. & Giladi, N. 2004, "Falls and freezing of gait in Parkinson's disease: A review of two interconnected, episodic phenomena", *Movement Disorders,* vol. 19, no. 8, pp. 871-884.

Bohannon, R.W. 2006, "Reference values for the timed up and go test: a descriptive meta-analysis.", *Journal of Geriatric Physical Therapy (2001),* vol. 29, no. 2, pp. 64-8.

Bolland, M.J., Siu, A.T.Y., Mason, B.H., Horne, A.M., Ames, R.W., Grey, A.B., Gamble, G.D. & Reid, I.R. 2011, "Evaluation of the FRAX and Garvan Fracture Risk Calculators in Older Women", *Journal of Bone and Mineral Research,* vol. 26, no. 2, pp. 420-427.

Bonnick, S.L. & Shulman, L. 2006, "Monitoring osteoporosis therapy: Bone mineral density, bone turnover markers, or both?", *American Journal of Medicine,* vol. 119, no. 4, pp. 25S-31S.

Boockvar, K. & Lachs, M. 2002, "Hospitalization risk following admission to an academic nursing home.", *Journal of the American Medical Directors Association,* vol. 3, no. 3, pp. 130-5.

Boonen, S., Autier, P., Barette, M., Vanderschueren, D., Lips, P. & Haentjens, P. 2004, "Functional outcome and quality of life following hip fracture in elderly women: a prospective controlled study", *Osteoporosis International,* vol. 15, no. 2, pp. 87-94.

Borissova, A., Shinkov, A., Kovatcheva, R., Vlahov, J., Dakovska, L. & Todorov, T. 2015, "Changes in the prevalence of diabetes mellitus in Bulgaria (2006-2012)." *Clinical Medicine Insights. Endocrinology and Diabetes,* vol. 8, pp. 41-5.

Boschitsch, E 2019, Diagnostics and fracture risk prediction, *Maturitas,* vol. 124, pp. 114

Bouxsein, M.L. 2003, "Bone quality: where do we go from here?", *Osteoporosis International,* vol. 14, pp. S118-S127.

Bowers, D. 1996, *Statistics from scratch. An Introduction for Health Care Professionals,* 20th ed., John Wiley & Sons Ltd, west Sussex, England.

Bowers, D. 2000, *Statistics from scratch. An Introduction for Health Care Professionals,* 5th ed., John Wiley & Sons Ltd, West Sussex, England.

Boyce, B.F. & Xing, L. 2007, "The RANKL/RANK/OPG pathway.", *Current Osteoporosis Reports,* vol. 5, no. 3, pp. 98-104.

Bradley, A.P. 1997, "The use of the area under the roc curve in the evaluation of machine learning algorithms", *Pattern Recognition,* vol. 30, no. 7, pp. 1145-1159.

Bradshaw, S.A., Playford, E.D. & Riazi, A. 2012, "Living well in care homes: a systematic review of qualitative studies", *Age and Ageing,* vol. 41, no. 4, pp. 429-440.

Brauer, C.A., Coca-Perraillon, M., Cutler, D.M. & Rosen, A.B. 2009, "Incidence and Mortality of Hip Fractures in the United States", *JAMA-Journal of the American Medical Association,* vol. 302, no. 14, pp. 1573-1579.

Brennan, J., Johansen, A., Butler, J., Stone, M., Richmond, P., Jones, S. & Lyons, R.A. 2003, "Place of residence and risk of fracture in older people: a population-based study of over 65-year-olds in Cardiff", *Osteoporosis International,* vol. 14, no. 6, pp. 515-519.

Brier, G.W. 1950, "Verification of forecasts expressed in terms of probability", *Monthly Weather Review,* pp. 1-3.

British Association of Parenteral and Enteral Nutrition (BAPEN) 2018, *BAPEN Malnutrition Self-Screening Tool*. Available: https://www.bapen.org.uk [2018, July/Monday].

British Orthopaedic Association 2007, *The Care of Patients with Fragility Fracture (The Blue Book),* British Orthopaedic Association, London.

Brown, H. 1995, "On the use of a pilot sample for sample size determination", *Statistics in Medicine,* vol. 14, pp. 1933-1940.

Brownbill, R.A. & Ilich, J.Z. 2003, "Hip geometry and its role in fracture: what do we know so far?" *Current Osteoporosis Reports,* vol. 1, no. 1, pp. 25-31.

Browner, W. 2007, *Predicting fracture risk: tougher than it looks*, BoneKEy.

Burge, R., Dawson-Hughes, B., Solomon, D.H., Wong, J.B., King, A. & Tosteson, A. 2007, "Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025", *Journal of Bone and Mineral Research,* vol. 22, no. 3, pp. 465-475.

Burge, R.T., Worley, D., Johansen, A., Bhattacharyya, S. & Bose, U. 2001, "The cost of osteoporotic fractures in the UK; projections for 2000-2020", *Journal of Medical Economics,* vol. 4, pp. 51-62.

Burger, H., De Laet, C.E.D.H., Weel, A.E.A.M., Hofman, A. & Pols, H.A.P. 1999, "Added value of bone mineral density in hip fracture risk scores", *Bone,* vol. 25, no. 3, pp. 369-374.

Burger, H., van Daele, P.L.A., Grashuis, K., Hofman, A., Grobbee, D.E., Schutte, H.E., Birkenhager, J.C. & Pols, H.A.P. 1997, "Vertebral deformities and functional impairment in men and women", *Journal of Bone and Mineral Research,* vol. 12, no. 1, pp. 152-157.

Butler, M., Norton, R., Lee Joe, T., Cheng, A. & Campbell, A.J. 1996, "The risks of hip fracture in older people from private homes and institutions", *Age and Ageing,* vol. 25, no. 5, pp. 381-385.

Cabinet Office 2018, *Consultation principles: guidance*. Available: https://www.gov.uk [2018, November/Sunday].

Cali, C.M. & Kiel, D.P. 1995, "An Epidemiologic-Study of Fall-Related Fractures among Institutionalized Older-People", *Journal of the American Geriatrics Society,* vol. 43, no. 12, pp. 1336-1340.

Callas, P.W., Pastides, H. & Hosmer, D.W. 1998, "Empirical comparisons of proportional hazards, Poisson, and logistic regression modelling of occupational cohort data", *American Journal of Industrial Medicine,* vol. 33, no. 1, pp. 33-47.

Cameron, I.D., Chen, J.S., March, L.M., Simpson, J.M., Cumming, R.G., Seibel, M.J. & Sambrook, P.N. 2009, "Hip Fracture Causes Excess Mortality Due to cardiovascular and Infectious Diseases in Institutionalised Older People: a Prospective Five Year Study", *Journal of Bone and Mineral Research,* vol. 25, no. 4, pp. 866-872.

Campbell, A.J., Reinken, J., Allan, B.C. & Martinez, G.S. 1981, "Falls in Old Age a Study of Frequency and Related Clinical Factors", *Age and Ageing,* vol. 10, no. 4, pp. 264-270.

Campbell, A.J., Spears, G.F.S., Borrie, M.J. & Fitzgerald, J.L. 1988, "Falls, Elderly Women and the Cold", *Gerontology,* vol. 34, no. 4, pp. 205-208.

Campbell, J. & Machin, D. 2000, *Medical Statistics, A common sense approach,* Third ed., John Wiley& Sons Ltd, West Sussex, England.

Canadian Institute for Health Information (CIHI) 2011, *Health Care in Canada*. Available: https://secure.cihi.ca/free_products/HCIC_2011_seniors_report_en.pdf [2018, August/Wednesday].

Care Quality Commission (CQC) 2015, *Care Standards*, Care Quality Commission, London.

Carehome.co.uk 2018, *Care homes in London*. Available: carehome.co.uk [2018, April/Monday].

Cartwright, J.C. 2002, "Nursing homes and assisted living facilities as places for dying.", *Annual Review of Nursing Research,* vol. 20, pp. 231-64.

Caspersen, C.J., Thomas, G.D., Boseman, L.A., Beckles, G.L.A. & Albright, A.L. 2012, "Aging, Diabetes, and the Public Health System in the United States", *American Journal of Public Health,* vol. 102, no. 8, pp. 1482-1497.

Cauley, J.A., Challous, D., Kassem, A.M.,& Fuleihan, G 2014. Geographic and ethnic disparities in osteoporotic fractures. *Nature Reviews Endocrinology,* vol. 10, pp. 338-351.

Cauley, J., El-Hajj Fuleihan, G., Arabi, A. & et al 2010, *FRAX International Task Force and FRAX International US subgroup report. Resource documents for the IOF/ISCD FRAX Initiative*, International Osteoporosis Foundation/ International Society for Clinical Densitometry.

Cauley, J.A., El-Hajj Fuleihan, G., Arabi, A., Fujiwara, S., Ragi-Eis, S., Calderon, A., Chionh, S.B., Chen, Z., Curtis, J.R., Danielson, M.E., Hanley, D.A., Kroger, H., Kung, A.W.C., Lesnyak, O., Nieves, J., Pluskiewicz, W., El Rassi, R., Silverman, S., Schott, A., Rizzoli, R., Luckey, M. & FRAX Position Dev Conf Members 2011, "Official Positions for FRAX (R) Clinical Regarding International Differences", *Journal of Clinical Densitometry,* vol. 14, no. 3, pp. 240-262.

Cauley, J.A., Palermo, L., Voot, M., Ensrud, K.E., Ewing, S., Hochberg, M., Nevitt, M.C. & Black, D.M. 2008, "Prevalent vertebral fractures in black women and white women", *Journal of Bone and Mineral Research,* vol. 23, no. 9, pp. 1458-1467.

Cauley, J.A., Thompson, D.E., Ensrud, K.C., Scott, J.C. & Black, D. 2000, "Risk of mortality following clinical fractures", *Osteoporosis International,* vol. 11, no. 7, pp. 556-561.

Cederholm, T., Cruz-Jentoft, A.J. & Maggi, S. 2013, "Sarcopenia and fragility fractures", *European Journal of Physical and Rehabilitation Medicine,* vol. 49, no. 1, pp. 111-117.

Center, J.R., Nguyen, T.V., Schneider, D., Sambrook, P.N. & Eisman, J.A. 1999, "Mortality after all major types of osteoporotic fracture in men and women: an observational study", *Lancet,* vol. 353, no. 9156, pp. 878-882.

Centers for Disease Control and Prevention (CDC) 2001, *National Health and Nutrition Examination Survey (NHANES),* Centers for Disease Control and Prevention, Bethesda, USA.

Centers for Disease Control and Prevention (CDC) 2016, *Long-Term Care Providers and Services Users in the United States: Data from the National Study of Long-Term Care Providers*, Centers for disease Control and Prevention, Atlanta, USA.

Centers for Disease Control and Prevention 2006, *Fatalities and injuries from falls among Older Adults-United States, 1993-2003 and 2001-2006*, US Department of Health and Human Services, Maryland, USA.

Centers for Disease Control and Prevention 2012, *Falls in Nursing Homes CDC 24/7: Saving Lives. Protecting People* Centres for Disease Control and Prevention, Atlanta, USA.

Cespedes, A. 2017. *How to Calculate BMI by Hand*. Available: https://www.livestrong.com/article/91064-side-effects-being-underweight/ [2018, May/Sunday].

Chandler, J.M., Zimmerman, S.I., Girman, C.J., Martin, A.R., Hawkes, W., Hebel, J.R., Sloane, P.D., Holder, L. & Magaziner, J. 2000, "Low bone mineral density and risk of fracture in white female nursing home residents", *JAMA-Journal of the American Medical Association*, vol. 284, no. 8, pp. 972-977.

Chapuy, M.C., Arlot, M.E., Duboeuf, F., Brun, J., Crouzet, B., Arnaud, S., Delmas, P.D. & Meunier, P.J. 1992, "Vitamin-D(3) and Calcium to Prevent Hip-Fractures in Elderly Women", *New England Journal of Medicine*, vol. 327, no. 23, pp. 1637-1642.

Chapuy, M. C, Schott, A.M., Garnero, P., Has, D., Delmas, P.D., & Meunier P.J., 1996, Healthy elderly French women living at home have secondary hyperparathyroidism and high bone turnover in winter. EPIDOS Study Group. *Journal of Clinical Endocrinology and Metabolism*, vol 18, no.3, pp 1129-1133.

Charlson, M.E., Pompei, P., Ales, K.L. & Mackenzie, C.R. 1987, "A New Method of Classifying Prognostic Co-Morbidity in Longitudinal-Studies - Development and Validation", *Journal of Chronic Diseases*, vol. 40, no. 5, pp. 373-383.

Chen, J., Simpson, J., March, L. & et al 2008, "Risk factors for fracture following a fall among older people in residential care facilities in Australia", *Journal of American Geriatrics Society*, vol. 56, no. 11, pp. 2020-2026.

Chen, J.S., Seibel, M.J., Zochling, J., March, L., Cameron, I.D., Cumming, R.G., Schwarz, J., Simpson, J.M. & Sambrook, P.N. 2006, "Calcaneal ultrasound but not bone turnover predicts fractures in Vitamin D deficient frail elderly at high risk of falls", *Calcified tissue International*, vol. 79, no. 1, pp. 37-42.

Chen, P., Krege, J.H., Adachi, J.D., Prior, J.C., Tenenhouse, A., Brown, J.P., Papadimitropoulos, E., Kreiger, N., Olszynski, W.P., Josse, R.G., Goltzman, D. & CaMOS, R.,Group 2009, "Vertebral fracture status and the World Health Organization risk factors for predicting osteoporotic fracture risk", *Journal of Bone & Mineral Research*, vol. 24, no. 3, pp. 495-502.

Chrischilles, E.A., Butler, C.D., Davis, C.S. & Wallace, R.B. 1991, "A Model of Lifetime Osteoporosis Impact", *Archives of Internal Medicine*, vol. 151, no. 10, pp. 2026-2032.

Christensen, K., Doblhammer, G., Rau, R. & Vaupel, J.W. 2009, "Ageing populations: the challenges ahead", *Lancet*, vol. 374, no. 9696, pp. 1196-1208.

Christensen, P., Brixen, K. & Kristiansen, I. 2003, *Danish Osteoporosis Outcome Model (DOOM)*, University of Soutjern Denmark, Denmark.

Clark, P., Cons-Molina, F., Deleze, M., Ragi, S., Haddock, L., Zanchetta, J.R., Jaller, J.J., Palermo, L., Talavera, J.O., Messina, D.O., Morales-Torres, J., Salmeron, J., Navarrete, A., Suarez, E., Perez, C.M. & Cummings, S.R. 2009, "The prevalence of radiographic vertebral fractures in Latin American countries: the Latin American Vertebral Osteoporosis Study (LAVOS)", *Osteoporosis International*, vol. 20, no. 2, pp. 275-282.

Clifford, P.C 1980. Fractures of the neck of humerus: A review of late results. *Injury* vol. 12, pp. 991 - 995

Clinical guide to prevention and treatment of osteoporosis 2013, National Osteoporosis Foundation (NOF), Washington DC.

Close, J.C.T., 2001, Interdisciplinary practice in the prevention of falls – a review of working models of care, *Age and Ageing*, Vol. 30, no. 4. pp 8-12

Close, J., Ellis, M., Hooper, R., Glucksman, E., Jackson, S. & Swift, C. 1999, "Prevention of falls in the elderly trial (PROFET): a randomised controlled trial", *Lancet*, vol. 353, no. 9147, pp. 93-97.

Coleman, P. 1984, "The Netherlands: poverty and disability in old age" in *Responses to Poverty: lessons from Europe*, eds. R. Walker, R. Lawson & P. Townsend, Heinmann, London, pp. 266-282.

Collins, G.S. & Michaelsson, K. 2012, "Fracture Risk Assessment: State of the Art, Methodologically Unsound, or Poorly Reported?", *Current Osteoporosis Reports*, vol. 10, no. 3, pp. 199-207

Collins, G.S., Mallett, S. & Altman, D.G. 2011, "Predicting risk of osteoporotic and hip fracture in the United Kingdom: prospective independent and external validation of QFractureScores", *British Medical Journal*, vol. 342, pp. d3651.

Colon-Emeric, C., Kuchibhatla, M., Pieper, C., Hawkes, W., Fredman, L., Magaziner, J., Zimmerman, S. & Lyles, K.W. 2003a, "The contribution of hip fracture to risk of subsequent fractures: data from two longitudinal studies", *Osteoporosis International*, vol. 14, no. 11, pp. 879-883.

Colon-Emeric, C.S., Biggs, D.P., Schenck, A.P. & Lyles, K.W. 2003b, "Risk factors for hip fracture in skilled nursing facilities: who should be evaluated?", *Osteoporosis International*, vol. 14, no. 6, pp. 484-489.

Commission for Social Care Inspection (CSCI) 2006, *Annual report and Accounts 2005-6*, The Stationary Office, London.

Committee for Proprietary Medicinal Product (CPMP) 2002, *Note for guidance on post menopausal osteoporosis in women 2001* [Homepage of Committee for Proprietary Medicinal product (CPMP)], [Online]. Available: http://www.emea.eu.int/pdfs/human/ewp/055295en.pdf [2018, June/Monday].

Compston, J., Cooper, A., Cooper, C., Gittoes, N., Gregson, C., Harvey, N., Hope, S., Kanis, A., McCloskey, E.V., Poole, K.E.S., Reid, D.M., Selby, P., Thompson, A., Vine, N. & The National Osteoporosis Guideline Group 2017, UK clinical guideline for the prevention and treatment of osteoporosis. *Archives of Osteoporosis* vol. 12, no.1

Compston, J. & Rosen, C.J. 2006, *Fast Facts: Osteoporosis*, 5th ed., Health Press Limited, Oxford.

Compston, J. 2006, "Bone quality: What is it and how is it measured? (Online version ISSN 1677-9487), *Arquivos Brasileiros de Endocrinologia & Metabologia*, vol. 50, no. 4.

Compston, J.E., Papapoulos, S.E., Blanchard, F. & Working Party European Union Member States 1998, "Report on osteoporosis in the European community: Current status and recommendations for the future", *Osteoporosis International*, vol. 8, no. 6, pp. 531-534.

Cook, D.J., Guyatt, G.H., Adachi, J.D., Epstein, R.S., Juniper, E.F., Austin, P.A., Clifton, J., Rosen, J., Kesennich, C.R., Stock, J.L., Overdorf, J., Miller, P.D., Erickson, A.L., McLung, M., Love, B. & Griffith, L.E. 1997, "Measuring quality of life in women with osteoporosis", *Osteoporosis International*, vol. 7, no. 5, pp. 478-487.

Cooper, C., Atkinson, E.J., Jacobsen, S.J., Ofallon, W.M. & Melton, L.J. 1993, "Population-Based Study of Survival After Osteoporotic Fractures", *American Journal of Epidemiology*, vol. 137, no. 9, pp. 1001-1005.

Cooper, C., Atkinson, E.J., O'Fallon, W.M. & Melton, L.J. 1992, "Incidence of Clinically Diagnosed Vertebral Fractures - a Population-Based Study in Rochester, Minnesota, 1985-1989", *Journal of Bone and Mineral Research*, vol. 7, no. 2, pp. 221-227.

Cooper, C., Campion, G. & Melton, L.J. 1992, "Hip-Fractures in the Elderly - a Worldwide Projection", *Osteoporosis International*, vol. 2, no. 6, pp. 285-289.

Crandall, C.J., Newberry, S.J., & Diamant, A., 2014, Comparative effectiveness of pharmacologic treatments to prevent fractures: an updated systematic review, *Annals of Internal Medicine*, vol. 161, pp. 711 - 723

Crepaldi, G. & Maggi, S. 2005, "Sarcopenia and osteoporosis: A hazardous duet.", *Journal of Endocrinological Investigation*, vol. 28, no. 10 Suppl., pp. 66-8.

Crilly, R., Tanner, D., Kloseck, M. & et al 2010, "Hip fractures in long-term care: Is the excess explained by the age and gender distribution of the residents?", *Journal of Aging Research*, vol. 2010, pp. 291258.

Cryer, C. & Patel, S. 2002, *Falls, Fragility & Fractures*, Alliance for Better Bone Health, Surrey, England.

Cummings, S., Faulkner, K.A. & Cauley, J. 1993, *Lower rates of hip fracture in Asian women may be due to their shorter hip axis length: presented at the Fourth International Symposium on Osteoporosis*, Hong Kong.

Cummings, S.R. & Black, D. 1995, "Bone mass measurements and risk of fracture in Caucasian women: A review of findings from prospective studies", *American Journal of Medicine*, vol. 98, no. 2, pp. 24S-28S.

Cummings, S.R. & Melton, L.J. 2002, "Epidemiology and outcomes of osteoporotic fractures", *Lancet*, vol. 359, no. 9319, pp. 1761-1767.

Cummings, S.R. & Nevitt, M.C. 1989, "A Hypothesis - the Causes of Hip-Fractures", *Journals of Gerontology*, vol. 44, no. 4, pp. M107-M111.

Cummings, S.R. 2002, "How drugs decrease fracture risk: Lessons from trials." *Journal of Musculoskeletal & Neuronal Interactions*, vol. 2, no. 3, pp. 198-200.

Cummings, S.R., Bates, D. & Black, D.M. 2002, "Clinical use of bone densitometry: scientific review", *JAMA*, vol. 288, no. 15, pp. 1889-97.

Cummings, S.R., Nevitt, M.C., Browner, W.S., Stone, K., Fox, K.M., Ensrud, K.E., Cauley, J.C., Black, D. & Vogt, T.M. 1995, "Risk-Factors for Hip Fracture in White Women", *New England Journal of Medicine*, vol. 332, no. 12, pp. 767-773.

Cummings, S.R., San Martin, J., McClung, M.R., Siris, E.S., Eastell, R., Reid, I.R., Delmas, P., Zoog, H.B., Austin, M., Wang, A., Kutilek, S., Adami, S., Zanchetta, J., Libanati, C., Siddhanti, S., Christiansen, C. & FREEDOM Trial 2009, "Denosumab for Prevention of Fractures in Postmenopausal Women with Osteoporosis", *New England Journal of Medicine*, vol. 361, no. 8, pp. 756-765.

Cummings-Vaughn, L.A. & Gammack, J.K. 2011, "Falls, osteoporosis, and hip fractures", *Medical Clinics of North America*, vol. 95, no. 3, pp. 495-506, x.

Cummins, N.M., Poku, E.K., Towler, M.R., O'Driscoll, O.M. & Ralston, S.H. 2011, "Clinical Risk Factors for Osteoporosis in Ireland and the UK: A Comparison of FRAX and QFractureScores", *Calcified Tissue International*, vol. 89, no. 2, pp. 172-177.

Dagan, N., Cohen-Stavi, C., Leventer-Roberts, M. & Balicer, R.D. 2017, "External validation and comparison of three prediction tools for risk of osteoporotic fractures using data from population based electronic health records: retrospective cohort study", *BMJ-British Medical Journal*, vol. 356, pp. i6755.

Dargent-Molina, P., Douchin, M.N., Cormier, C., Meunier, P.J., Breart, G. & EPIDOS Study Grp 2002, "Use of clinical risk factors in elderly women with low bone mineral density to identify women at higher risk of hip fracture: The EPIDOS prospective study", *Osteoporosis International*, vol. 13, no. 7, pp. 593-599.

Dargent-Molina, P., Piault, S. & Breart, G. 2005, "A triage strategy based on clinical risk factors for selecting elderly women for treatment or bone densitometry: the EPIDOS prospective study", *Osteoporosis International*, vol. 16, no. 8, pp. 898-906.

Dargent-Molina, P., Schott, A.M., Hans, D., Favier, F., Grandjean, H., Baudoin, C., Meunier, P.J., Breart, G. & EPIDOS Study Grp 1999, "Separate and combined value of bone mass and gait speed measurements in screening for hip fracture risk: Results from the EPIDOS study", *Osteoporosis International,* vol. 9, no. 2, pp. 188-192.

Dawson-Hughes, B., Tosteson, A.N.A., Melton, L.J.,III, Baim, S., Favus, M.J., Khosla, S. & Lindsay, R.L. 2008, "Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA", *Osteoporosis International,* vol. 19, no. 4, pp. 449-458.

De Laet, C., Kanis, J.A., Oden, A., Johanson, H., Johnell, O., Delmas, P., Eisman, J.A., Kroger, H., Fujiwara, S., Garnero, P., McCloskey, E.V., Mellstrom, D., Melton, L.J., Meunier, P.J., Pols, H.A.P., Reeve, J., Silman, A. & Tenenhouse, A. 2005, "Body mass index as a predictor of fracture risk: A meta-analysis", *Osteoporosis International,* vol. 16, no. 11, pp. 1330-1338.

De Laet, C.E., van Hout, B.A., Hofman, A. & Pols, H.A. 1996, "[Costs due to osteoporosis-induced fractures in The Netherlands; possibilities for cost control].", *Nederlands tijdschrift voor geneeskunde,* vol. 140, no. 33, pp. 1684-8.

De Laet, C.E.D.H., Van Hout, B.A., Burger, H., Weel, A.E.A.M., Hofman, A. & Pols, H.A.P. 1998, "Hip fracture prediction in elderly men and women: Validation in the Rotterdam study", *Journal of Bone and Mineral Research,* vol. 13, no. 10, pp. 1587-1593.

Deandrea, S., Bravi, F., Turati, F., Lucenteforte, E., La Vecchia, C. & Negri, E. 2013, "Risk factors for falls in older people in nursing homes and hospitals: a systematic review and meta-analysis", *Archives of Gerontology and Geriatrics,* vol. 56, no. 3, pp. 407-415.

Deandrea, S., Lucenteforte, E., Bravi, F., Foschi, R., La Vecchia, C. & Negri, E. 2010, "Risk Factors for Falls in Community-dwelling Older People: a Systematic Review and Meta-analysis", *Epidemiology,* vol. 21, no. 5, pp. 658-668.

Delmas, P.D. 2000,"Markers of bone turnover for monitoring treatment of osteoporosis with antiresorptive drugs", *Osteoporosis International,* vol. 11, pp. 66-76.

Delmas, P.D. 2002, "Treatment of postmenopausal osteoporosis", *Lancet,* vol. 359, no. 9322, pp. 2018-2026.

Department of Health (DH) 1992, *Residential Accommodation for Elderly and Younger Physically handicapped People: year ending 31 May 1991. Government Statistical Offic*e, Department of Health, London.

Department of Health (DOH) 2001, *Guide to Consent for Examination and Treatment*, Department of Health (DOH), London.

Department of Health 2001, *National Service Framework for Older Peopl*e, Department of Health, London.

Derbyshire County Council 2017, *Focus groups*, Derbyshire County Council, Matlock, UK.

Derbyshire County Council *Consultation methods- advantages and disadvantages*, Derbyshire County Council.

Deurenberg-Yap, M., Schmidt, G., van Staveren, W.A. & Deurenberg, P. 2000, "The paradox of low body mass index and high body fat percentage among Chinese, Malays and Indians in Singapore", *International Journal of Obesity*, vol. 24, no. 8, pp. 1011-1017.

Dey, D.K., Rothenberg, E., Sundh, V., Bosaeus, I., & Steen, B. 2001. Height and body weight in elderly adults: a 21-year population study on secular trends and related factors in 70-year olds. *The Journals of Gerontology. Series A, Biological sciences and medical sciences*, vol. 56, pp. M780-M784

Diagnostic Test Accuracy Working Group, The Cochrane Collaboration 2009, *Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy*, Version 1.0.1 edn, John Wiley & Sons, Chichester, UK.

Diez-Perez, A., Gonzalez-Macias, J., Marin, F., Abizanda, M., Alvarez, R., Gimeno, A., Pegenaute, E., Vila, J. & ECOSAP Study Investigators 2007, "Prediction of absolute risk of non-spinal fractures using clinical risk factors and heel quantitative ultrasound", *Osteoporosis International*, vol. 18, no. 5, pp. 629-639.

Diong, J. 2016, *Limitations of P values*. Available: https//scientificallysound.org [2018, June/2018].

Donnelly, N., Hickey, A., Burns, A. & et al 2015, "Systematic Review and Meta-Analysis of the impact of Carer Stress on Subsequent Institutionalisation of Community Dwelling Older People", *Plos One*.

Douglas, S., Bunyan, A., Chiu, K.H., Twaddle, B. & Maffulli, N. 2000, "Seasonal variation of hip fracture at three latitudes", *Injury-International Journal of the Care of the Injured*, vol. 31, no. 1, pp. 11-19.

Downton, J.H. & Andrews, K. 1991, "Prevalence, characteristics and factors associated with falls among the elderly living at home.", *Aging (Milan, Italy)*, vol. 3, no. 3, pp. 219-28.

Dufresne, T.E., Chmielewski, P.A., Manhart, M.D., Johnson, T.D. & Borah, B. 2003, "Risedronate preserves bone architecture in early postmenopausal women in 1 year as measured by three-dimensional microcomputed tomography", *Calcified tissue international*, vol. 73, no. 5, pp. 423-432.

Duncan, R, Robinson, L, Francis, R. M, Jagger, C, & Kingston, A., 2014, Magnitude of fragility fracture in the very old-are we meeting their needs? *Osteoporosis International*, vol. 26, no. 1, pp. 123 – 130.

Duque, G., Lord, S.R., Mak, J., Ganda, K., Close, J.J.T., Ebeling, P., Papaioannou, A. & Inderjeeth, C.A. 2016, "Treatment of Osteoporosis in Australian Residential Aged Care Facilities: Update on Consensus Recommendations for Fracture Prevention.", *Journal of the American Medical Directors Association*, vol. 17, no. 9, pp. 852-9.

Eastell, R. 1998, "Treatment of postmenopausal osteoporosis", *New England Journal of Medicine*, vol. 338, no. 11, pp. 736-746.

Eastwood, E.A., Magaziner, J., Wang, J., Silberzweig, S.B., Hannan, E.L., Strauss, E. & Siu, A.L. 2002, "Patients with hip fracture: Subgroups and their outcomes", *Journal of the American Geriatrics Society,* vol. 50, no. 7, pp. 1240-1249.

Eddy, D., Johnston, C. & Cummings SR, e.a. 1998, "Osteoporosis: and cost-effectiveness analysis. Status report", *Osteoporosis International,* vol. 8, pp. I-S82.

Edwards, B.J., Bunta, A.D., Simonelli, C., Bolander, M. & Fitzpatrick, L.A. 2007, "Prior fractures are common in patients with subsequent hip fractures", *Clinical Orthopaedics and Related research,* , no. 461, pp. 226-230.

Elixhauser, A., Steiner, C., Harris, D.R. & Coffey, R.N. 1998, "Comorbidity measures for use with administrative data", *Medical Care,* vol. 36, no. 1, pp. 8-27.

Elliott, M.B.,N. 2003, "Fracture risks for women in long-term care; high prevalence of calcaneal osteoporosis and hypervitaminosis D", *Pharmacotherapy,* vol. 23, no. 6, pp. 702-710.

Elvey, M.H., Pugh, H., Schaller, G., Dhotar, G., Patel, B. & Oddy, M.J. 2014, "Failure in the application of fragility fracture prevention guidelines", *Annals of the Royal College of Surgeons of England,* vol. 96, no. 5, pp. 381-385.

Ensrud, K.E., Lipschutz, R.C., Cauley, J.A., Seeley, D., Nevitt, M.C., Scott, J., Orwoll, E.S., Genant, H.K. & Cummings, S.R. 1997, "Body size and hip fracture risk in older women: A prospective study", *American Journal of Medicine,* vol. 103, no. 4, pp. 274-280.

Ensrud, K.E., Nevitt, M.C., Yunis, C., Hulley, S.B., Grimm, R.H. & Cummings, S.R. 1992, "Postural hypotension and postural dizziness in elderly women. The study of osteoporotic fractures. The Study of Osteoporotic Fractures Research Group", *Archives of Internal Medicine,* vol. 152, no. 5, pp. 1058-64.

European Medicines Agency (EMA) 2005, *Guideline on the evaluation of new Medicinal products in the treatment of primary osteoporosis*, European Medicine Agency, London.

European Medicines Agency (EMA) 2006, *Guideline on the Evaluation of Medicinal Products in the Treatment of Primary Osteoporosis*, European Medicines Agency, London.

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.2009,. Statistical power analyses using GPower 3.1: Tests for correlation and regression analyses. *Behavior Research Methods*, vol 41, no. 4, pp. 1149-1160.

Faulkner, K.G., Cummings, S.R., Black, D., Palermo, L., Gluer, C.C. & Genant, H.K. 1993, "Simple measurement of femoral geometry predicts hip fracture: The study of osteoporotic fractures", *Journal of Bone and Mineral Research,* vol. 8, no. 10, pp. 1211-1217.

Fawcett, T. 2004, *ROC graphs: notes and practical considerations for data mining researchers.* Kluwer Academic Publishers, Netherlands.

Fazzalari N 2009, *Why is the secondary prevention of fragility fracture important/ -The Australian Reality*.

Felson, D. 2018, *Test validity*. Available: http://sphweb.bumc.bu.edu/otIt/MPH-Modules/EP/EP713_Screening [2018, May/Tuesday].

Fenton, K 2014. The human cost of falls. *Blog : Public health matters, Public Health England*

Ferri, C., Flach, P., Hernandez-Orallo, J. & Senad, A. 2005, "Modifying ROC curves to incoporate predicted probabilities.", *Proceedings of the Second Workshop on ROC Analysis in Machine Learning (ed, by N. Laciche, C.Ferri, S. Macskassy and A. Rakotomamonjy), pp. 33-40. International Conference on Machine Leraning*, pp. 33.

Fiatarone Singh, M.A., Singh, N.A., Hansen, R.D., Finnegan, T.P., Allen, B.J., Diamond, T.H., Diwan, A.D., Lloyd, B.D., Williamson, D.A., Smith, E.U.R., Grady, J.N., Stavrinos, T.M. & Thompson, M.W. 2009, "Methodology and baseline characteristics for the Sarcopenia and Hip Fracture study: a 5-year prospective study.", *The Journals of Gerontology.Series A, Biological Sciences and Medical Sciences*, vol. 64, no. 5, pp. 568-74.

Fielding, A.H. & Bell, J.F. 1997, "A review of methods for the assessment of prediction errors in conservation presence/absence models", *Environmental Conservation*, vol. 24, no. 1, pp. 38-49.

Finnern, H.W. & Sykes, D.P. 2003, "The hospital cost of vertebral fractures in the EU: estimates using national datasets", *Osteoporosis International*, vol. 14, no. 5, pp. 429-436.

Forder, J. & Fernandez, J. 2011, *Length of stay in Care Homes. Report commissioned by BUPA Care Services, PSSRU. Discussion Paper 276*9, BUPA Care Services, Canterbury.

Forman, G. & Cohen, I. 2005, "Beware the null hypothesis: Critical value tables for evaluating classifiers", *Machine Learning: Ecml 2005, Proceedings*, vol. 3720, pp. 133-145.

Forsen, L., Sogaard, A.J., Meyer, H.E., Edna, T.H. & Kopjar, B. 1999, "Survival after hip fracture: Short- and long-term excess mortality according to age and gender", *Osteoporosis International*, vol. 10, no. 1, pp. 73-78.

Fossey, J., Ballard, C., Juszczak, E., James, I., Aldler, N., Jacoby, R. & Howard, R. 2006, "Effect of enhanced psychosocial care on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial", *British Medical Journal*, vol. 332, no. 7544, pp. 756-758A.

Fried, L.P. & Guralnik, J.M. 1997, "Disability in older adults: Evidence regarding significance, aetiology, and risk", *Journal of the American Geriatrics Society*, vol. 45, no. 1, pp. 92-100.

Friedman, S.M., Menzies, I.B., Bukata, S.V., Mendelson, D.A. & Kates, S.L. 2010, "Dementia and hip fractures: development of a pathogenic framework for understanding and studying risk.", *Geriatric Orthopaedic Surgery & Rehabilitation*, vol. 1, no. 2, pp. 52-62.

Friedman, S.M., Williamson, J.D., Lee, B.H., Ankrom, M.A., Ryan, S.D. & Denman, S.J. 1995, "Increased Fall Rates in Nursing-Home Residents After Relocation to a New Facility", *Journal of the American Geriatrics Society*, vol. 43, no. 11, pp. 1237-1242.

Froggatt, K. & Davies, S. 2009, *Understanding care homes: A research and development perspective*, Jessica Kingsley, London.

Froggatt, K.A., Wilson, D., Justice, C., Macadam, M., Leibovici, K., Kinch, J., Thomas, R. & Choi, J. 2006, "End-of-life care in long-term care settings for older people: a literature review.", *International Journal of Older People Nursing*, vol. 1, no. 1, pp. 45-50.

Frost, H.M. 1997, "On our age-related bone loss: Insights from a new paradigm", *Journal of Bone and Mineral Research*, vol. 12, no. 10, pp. 1539-1546.

Fuggle, N., Curtis, E.M., ward, K. A., Harvey, N. C., Dennison, E. M., & Cooper, C 2019, Fracture prediction, imaging and screening in osteoporosis, *Nature Reviews. Endocrinology*

Fujita, T. 1994, "Osteoporosis in Japan - Factors Contributing to the Low Incidence of Hip Fracture", *Advances in Nutritional Research, Vol 9*, vol. 9, pp. 89-99.

Fuleihan G E, Aclib G 2011, *THE MIDDLE EAST & AFRICA REGIONAL AUDIT Epidemiology, costs & burden of osteoporosis in 2011*, International Osteoporosis Foundation, Switzerland.

Gallagher, J.C., Melton, L.J., Riggs, B.L. & Bergstrath, E. 1980, "Epidemiology of Fractures of the Proximal Femur in Rochester, Minnesota", *Clinical Orthopaedics and Related Research*, , no. 150, pp. 163-171.

Garnero, P., Hausherr, E., Chapuy, M.C., Marcelli, C., Grandjean, H., Muller, C., Cormier, C., Breart, G., Meunier, P.J. & Delmas, P.D. 1996, "Markers of bone resorption predict hip fracture in elderly women: The EPIDOS prospective study", *Journal of Bone and Mineral Research*, vol. 11, no. 10, pp. 1531-1538.

Gates, S., Smith, L.A., Fisher, J.D. & Lamb, S.E. 2008, "Systematic review of accuracy of screening instruments for predicting fall risk among independently living older adults", *Journal of Rehabilitation Research and Development*, vol. 45, no. 8, pp. 1105-1116.

Genant, H.K., Cooper, C., Poor, G., Reid, I., Ehrlich, G., Kanis, J., Nordin, B.E.C., Barrett-Connor, E., Black, D., Bonjour, J.P., Dawson-Hughes, B., Delmas, P.D., Dequeker, J., Eis, S.R., Gennari, C., Johnell, O., Johnston, C.C., Lau, E.M.C., Liberman, U.A., Lindsay, R., Martin, T.J., Masri, B., Mautalen, C.A., Meunier, P.J., Miller, P.D., Mithal, A., Morii, H., Papapoulos, S., Woolf, A., Yu, W. & Khaltaev, N. 1999, "Interim report and recommendations of the World Health Organization task-force for osteoporosis", *Osteoporosis International*, vol. 10, no. 4, pp. 259-264.

Gerdhem, P., Ringsberg, K., Obrant, K. & Akesson, K. 2005, "Association between 25-hydroxy Vitamin D levels, physical activity, muscle strength and fractures in the prospective population-based OPRA Study of Elderly Women", *Osteoporosis International*, vol. 16, no. 11, pp. 1425-1431.

Ginde, A.A., Liu, M.C. & Camargo, C.A.,Jr. 2009, "Demographic Differences and Trends of Vitamin D Insufficiency in the US Population, 1988-2004", *Archives of Internal Medicine*, vol. 169, no. 6, pp. 626-632.

Gingaras C, *How to interprete odds ratios that are smaller than* 1. Available: https://www.researchgate.net/post/How_to_interpret_oods_ratios_that-are_smaller_than_1 [2018, May/Saturday].

Girman, C.J., Chandler, J.M., Zimmerman, S.I., Martin, A.R., Hawkes, W., Hebel, J.R., Sloane, P.D. & Magaziner, J. 2002a, "Prediction of fracture in nursing home residents", *Journal of the American Geriatrics Society,* vol. 50, no. 8, pp. 1341-1347.

Glass, D. 2010, "Signalling pathways perturbing muscle mass", *Current Opinion in Clinical Nutrition and Metabolic Care,* vol. 13, pp. 226-229.

Gluer, C.C., Cummings, S.R., Pressman, A., Li, J., Gluer, K., Faulkner, K.G., Grampp, S. & Genant, H.K. 1994, "Prediction of hip fractures from pelvic radiographs: The study of osteoporotic fractures", *Journal of Bone and Mineral Research,* vol. 9, no. 5, pp. 671-677.

Godfrey, M. & Denby, T. 2004, *Depression and Older People: Towards Securing Well-being in Later Life,* The University of Chicago Press Books, Chicago, USA.

Goeree, E., O`Brien, B. & Pettit, D. 1991, "An assessment of burden of illness due to osteoporosis in Canada", *Journal of the Society of Obstetricians and Gynaecologists of Canada,* vol. 18, pp. 15-24.

Goh, J.C.H., Low, S.L. & DasDe, S. 2004, "Bone mineral density and hip axis length in Singapore's multiracial population", *Journal of Clinical Densitometry,* vol. 7, no. 4, pp. 406-412.

Gordon, A., Lee, F., Franklin, M. & Bradshaw, L. 2014, "Health status of UK care home residents: a cohort study", *Age and Ageing,* vol. 43, no. 1, pp. 97-103.

Greenspan, S.L., Myers, E.R., Kiel, D.P., Parker, R.A., Hayes, W.C. & Resnick, N.M. 1998, "Fall direction, bone mineral density, and function: Risk factors for hip fracture in frail nursing home elderly", *American Journal of Medicine,* vol. 104, no. 6, pp. 539-545.

GRIFFIN, M., RAY, W., FOUGHT, R. & MELTON, L. 1992, "Black-White Differences in Fracture Rates", *American Journal of Epidemiology,* vol. 136, no. 11, pp. 1378-1385.

Grimley Evans, J., Franklin Williams, T., Lynn Beattie, B. & et al 2000, *Oxford Textbook of Geriatric Medicine,* 2nd ed., Oxford University Press, United States Of America (USA).

Grisso, J.A., Chiu, G.Y., Maislin, G., Steinmann, W.C. & Portale, J. 1991, "Risk-Factors for Hip-Fractures in Men - a Preliminary-Study", *Journal of Bone and Mineral Research,* vol. 6, no. 8, pp. 865-868.

Grisso, J.A., Kelsey, J.L., Strom, B.L., Chiu, G.Y., Maislin, G., Obrien, L.A., Hoffman, S. & Kaplan, F. 1991b, "Risk-Factors for Falls as a Cause of Hip Fracture in Women", *New England Journal of Medicine,* vol. 324, no. 19, pp. 1326-1331.

Grisso, J.A., Wishner, A.R., Schwarz, D.F., Weene, B.A., Holmes, J.H. & Sutton, R.L. 1991c, "A Population-Based Study of Injuries in Inner-City Women", *American Journal of Epidemiology,* vol. 134, no. 1, pp. 59-68.

Guideline Development Group 2012, *Osteoporosis: Assessing the Risk of Fragility Fracture*, The Guideline Development Group, Royal College of Physicians, London.

Guideline for Good Clinical Practice-ICH 2016, *Guideline for Good Clinical Practice, ICH Harmonised Tripartite Guideline*. Available: https//www.ich.org/fileadmin/Public_Web_Site/ICH_/E6/E6_R1_Guideline.pdf [2018, November/Sunday].

Guidelines for the Prevention of Falls in Older People 2001, , American Geriatrics Society, British Geriatrics Society, American Academy of Orthopaedic Surgeons, New York, USA.

Gupta, A. 2008, *Measurement Scales Used in Elderly Care*, 1st ed., Radcliffe Publishing Ltd, Oxon, United Kingdom.

Haboubi, N.Y., Hudson, P.R. & Pathy, M.S. 1990, "Measurement of Height in the Elderly", *Journal of the American Geriatrics Society*, vol. 38, no. 9, pp. 1008-1010.

Haddock, C. K., Rindskopf, D., & Shadish, W. R. 1998. “Using odds ratios as effect sizes for meta-analysis of dichotomous data: A primer on methods and issues”. *Psychological Methods*, vol.3, pp. 339–353.

Hajcsar, E.E., Hawker, G. & Bogoch, E.R. 2000, "Investigation and treatment of osteoporosis in patients with fragility fractures", *Canadian Medical Association Journal*, vol. 163, no. 7, pp. 819-822.

Hall, D.M.B. & Stewart-Brown, K. 1998, "Screening in child health", *British Medical Bulletin*, vol. 54, no. 4, pp. 929-943.

Hall, S., Longhurst, S. & Higginson, I.R. 2009, "Challenges to conducting research with older people living in nursing homes", *BMC Geriatrics*, vol. 9, no. 38, pp. 3-10.

Hamilton, E. 2011, *Carers` stress and burnt out. Aged Carer pages1-7*, womenshealth.gov.

Hannan, E.L., Magaziner, J., Wang, J.J., Eastwood, E.A., Silberzweig, S.B., Gilbert, M., Morrison, R.S., McLaughlin, M.N., Orosz, G.M. & Siu, A.L. 2001, "Mortality and locomotion 6 months after hospitalization for hip fracture - Risk factors and risk-adjusted hospital outcomes", *JAMA-Journal of the American Medical Association*, vol. 285, no. 21, pp. 2736-2742.

Hans, D., Durosier, C., Kanis, J.A., Johansson, H., Schott-Pethelaz, A.M. & Krieg, M.A. 2008, "Assessment of the 10-year probability of osteoporotic hip fracture combining clinical risk factors and heel bone ultrasound: the EPISEM prospective cohort of 12,958 elderly women", *Journal of Bone & Mineral Research*, vol. 23, no. 7, pp. 1045-51.

Hans, D., Stenova, E., & Lamy, O 2017, The Trabecular Bone Score (TBS) Complements DXA and the FRAX as a Fracture Risk Assessment Tool in Routine Clinical Practice, *Current Osteoporosis Reports*, vol. 15. Pp. 521- 531

Hanson, J., Gilliam, R. & Lee, T. 2010, "Successful Clinical Trial Research in Nursing Homes: The Improving Decision-Making Study", *Clinical Trials,* vol. 7, no. 6, pp. 735-743.

Harding, M. 2018, "Hip fracture", *Health Information,*.

Harrell, F.E., Lee, K.L. & Mark, D.B. 1996, "Multivariable prognostic models: Issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors", *Statistics in Medicine,* vol. 15, no. 4, pp. 361-387.

Harris, S. & Dawsonhughes, B. 1992, "Rates of Change in Bone-Mineral Density of the Spine, Heel, Femoral-Neck and Radius in Healthy Postmenopausal Women", *Bone and Mineral,* vol. 17, no. 1, pp. 87-95.

Harvey, N., Dennison, E. & Cooper, C. 2008, "Epidemiology of osteoporotic fractures. In: Rosen C,ed.Primer on the metabolic bone diseases and disorders of mineral metabolism." in *Primer on the metabolic diseases and disorders of mineral metabolism*, ed. Rosen C, 7th edn, American Society for Bone Mineral Research, Philadelphia, pp. 198-203.

Hayes, W.C., Myers, E.R., Morris, J.N., Gerhart, T.N., Yett, H.S. & Lipsitz, L.A. 1993, "Impact Near the Hip Dominates Fracture Risk in Elderly Nursing-Home Residents Who Fall", *Calcified Tissue International,* vol. 52, no. 3, pp. 192-198.

Hayes, W.C., Piazza, S.J. & Zysset, P.K. 1991, "Biomechanics of Fracture Risk Prediction of the Hip and Spine by Quantitative Computed Tomography", *Radiologic Clinics of North America,* vol. 29, no. 1, pp. 1-18.

Health Education Authority 1999 1999, *Older People and accidents; Fact sheet 2*, Health Education Authority, London.

Hedlund, R. & Lindgren, U. 1987, "Trauma Type, Age, and Gender as Determinants of Hip Fracture", *Journal of Orthopaedic Research,* vol. 5, no. 2, pp. 242-246.

Hellec, B., Campbell-Scherer, D. & Allan, G.M. 2015, "The skinny on BMI and mortality", *Canadian Family Physician,* vol. 61, no. 11, pp. 970-970.

Hellmeier, U., Patsch, J. M., Baum, T., Burghardt, A. J., & Link, T. M, 2016, Serum miRNA Signatures Are Indicative of Skeletal Fractures in Postmenopausal Women With and Without Type 2 Diabetes and Influence Osteogenic and Adipogenic Differentiation of Adipose Tissue-Derived Mesenchymal Stem Cells in Vitro, *Journal of Bone and Mineral Research*, vol. 31, pp. 2173 – 2192.

Henry, M.J., Pasco, J.A., Merriman, E.N., Zhang, Y., Sanders, K.M., Kotowicz, M.A. & Nicholson, G.C. 2011, "Fracture risk score and absolute risk of fracture", *Radiology,* vol. 259, no. 2, pp. 495-501.

Henry, M.J., Pasco, J.A., Seeman, E., Nicholson, G.C., Sanders, K.M. & Kotowicz, M.A. 2002, "Fracture thresholds revisited. Geelong Osteoporosis Study", *Journal of Clinical Epidemiology,* vol. 55, no. 7, pp. 642-6.

Hill, K., Schwarz, J., Flicker, L. & Carroll, S. 1999, "Falls among healthy, community-dwelling, older women: a prospective study of frequency, circumstances, consequences and prediction accuracy", *Australian and New Zealand Journal of Public Health*, vol. 23, no. 1, pp. 41-48.

Hill, R. 1998, "What sample size is "enough" in internet survey research? Interpersonal Computing and Technology", *An Electronic Journal for the 21st Century*, vol. 6, pp. 3-4.

Hills, D. 1991, *Carer support in the Community HMSO*, London.

Hippisley-Cox, J. & Coupland, C. 2009, "Predicting risk of osteoporotic fracture in men and women in England and Wales: prospective derivation and validation of QFractureScores", *BMJ*, vol. 339.

Holick, M. F., Chen, T. C., 2008, "Vitamin D deficiency: a worldwide problem with health consequences". *American Journal of Clinical Nutrition*, vol. 87, no 4

Holloway, K.L, Kotowicz, M. A, Lane, S. E, Brennan, S. L, & Pasco, J. A, 2015, FRAX (Aus) and falls risk: Association in men and women, *Bone* vol 76, pp. 1 – 4.

Holmberg, A.H., Johnell, O., Nilsson, P.M., Nilsson, J., Berglund, G. & Akesson, K. 2006, "Risk factors for fragility fracture in middle age. A prospective population-based study of 33,000 men and women", *Osteoporosis International*, vol. 17, no. 7, pp. 1065-1077.

Honkanen, R.J., Honkanen, K., Kroger, H., Alhava, E., Tuppurainen, M. & Saarikoski, S. 2000, "Risk factors for premenopausal distal forearm fracture", *Osteoporosis International*, vol. 11, no. 3, pp. 265-270.

Hosmer, D. & Lemeshow, S. 2000, *Applied logistic regression*, 2nd ed. John Wiley & Sons, New York.

House of Commons (HC) 2007, The Electronic Patient Record. Sixth Report of Session 2006-2007. HC 4221. The Stationary Office.

Huang, C., Ross, P.D., Yates, A.J., Walker, R.E., Imose, K., Emi, K. & Wasnich, R.D. 1998, "Prediction of fracture risk by radiographic absorptiometry and quantitative ultrasound: A prospective study", *Calcified Tissue International*, vol. 63, no. 5, pp. 380-384.

Hui, L., Slemenda, W. & Johnston, C. 1998, "Age and bone mass as predictors of fracture in a prospective study", *Journal of Clinical Investigation*, vol. 81, pp. 1804-1809.

I1iffe, S., Patterson, L. & Gould M (ed.) 1998, *Health Care for Older People*, 1st ed., British Medical Journal, London.

Ikeda, M., Ishigaki, T. & Yamauchi, K. 2002, "Relationship between Brier score and area under the binormal ROC curve", *Computer Methods and Programs in Biomedicine*, vol. 67, no. 3, pp. 187-194.

INDEC 2001, *Residential care for older people in Argentina*, INDEC, Buenos Aires, Argentina.

Inelmen, E.M., Sergi, G., Coin, A., Miotto, F., Peruzza, S. & Enzi, G. 2003, "Can obesity be a risk factor in elderly people?", *Obesity reviews : an official journal of the International Association for the Study of Obesity*, vol. 4, no. 3, pp. 147-55.

Industrial Safety & Hygiene News (ISHN), 2017. Typical nursing home reports 100 – 200 patient falls per year. *Nursing Home Abuse Center*. www.nursinghomeabusecenter.org

International Osteoporosis Foundation (IOF) 2018, *Exemplary SEIOMM-UFO programme to improve secondary fracture prevention in Spain*. Available: iofbonehealth.org [2018, May/Sunday].

INVOLVE 2018, *INVOLVE Supporting public involvement in NHS, public health and social care researc*h. Available: http://www.invo.org.uk/resource-centre/libraries/library-of-research-projects/?sh=3&Keyword=ihama [2018, May/Wednesday].

Isaac, S. & Michael B 1995, *Handbook in research and evaluation*, Educational and Industrial Testing Services, San Diego, California.

Jalava, T., Sarna, S., Pylkkanen, L., Mawer, B., Kanis, J.A., Selby, P., Davies, M., Adams, J., Francis, R.M., Robinson, J. & McCloskey, E. 2003, "Association between vertebral fracture and increased mortality in osteoporotic patients", *Journal of Bone and Mineral Research*, vol. 18, no. 7, pp. 1254-1260.

Jamuna, D. 2003, *" Issues of elder care and elder abuse in the Indian context " in Liebig, P. and Irudaya Rajan,S., ed.. An ageing India, Perspectives, prospectives, prospects and policies*, Haworth Press, London.

Janghorbani, M., Van Dam, R.M., Willett, W.C. & Hu, F.B. 2007, "Systematic review of type 1 and type 2 diabetes mellitus and risk of fracture", *American Journal of Epidemiology*, vol. 166, no. 5, pp. 495-505.

Jarnlo, G. 2003, "Functional balance tests related to falls among elderly people living in the community", *European Journal of Geriatrics*, vol. 5, pp. 7-14.

Joakimsen, R.M., Fonnebo, V., Magnus, J.H., Tollan, A. & Sogaard, A.J. 1998, "The Tromso Study: Body height, body mass index and fractures", *Osteoporosis International*, vol. 8, no. 5, pp. 436-442.

Johansson, H., Oden, A., Johnell, O., Jonsson, B., de Laet, C., Oglesby, A., McCloskey, E.V., Kayan, K., Jalava, T. & Kanis, J.A. 2004, "Optimization of BMD measurements to identify high risk groups for treatment - A test analysis", *Journal of Bone and Mineral Research*, vol. 19, no. 6, pp. 906-913.

Johnell, O. & Kanis, J.A. 2004, "An estimate of the worldwide prevalence, mortality and disability associated with hip fracture", *Osteoporosis International*, vol. 15, no. 11, pp. 897-902.

Johnell, O. & Kanis, J.A. 2006, "An estimate of the worldwide prevalence and disability associated with osteoporotic fractures", *Osteoporosis International*, vol. 17, no. 12, pp. 1726-1733.

Johnell, O. 1997, "The socioeconomic burden of fractures: today and in the 21st century.", *The American Journal of Medicine,* vol. 103, no. 2A, pp. 20S-25S; discussion 25S-26S.

Johnell, O. 2005, "Review: no single physical examination sign rules in or out osteoporosis or spinal fracture", *Evidence Based Medicine,* vol. 10, no. 4, pp. 123-124.

Johnell, O., Borgstrom, F., Jonsson, B. & Kanis, J. 2007, "Latitude, socioeconomic prosperity, mobile phones and hip fracture risk", *Osteoporosis International,* vol. 18, no. 3, pp. 333-337.

Johnell, O., Gullberg, B., Allander, E., Kanis, J.A., Dilzen, G., Gennari, C., Lopezvaz, A.A., Lyritis, G., Mazzuoli, G.F., Miravet, L., Passeri, M., Perezcano, R., Rapado, A., Ribot, C., Dequeker, J., Loew, D., Khaltaev, N. & Pluss, M. 1992, "The Apparent Incidence of Hip Fracture in Europe - a Study of National Register Sources", *Osteoporosis International,* vol. 2, no. 6, pp. 298-302.

Johnell, O., Gullberg, B., Kanis, J.A., Allander, E. & Elefors, L. 1995, "Risk-Factors for Hip-Fractures in European Women", *Journal of Bone and Mineral Research,* vol. 10, pp. S504-S504.

Johnell, O., Kanis, J.A., Jonsson, B., Oden, A., Johansson, H. & De Laet, C. 2005, "The burden of hospitalised fractures in Sweden", *Osteoporosis International,* vol. 16, no. 2, pp. 222-228.

Jones, G., Nguyen, T., Sambrook, P.N., Kelly, P.J., Gilbert, C. & Eisman, J.A. 1994, "Symptomatic Fracture Incidence in Elderly Men and Women - the Dubbo-Osteoporosis-Epidemiology-Study (Does)", *Osteoporosis International,* vol. 4, no. 5, pp. 277-282.

Jones, S., Carley, S. & Harrison, M. 2004 , *An introduction to power and sample size estimatio*n. Available: http://dx.doi.org/10.1136/emj.20.5.453 [2018, June/Thursday].

Jonsson, B. 1998, "Targeting high-risk populations", *Osteoporosis International,* vol. 8, pp. S13-S16.

Julious, S.A. 2005, "Sample size of 12 per group rule of thumb for a pilot study", *Pharmaceutical Statistics,* vol. 4, no. 4, pp. 287-291.

Kaasalainen, S., Williams, J., Hadjistavropoulos, T., Thorpe, L., Whiting, S., Neville, S. & Tremeer, J. 2010, "Creating Bridges Between Researchers and Long-Term Care Homes to Promote Quality of Life for Residents", *Qualitative Health Research,* vol. 20, no. 12, pp. 1689-1704.

Kado, D.M., Browner, W.S., Palermo, L., Nevitt, M.C., Genant, H.K., Cummings, S.R. & Study Osteoporotic Fractures Res Grp 1999, "Vertebral fractures and mortality in older women - A prospective study", *Archives of Internal Medicine,* vol. 159, no. 11, pp. 1215-1220.

Kalilani, L., Asgharnejad, M., Palokangas, T. & Durgin, T. 2016, "Comparing the Incidence of Falls/Fractures in Parkinson's Disease Patients in the US Population", *Plos One,* vol. 11, no. 9, pp. e0161689.

Kane, R.S., Burns, E.A. & Goodwin, J.S. 1995, "Minimal Trauma Fractures in Older Nursing-Home Residents - the Interaction of Functional Status, Trauma, and Site of Fracture", *Journal of the American Geriatrics Society,* vol. 43, no. 2, pp. 156-159.

Kanis, J.A., Johnell, O., Oden, A., Dawson, A., De Laet, C., & Jonsson, B. 2001, Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds, *Osteoporosis International,* vol. 12, pp. 989-995

Kanis , J., Johnell, O., Oden, A., De Laet, C., Jonsson, B. & Dawson, A. 2001, "Ten year risk of osteoporotic fracture and the effect of risk factors on screening strategies", *Bone,* vol. 30, no. 1, pp. 251-258.

Kanis, J. 2007, *ASSESSMENT OF OSTEOPOROSIS AT THE PRIMARY HEALTH CARE LEVEL*
Report of a WHO Scientific Group, World Health Organisation, Sheffield, UK.

Kanis, J. 2012, "European guidance for the diagnosis and management of osteoporosis in postmenopausal women (On behalf of the Scientific Advisory Board of ESCEO and the Committee of Scientific Advisors of IOF)", *Osteoporosis International,*

Kanis, J., Johnell, O., Gullberg, B., Allander, E., Elffors, L., Ranstam, J., Dequeker, J., Dilsen, G., Gennari, C., Vaz, A.L., Lyritis, G., Mazzuoli, G., Miravet, L., Passeri, M., Cano, R.P., Rapado, A. & Ribot, C. 1999, "Risk factors for hip fracture in men from Southern Europe: The MEDOS study", *Osteoporosis International,* vol. 9, no. 1, pp. 45-54.

Kanis, J.A. 2002, "Diagnosis of osteoporosis and assessment of fracture risk", *Lancet,* vol. 359, no. 9321, pp. 1929-36.

Kanis, J.A. 2002, "Assessing the risk of vertebral osteoporosis", *Singapore Medical Journal,* vol. 43, no. 2, pp. 100-5.

Kanis, J.A., Borgstrom, F., De Laet, C., Johansson, H., Johnell, O., Jonsson, B., Oden, A., Zethraeus, N., Pfleger, B. & Khaltaev, N. 2005, "Assessment of fracture risk", *Osteoporosis International,* vol. 16, no. 6, pp. 581-589.

Kanis, J.A., Burlet, N., Cooper, C., Delmas, P.D., Reginster, J.-., Borgstrom, F., Rizzoli, R. & European Soc Clin & Econ Aspects O 2008, "European guidance for the diagnosis and management of osteoporosis in postmenopausal women (vol 19, p 399, 2008)", *Osteoporosis International,* vol. 19, no. 7, pp. 1103-1104.

Kanis, J.A., Johansson, H., & Johnell, O., 2005b, Alcohol intake as a risk factor for fracture, *Osteoporosis International,* vol. 16 pp. 737 - 742

Kanis, J.A., Johnell, O., & Oden, A., 2005a, Smoking and fracture risk: a meta-analysis, *Osteoporosis International,* vol. 16, pp. 155 – 162

Kanis, J.A., Johansson, H., Oden, A., Johnell, O., De Laet, C., Eisman, J.A., McCloskey, E.V., Mellstrom, D., Melton, L.J., Pols, H.A.P., Reeve, J., Silman, A.J. & Tenenhouse, A. 2004, "A family history of fracture and fracture risk: a meta-analysis", *Bone,* vol. 35, no. 5, pp. 1029-1037.

Kanis, J.A., Johnell, O., Oden, A., Dawson, A., De Laet, C. & Jonsson, B. 2001, "Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds", *Osteoporosis International,* vol. 12, no. 12, pp. 989-995.

Kanis, J.A., Johnell, O., Oden, A., Johansson, H. & McCloskey, E. 2008, "FRAX and the assessment of fracture probability in men and women from the UK", *Osteoporosis International,* vol. 19, no. 4, pp. 385-97.

Kanis, J.A., McCloskey, E.V., Johansson, H., Cooper, C., Rizzoli, R., Reginster, J., ESCEO & IOF 2013, "European guidance for the diagnosis and management of osteoporosis in postmenopausal women", *Osteoporosis International,* vol. 24, no. 1, pp. 23-57.

Kanis, J.A., Oden, A., Johansson, H. & McCloskey, E. 2012, "Pitfalls in the external validation of FRAX", *Osteoporosis International,* vol. 23, no. 2, pp. 423-431.

Kanis, J.A., Oden, A., Johnell, O., De Laet, C., Jonsson, B. & Oglesby, A.K. 2003, "The components of excess mortality after hip fracture", *Bone,* vol. 32, no. 5, pp. 468-473.

Kanis, J.A., Oden, A., McCloskey, E.V., Johansson, H., Wahl, D.A., Cooper, C. & IOF Working Grp Epidemiology Quali 2012, "A systematic review of hip fracture incidence and probability of fracture worldwide", *Osteoporosis International,* vol. 23, no. 9, pp. 2239-2256.

Kanis, J.A., Svedbom, A., Harvey, N. & McCloskey, E.V. 2014, "The Osteoporosis Treatment Gap", *Journal of Bone and Mineral Research,* vol. 29, no. 9, pp. 1926-1928.

Kanis,J.A et al on behalf of the Scientific Advisory Board of ESCEO and the Committee of Scientific Advisors of IOF 2013, "European guidance for the diagnosis and management of osteoporosis in postmenopausal women", *Osteoporosis International,* vol. 24,no1,pp 23-57.

Kannus, P., Palvanen, M., Kaprio, J., Parkkari, J. & Koskenvuo, M. 1999, "Genetic factors and osteoporotic fractures in elderly people: prospective 25 year follow up of a nationwide cohort of elderly Finnish twins", *British Medical Journal,* vol. 319, no. 7221, pp. 1334-1337.

Karakusevic, S. 2016, *Understanding patient flow in hospital*, Nuffield Trust, London.

Karampampa,K., Andersson,S., Drefahl,S., Ahlbom, A., & Modig, K 2014, Does improved survival lead to a more fragile population : time trends in second and third hospital admissions among men and women above the age of 60 in Sweden. *PloS One,* vol. 9. P.e99034.

Katz, P.R. 2011, "An International Perspective on Long Term Care: Focus on Nursing Homes", *Journal of the American Medical Directors Association,* vol. 12, no. 7, pp. 487-492.

Katz, P.R., Karuza, J. & Counsell, S.R. 1995, "Academics and the Nursing-Home", *Clinics in Geriatric Medicine,* vol. 11, no. 3, pp. 503-516.

Keegan, T.H.M., Kelsey, J.L., King, A.C., Quesenberry, C.P. & Sidney, S. 2004, "Characteristics of fallers who fracture at the foot, distal forearm, proximal humerus, pelvis, and shaft of the tibia/fibula compared with fallers who do not fracture", *American Journal of Epidemiology,* vol. 159, no. 2, pp. 192-203.

Kerr, G.K., Worringham, C.J., Cole, M.H., Lacherez, P.F., Wood, J.M. & Silburn, P.A. 2010, "Predictors of future falls in Parkinson disease", *Neurology,* vol. 75, no. 2, pp. 116-124.

Khan Academy 2018, *Identifying outliers with the 1.5 X IQR rul*e. Available: https://www.khanacademy.org/about/our-content-specialist [2018, June/Thursday].

Khan K 2003, *Systematic reviews to support evidenced-based medicine; How to review and apply findings of healthcare research*, Royal Society of Medicine, London.

Khatib, R., Santesso, N., Pickard, L., Osman, O., Giangregorio, L., Skidmore, C. & Papaioannou, A. 2014, "Fracture risk in long term care: a systematic review and meta-analysis of prospective observational studies", *BMC Geriatrics,* vol. 14, pp. 130.

Kiely, D.K., Kiel, D.P., Burrows, A.B. & Lipsitz, L.A. 1998, "Identifying nursing home residents at risk for falling", *Journal of the American Geriatrics Society,* vol. 46, no. 5, pp. 551-555.

King's Fund 2016, *Deficits in the NHS*, King's Fund, London.

Kinsella, K.T., C 1993, *An aging world II, International Population Reports P95/92-3*, US Department of Commerce, Bureau of the Census, Washington DC.

Kinsella, K.T., C 1993, *An aging world II, International Population Reports P95/92-3*, US Department of Commerce, Bureau of the Census, Washington DC.

Klotzbuecher, C.M., Ross, P.D., Landsman, P.B., Abbott, T.A. & Berger, M. 2000, "Patients with prior fractures have an increased risk of future fractures: A summary of the literature and statistical synthesis", *Journal of Bone and Mineral Research,* vol. 15, no. 4, pp. 721-739.

Kobayashi, M. & Usuda, S. 2016, "Development of a clinical assessment test of 180-degree standing turn strategy (CAT-STS) and investigation of its reliability and validity", *Journal of Physical Therapy Science,* vol. 28, no. 2, pp. 646-653.

Kocijan, R., Muschitz, C., Geiger, E., Skalicky,. S., Baierl, A., Dormann,. R., Plachel,. F., Feichtinger, X., Heimel, P., & Fahrieitner-Pammer, A., 2016, “Circulating microRNA Signatures in Patients With Idiopathic and Postmenopausal Osteoporosis and Fragility Fractures”, *The Journal of Clinical Endocrinology & Metabolism,*vol. 101., no. 11., pp. 4125- 4134.

Kontis, V., Bennett, J.E., Mathers, C.D., Li, G., Foreman, K. & Ezzati, M. 2017, "Future life expectancy in 35 industrialised countries: projections with a Bayesian model ensemble.", *Lancet (London, England), .*

Koops, L. & Lindley, R. 2002, "Thrombolysis For Acute Ischaemic Stroke: Consumer Involvement in Design Of New Randomised Controlled Trial", *British medical journal,* vol. 325, no. 7361, pp. 415-417.

Kotowicz, M.A., Melton, L.J., Cooper, C., Atkinson, E.J., O'Fallon, W.M. & Riggs, B.L. 1994, "Risk of Hip Fracture in Women with Vertebral Fracture", *Journal of Bone and Mineral Research,* vol. 9, no. 5, pp. 599-605.

Kwong, E., Lai, C. & Liu, F. 2014, "Quality of life in nursing home settings: Perspectives from elderly residents with frailty", *Clinical Nursing Studies,* vol. 2, no. 1, pp. 100-110.

LaFleur, J., McAdam-Marx, C., Kirkness, C. & Brixner, D.I. 2008, "Clinical risk factors for fracture in postmenopausal osteoporotic women: A review of the recent literature", *Annals of Pharmacotherapy,* vol. 42, no. 3, pp. 375-386.

Lalkhen, A. & McCluskey, A. 2008, "Clinical tests: sensitivity and specificity", *Continuing Education in Anaesthesia Critical Care & Pain,* vol. 8, no. 6, pp. 221-223.

Lamb, S.E., Jorstad-Stein, E.C., Hauer, K., Becker, C. & Prevention Falls Network Europe & 2005, "Development of a common outcome data set for fall injury prevention trials: The prevention of falls network Europe consensus", *Journal of the American Geriatrics Society,* vol. 53, no. 9, pp. 1618-1622.

LaMorte W, *The Difference Between "Probability" and "Odds"*. Available: http:sphweb.bumc.bu.edu/otIt/MPH-Modules/BS/BS704_Confidence_Intervals/BS7 [2018, May/Saturday].

Langsetmo, L., Nguyen, T.V., Nguyen, N.D., Kovacs, C.S., Prior, J.C., Center, J.R., Morin, S., Josse, R.G., Adachi, J.D., Hanley, D.A., Eisman, J.A. & Canadian, M.,Group 2011, "Independent external validation of nomograms for predicting risk of low-trauma fracture and hip fracture", *CMAJ Canadian Medical Association Journal,* vol. 183, no. 2, pp. E107-14.

Latham, N.K., Anderson, C.S., Lee, A., Bennett, D.A., Moseley, A., Cameron, I.D. & Fitness Collaborative Grp 2003, "A randomized, controlled trial of quadriceps resistance exercise and Vitamin D in frail older people: The Frailty Interventions Trial in Elderly Subjects (FITNESS)", *Journal of the American Geriatrics Society,* vol. 51, no. 3, pp. 291-299.

Lau, E.M.C. & Cooper, C. 1996, "The epidemiology of osteoporosis - The Oriental perspective in a world context", *Clinical Orthopaedics and Related Research,* , no. 323, pp. 65-74.

Laupacis, A., Sekar, N. & Stiell, I.G. 1997, "Clinical prediction rules - A review and suggested modifications of methodological standards", *JAMA-Journal of the American Medical Association,* vol. 277, no. 6, pp. 488-494.

Lauritzen, J.B., Petersen, M.M. & Lund, B. 1993, "Effect of External Hip Protectors on Hip-Fractures", *Lancet,* vol. 341, no. 8836, pp. 11-13.

Lauritzen, J.B., Schwarz, P., Lund, B., McNair, P., Transbol, I., 1993 Changing incidence and residual lifetime risk of common osteoporosis-related fractures. *Osteoporos International* vol. 3, pp. 127-132.

Last, A., 2004, Relative risks and odds ratios: What`s the difference? *MDedge Family Medicine* vol. 53, no. 2 pp. 108

Law, M., Withers, H., Morris, J. & Anderson, F. 2006, "Vitamin D supplementation and the prevention of fractures and falls: results of a randomised trial in elderly people in residential accommodation", *Age and Ageing,* vol. 35, no. 5, pp. 482-486.

Leary, S. 2005, TheNorth East Lincolnshire Falls Prevention Collaborative. https://www.service4.me.uk/kb5/nelincs/asch/service.page?id=Sw-2VPze5II

Leslie, W.D. & Lix, L.M. 2014, "Comparison between various fracture risk assessment tools", *Osteoporosis International,* vol. 25, no. 1, pp. 1-21.

Leslie, W.D., Lix, L.M., Wu, X. & Manitoba Bone Density Program 2013, "Competing mortality and fracture risk assessment", *Osteoporosis International,* vol. 24, no. 2, pp. 681-688.

Leys, C 2018. Risks to the NHS when referring to private hospitals. *Centre for Health and Public Interest.*

Lievesley, N. & Crosby, G. 2011, *The changing role of care homes*, Bupa and Centre for Policy on Ageing, London.

Lillholm, M., Ghosh, A., Pettersen, P.C., de Bruijne, M., Dam, E.B., Karsdal, M.A., Christiansen, C., Genant, H.K. & Nielsen, M. 2011, "Vertebral fracture risk (VFR) score for fracture prediction in postmenopausal women", *Osteoporosis International,* vol. 22, no. 7, pp. 2119-2128.

Lin, C., Liao, K. & Pu, J. 2011, "Associated Factors for falls among the Community-Dwelling Older People assessed by Annual Geriatric Health Examinations", *Plos One,* .

Lincolnshire County Council 2015, The Wellbeing Service. (URL=/health-andwellbeing/the-wellbeing-service/access-the wellbeing-service/124175.article)

Linnane, E., Paul, A. & Parry, R. 1999, "Screening of new-born infants for cholestatic hepatobiliary disease - Does test fulfil screening criteria?", *British Medical Journal,* vol. 319, no. 7222, pp. 1435-1436.

Lips, P., Karpf, D., Seeman, E., Cooper, C., Black, D., Johnell, O., Lyons, A., Cummings, S., Slemenda, C. & Ross, P. 1997, "Epidemiology and predictors of fractures associated with osteoporosis", *American Journal of Medicine,* vol. 103, no. 2, pp. 3S-11S.

Lippuner, K, von Overbeck, J., Perrelet, R., Bosshard, H., & Jaeger, P 1997. Incidence and direct costs of hospitalisation due to osteoporotic fractures in Switzerland. *Osteoporosis International,* vol. 7 pp. 414 – 425.

Little, R. & Rubin, D. 1987, *Statistical Analysis with Missing Data,* Wiley, New York.

Lobo, J., Jimenez-Valverde, A. & Real, R. 2008, "AUC: a misleading measureof the predictive performance of predictive distribution models", *Global Ecology and Biogeography*, vol. 17, pp. 145-151.

Local Government Association (LGA) 2018 , *Hospital admissions due to falls by older people set to reach nearly 1000 a day*. Available: http://www.local.gov.uk/about/news/hospital-admissions-due-falls-older-people-set-reach-nearly-1000-day [2018, May/Friday].

Looker, A.C., Orwoll, E.S., Johnston, C.C., Lindsay, R.L., Wahner, H.W., Dunn, W.L., Calvo, M.S., Harris, T.B. & Heyse, S.P. 1997, "Prevalence of low femoral bone density in older US adults from NHANES III", *Journal of Bone and Mineral Research*, vol. 12, no. 11, pp. 1761-1768.

Lord, S.R., Mclean, D. & Stathers, G. 1992, "Physiological Factors Associated with Injurious Falls in Older-People Living in the Community", *Gerontology*, vol. 38, no. 6, pp. 338-346.

Lubitz, J., Cai, L.M., Kramarow, E. & Lentzner, H. 2003, "Health, life expectancy, and health care spending among the elderly", *New England Journal of Medicine*, vol. 349, no. 11, pp. 1048-1055.

Luff, R., Ferreira, Z. & Meyer, J. 2011, *Improving the evidence base for adult social care practic*e, National Institute for Health Research, London.

Luthje, P. 1985, "Incidence of Hip Fracture in Finland - a Forecast for 1990", *Acta Orthopaedica Scandinavica*, vol. 56, no. 3, pp. 223-225.

Luthje, P. 1991, The incidence of hip fractures in Finland in the year 2000, *Acta Orthopaedica Scandinavia*, vol 62, sppl. 241, pp. 35-37.

Luukinen, H., Koski, K., Hiltunen, L. & Kivela, S.L. 1994, "Incidence Rate of Falls in an Aged Population in Northern Finland", *Journal of Clinical Epidemiology*, vol. 47, no. 8, pp. 843-850.

Lyles, K.W., Schenck, A.P. & Colon-Emeric, C.S. 2008, "Hip and other osteoporotic fractures increase the risk of subsequent fractures in nursing home residents", *Osteoporosis International*, vol. 19, no. 8, pp. 1225-1233.

Maalouf, G., Gannage-Yared, M.H., Ezzedine, J., Larijani, B., Badawi, S., Rached, A., Zakroui, L., Masri, B., Azar, E., Saba, E., Nammari, R., Adib, G., Abou Samra, H., Alrawi, Z., Salman, S., El Muntasser, K., Tarseen, R., El Kharousi, W., Al-Lamki, M., Alothman, A.N., Almarzook, N., El Dessouki, M., Sulaimani, R., Saleh, J., Suhaili, A.R., Khan, A., Delmas, P. & Seeman, E. 2007, "Middle East and North Africa consensus on osteoporosis", *Journal of Musculoskeletal & Neuronal Interactions*, vol. 7, no. 2, pp. 131-143.

Maas, M.L., Kelley, L.S., Park, M. & Specht, J.R. 2002, "Issues in conducting research in nursing homes", *Western Journal of Nursing Research*, vol. 24, no. 4, pp. 373-389.

Magaziner, J., Hawkes, W., Hebel, J.R., Zimmerman, S.I., Fox, K.M., Dolan, M., Felsenthal, G. & Kenzora, J. 2000, "Recovery from hip fracture in eight areas of function", *Journals*

of Gerontology Series A-Biological Sciences and Medical Sciences, vol. 55, no. 9, pp. M498-M507.

Magaziner, J., Simonsick, E.M., Kashner, T.M., Hebel, J.R. & Kenzora, J.E. 1989, "Survival Experience of Aged Hip Fracture Patients", *American Journal of Public Health*, vol. 79, no. 3, pp. 274-278.

Maggi, S., Kelsey, J.L., Litvak, J. & Heyse, S.P. 1991, "Incidence of hip fractures in the elderly: a cross-national analysis.", *Osteoporosis International : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*, vol. 1, no. 4, pp. 232-41.

Mallett, S., Royston, P., Dutton, S., Waters, R. & Altman, D.G. 2010, "Reporting methods in studies developing prognostic models in cancer: a review", *BMC Medicine*, vol. 8, pp. 20.

Manel, S., Williams, H.C. & Ormerod, S.J. 2001, "Evaluating presence-absence models in ecology: the need to account for prevalence", *Journal of Applied Ecology*, vol. 38, no. 5, pp. 921-931.

March, L., Chamberlain, A. & Cameron, L. 1996, *Prevention, treatment and Rehabilitation of femoral neck of femur fracture. Report from the Northern Sydney Area*, Sydney.

Marks, R. 2010. Hip fracture epidemiological trends, outcomes, and risk factors 1970-2009. *International Journal of General Medicine*, vol.3 pp. 1-17.

Marottoli, R.A., Berkman, L.F. & Cooney, L.M. 1992, "Decline in Physical Function Following Hip Fracture", *Journal of the American Geriatrics Society*, vol. 40, no. 9, pp. 861-866.

Marshall, D., Johnell, O. & Wedel, H. 1996, "Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures", *BMJ*, vol. 312, no. 7041, pp. 1254-9.

Martin, J., Meltzer, H. & Elliot, D. 1998, *Prevalence of Disability among Adults*, Her Majesty`s Stationary Office (HMSO), London.

Maslach, C., Jackson, S. & Leiter, M. 1986, *Maslach Burnout Inventory Manual*, 2nd edn, Consulting Psychologists Press, Palo, Alto, California.

McClung, M.R., Geusens, P., Miller, P.D., Zippel, H., Bensen, W.G., Roux, C., Adami, S., Fogelman, I., Diamond, T., Eastell, R., Meunier, P.J., Reginster, J.Y., Wasnich, R.D., Greenwald, M., Kaufman, J., Chestnut, C.H. & Hip Intervention Program Study Grp 2001, "Effect of risedronate on the risk of hip fracture in elderly women", *New England Journal of Medicine*, vol. 344, no. 5, pp. 333-340.

McCrum-Gardner, E. 2010, "Sample size and power calculations made simple", *International Journal of Therapy and Rehabilitation*, vol. 17, no. 1, pp. 10-14.

McGrother, C.W., Donaldson, M.M., Clayton, D., Abrams, K.R. & Clarke, M. 2002, "Evaluation of a hip fracture risk score for assessing elderly women: the Melton

Osteoporotic Fracture (MOF) study", *Osteoporosis International,* vol. 13, no. 1, pp. 89-96.

McLellan, A. 2003, *Effectiveness of Strategies for the secondary Prevention of Osteoporotic Fractures In Scotland*, NHS Quality Improvement Scotland, Scotland.

McPherson, J.M., Jetz, W. & Rogers, D.J. 2004, "The effects of species' range sizes on the accuracy of distribution models: ecological phenomenon or statistical artefact?", *Journal of Applied Ecology,* vol. 41, no. 5, pp. 811-823.

MEDCALC 2018, *MEDCALC. Easy-to-use statistical softwar*e. Available: https://www.medcalc.org/calc/diagnostic_test.php [2018, May/Thursday].

Medical Research Council (MRC) 2008, *Developing and Evaluating Complex Interventions: new Guidance*., Medical Research Council (MRC), London.

Meeta, Digumarti, L., Agarwal, N., Vaze, N., Shah, R. & Malik, S. 2013, "Clinical practice guidelines on menopause: An executive summary and recommendations.", *Journal of Mid-Life Health,* vol. 4, no. 2, pp. 77-106.

Melton, L.J. 1993, "Hip-Fractures - a Worldwide Problem Today and Tomorrow", *Bone,* vol. 14, pp. S1-S8.

Melton,L.J III., Atkinson,A.J., O`Connor,M.K., O`fallon, W.M., & Lawrence Riggs, B 2009. Determinants of Bone Loss from the Femoral Neck in Women of Different Ages. *Journal of Bone and Mineral Research,* vol. 15, no. 1 (http://doi.org/10.1359/jbmr.2000.15.1.24)

Melton, L & Cooper C. 2001. In Osteoporosis 2nd edn. Vol. 1 (eds Marcus, R., Feldman, D. & Kelsey, J.) 557 – 567 (Academic Press, San Diego.)

Melton, L.J. 2003, "Adverse outcomes of osteoporotic fractures in the general population", *Journal of Bone and Mineral Research,* vol. 18, no. 6, pp. 1139-1141.

Melton, L.J., Ilstrup, D.M., Riggs, B.L. & Beckenbaugh, R.D. 1982, "50-Year Trend in Hip Fracture Incidence", *Clinical Orthopaedics and Related Research,* , no. 162, pp. 144-149.

Memon, A., Pospula, W.M., Tantawy, A.Y., Abdul-Ghafar, S., Suresh, A. & Al-Rowaih, A. 1998, "Incidence of hip fracture in Kuwait", *International Journal of Epidemiology,* vol. 27, no. 5, pp. 860-865.

Mentes, J.C. & Tripp-Reimer, T. 2002, "Barriers and facilitators in nursing home intervention research", *Western Journal of Nursing Research,* vol. 24, no. 8, pp. 918-936.

Metz, C.E. 1978, "Basic Principles of Roc Analysis", *Seminars in Nuclear Medicine,* vol. 8, no. 4, pp. 283-298.

Meyer, H.E., Tverdal, A. & Falch, J.A. 1993, "Risk-Factors for Hip Fracture in Middle-Aged Norwegian Women and Men", *American Journal of Epidemiology,* vol. 137, no. 11, pp. 1203-1211.

Mills, H.J., Horne, G 1985. Fractures of the proximal humerus in adults. *The Journal of Trauma and Acute Care Surgery.* Vol. 25, pp. 801 - 805

Mithal A, E.P. 2013, *THE ASIA-PACIFIC REGIONAL AUDIT Epidemiology, costs & burden of osteoporosis in 2013*, International Osteoporosis Foundation, Switzerland.

Mithal, A. & Lau E 2010, *The Asian Audit. Epidemiology, costs and burden of osteoporosis in Asia 2009*, International Osteoporosis Foundation, Nyon, Switzerland.

Mithal, A. & Lau, E. 2009, *The Asian Audit Epidemiology, costs and burden of osteoporosis in Asia 2009*, International Osteoporosis Foundation, Switzerland.

Modig,K., Andersson,T., & Drefahl, A. 2013 age-Specific trends in morbidity, mortality and case-fatality from cardiovascular diseases, myocardial infarction and stroke in advanced age; evaluation in the Swedish population. *PloS One,* vol.8 p.e64928

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G. & PRISMA Grp 2010, "Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement", *International Journal of Surgery,* vol. 8, no. 5, pp. 336-341.

Moons, K.G.M. 2010, "Criteria for Scientific Evaluation of Novel Markers: A Perspective", *Clinical Chemistry,* vol. 56, no. 4, pp. 537-541.

Moons, K.G.M., Donders, R.A.R.T., Stijnen, T. & Harrell Jnr, F.E. 2006, "Using the outcome for imputation of missing predictor values was preferred", *Journal of Clinical Epidemiology,* vol. 59, no. 10, pp. 1092-1101.

Moons, K.G.M., Kengne, A.P., Woodward, M., Royston, P., Vergouwe, Y., Altman, D.G. & Grobbee, D.E. 2012, "Risk prediction models: I. Development, internal validation, and assessing the incremental value of a new biomarker", *Heart,* vol. 98, no. 9, pp. 683-690.

Moons, K.G.M., Royston, P., Vergouwe, Y., Grobbee, D.E. & Altman, D.G. 2009, "Prognosis and prognostic research: what, why, and how?", *British Medical Journal,* vol. 338, pp. b375.

Moons, K.G.M., van Es, G.A., Michel, B.C., Buller, H.R., Habbema, J.D.F. & Grobbee, D.E. 1999, "Redundancy of single diagnostic test evaluation", *Epidemiology,* vol. 10, no. 3, pp. 276-281.

Morales-Torres, J., Gutierrez-Urena, S. & PANLAR 2004, "The burden of osteoporosis in Latin America", *Osteoporosis International,* vol. 15, no. 8, pp. 625-632.

Moran, C., Lecky, F., Bouamra, O., Lawrence, T., Edwards, A., & Woodford, M. 2018. Changing the System – major Trauma patients and their Outcomes in the NHS (England), *Research Paper,* vol. 2, pp. 13-21

Morrison, R.S., Magaziner, J., McLaughlin, M.A., Orosz, G., Silberzweig, S.B., Koval, K.J. & Siu, A.L. 2003, "The impact of post-operative pain on outcomes following hip fracture", *Pain,* vol. 103, no. 3, pp. 303-311.

Morse, J 1994. Preventing Patient Falls. London: Sage

Murray, C. & Lopez, A. 1996, *Global and regional descriptive epidemiology of disability: Incidence, prevalence, health expectances and years lived with disability. In: Murray C, Lopez A., eds. The Global Burden of Diseases*, World Health Organisation, Switzerland.

Murray, C.J.L., Ezzati, M., Flaxman, A.D., Lim, S., Lozano, R., Michaud, C., Naghavi, M., Salomon, J.A., Shibuya, K., Vos, T., Wikler, D. & Lopez, A.D. 2012, "GBD 2010: design, definitions, and metrics", *Lancet*, vol. 380, no. 9859, pp. 2063-2066.

Nakamura, K., Oyama, M., Takahashi, S., Yoshizawa, Y., Kobayashi, R., Oshiki, R., Saito, T. & Tsuchiya, Y. 2010, "Fracture incidence in nursing homes in Japan", *Osteoporosis International*, vol. 21, no. 5, pp. 797-803.

National Center for Health Statistics (NCHS) 2004, *Trend tables on 65 and older population*, National Center for Health Statistics (NCHS), USA.

National Institute for Clinical Excellence (NICE) 2012, *Individual research recommendation detail*s, National Institute for Clinical Excellence, London.

National Institute for Clinical Excellence (NICE) 2012b, *Osteoporosis: fragility fracture risk Short clinical guideline- CG146*, National Institute for Health and Clinical Excellence, London.

National Institute for Health and Care Excellence 2008, *Guide to methods of Technology Appraisal*, National Institute for Health and Care Excellence, London.

National Institute for Health and Care Excellence 2014, *Falls-risk assessment*, National Institute for Health and Care Excellence, London.

National Institute for Health and Clinical Excellence (NICE) 2011, *Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (amended) NICE technology appraisal guidance 161 (amended)*, National Institute for Health and Clinical Excellence, London.

National Institute for Health and Clinical Excellence (NICE) 2014, *Hip Fracture : Management NICE guidelines (CG124*), 2014th ed., NICE, London.

National Institute for Health and Clinical Excellence 2016. Osteoporosis- Prevention of fragility fractures (/guidance/cg146)

National Institute for Health and Clinical Excellence 2018, NICE impact falls and fragility fractures. www.nice.org.uk

National Institute for Health Research (NIRH). The ENRICH toolkit. Enabling Research in Care Homes: a simple guide for researchers, care home staff and residents. http://www.enrich.dendron.nihr.ac.uk/

National Institute for Health Research (NIHR) 2016, *Understanding Care Homes*, National Institute for Health Research, London.

National Osteoporosis Guideline Group (NOGG) 2018, *Guideline for the diagnosis and management of osteoporosis in postmenopausal men and women from the age of 50 in the UK*, National Osteoporosis Guideline Group, London. (https://www.sheffield.ac.uk/NOGG/)

National Osteoporosis Foundation, 2008, Clinician`s guide to prevention and treatment of osteoporosis. http;//www.nof.org/professionals/cliniciansguide-form.asp

National Osteoporosis Society (NOS) 2013, *Vitamin D and Bone Health. A Practical Clinical Guideline for Patient Management*, National Osteoporosis Society, Camerton, Bath, UK.

Navarro-Valverde, C., Caballero-Villarraso, J., Mata-Granados, J. M., Casado-Diaz, A, Sosa-Henriquez, M, Malouf-Sirra,J., Nogues-Solan, X., Rodriguez-Manas, L., Cortes-Gil, X, Delgadillo-Duarte, J, & Quesada-Gomez, J 2017, "High Serum as a Relevant Contributor to low Bone Mineral Density in Postmenopausal Osteoporotic Women", *Calcified Tissue International*, vol. 102, pp. 651- 656

Nayak, S., Edwards, D.L., Saleh, A.A. & Greenspan, S.L. 2014, "Performance of risk assessment instruments for predicting osteoporotic fracture risk: a systematic review", *Osteoporosis International*, vol. 25, no. 1, pp. 23-49.

Nelson, H.D., Haney, E.M., Dana, T., Bougatsos, C. & Chou, R. 2010, "Screening for Osteoporosis: An Update for the US Preventive Services Task Force", *Annals of Internal Medicine*, vol. 153, no. 2, pp. 99-W43.

Netten, A., Darton, R. & Curtis, L. 2002, *Self-Funded Admissions to Care Homes.*, Personal Social Services Research Unit.

Netter, A., Beadle-Brown, J., Trukeschitz, B., Towers, A., Welch, E., Forder, J., Smith, J. & Alden, E. 2010, *Measuring outcomes of care homes: Final Repor*t, Personal Social Services Research Unit (PSSRU), Canterbury, Kent.

Nevitt, C. & Cummings, R. 1992a, "Falls and fractures in older women." in *Falls, balance and gait disorders in the elderl*y, eds. Vellas B & Toupet M, Rubenstein L, Albarede JlLChristen Y, Elsevier, Paris, pp. 69-80.

Nevitt, M.C., Cummings, S.R., Black, D., Genant, H.K., Arnaud, C., Browner, W., Faulker, K., Fox, C., Gluer, C., Harvey, S., Hulley, S.B., Palermo, L., Seeley, D., Steiger, P., Jergas, M., Sherwin, R., Scott, J., Fox, K., Lewis, J., Bahr, M., Trusty, S., Hohman, B., Emerson, L., Rebar, D., Oliner, E., Ensrud, K., Grimm, R., Bell, C., Thomas, D., Jacobson, K., Jackson, S., Mitson, E., Stocke, L., Frank, P., Cauley, J.A., Kuller, L.H., Harper, L., Nasim, M., Bashada, C., Buck, L., Githens, A., Medve, D., Rudovsky, S., Vogt, T.M., Vollmer, V.M., Glauber, H., Orwoll, E., Blank, J., Mastelsmith, B., Bright, R. & Downing, J. 1993a, "Type of Fall and Risk of Hip and Wrist Fractures - the Study of Osteoporotic Fractures", *Journal of the American Geriatrics Society*, vol. 41, no. 11, pp. 1226-1234.

Newman, E.D., Ayoub, W.T., Starkey, R.H., Diehl, J.M. & Wood, G.C. 2003, "Osteoporosis disease management in a rural health care population: hip fracture reduction and reduced costs in postmenopausal women after 5 years", *Osteoporosis International*, vol. 14, no. 2, pp. 146-151.

Nguyen, N.D., Eisman, J.A., Center, J.R. & Nguyen, T.V. 2007b, "Risk factors for fracture in non-osteoporotic men and women", *Journal of Clinical Endocrinology & Metabolism*, vol. 92, no. 3, pp. 955-962.

Nguyen, N.D., Frost, S.A., Center, J.R., Eisman, J.A. & Nguyen, T.V. 2008, "Development of prognostic nomograms for individualizing 5-year and 10-year fracture risks", *Osteoporosis International*, vol. 19, no. 10, pp. 1431-1444.

Nguyen, N.D., Frost, S.A., Center, J.R., Eisman, J.A. & Nguyen, T.V. 2007a, "Development of a nomogram for individualizing hip fracture risk in men and women", *Osteoporosis International*, vol. 18, no. 8, pp. 1109-1117.

Nguyen, T.H., Thuc-Nhi Nguyen, Fischer, T., Ha, W. & Tran, T.V. 2015, "Type 2 diabetes among Asian Americans: Prevalence and prevention", *World Journal of Diabetes*, vol. 6, no. 4, pp. 543-547.

NHG Standaard Osteoporose 2005, *Revised Guidelines of Osteoporosis*, The Dutch College of General Practitioners, The Netherlands.

NHS RightCare, NHS RightCare Pathways. https://www.england.nhs.uk/rightcare/products/pathways/. [2019/August/Sunday]

NICE 2013, *Clinical Guidelines CG161 (2013). Falls: the assessment and prevention of falls in older peopl*e, National Institute for Care Excellence, London.

NICE CKS 2016, Osteoporosis - prevention of fragility fractures. Last revised in December 2016. https://cks.nice.org.uk/osteoporosis-prevention-of-fragility-fractures

NICE 2017, Quality standard (/guidance/qs149). (http://www.shef.ac.uk/NOGG/mainrecommendations.html (2017) (https://cks.nice.org.uk/osteoporosis-prevention-of-fragility-fractures) (2016)

NICE 2009, Hip fracture final scope. https://www.nice.org.uk/guidance/cg124/documents/hip-fracture-final-scope

Nijs, K.A.N.D., de Graaf, C., Kok, F.J. & van Staveren, W.A. 2006, "Effect of family style mealtimes on quality of life, physical performance, and body weight of nursing home residents: cluster randomised controlled trial", *British Medical Journal*, vol. 332, no. 7551, pp. 1180-1183.

Niles, R. 2006, ""Robert Niles Journalism Help: Statistics Every Writer Should Know"", [Online],

Nilsson, B.E. 1970, "Spinal osteoporosis and femoral neck fracture.", *Clinical Orthopaedics and Related Research*, vol. 68, pp. 93-5.

Nimmo, A.W., Peterkin, G. & Coid, D.R. 2006, "Mortality in general practice: Problems concerning deaths in institutions", *Public Health,* vol. 120, no. 7, pp. 671-675.

NOGG (2016) ,*Osteoporosis.Clinical guideline for prevention and treatment. Executive summary. National Osteoporosis Guideline Group.* www.shef.ac.uk/NOGG<www.shef.ac.uk/NOGG/downloads.html>

Nordin, B.E.C 1966, International patterns of osteoporosis. *Clinical Orthopaedics and Related Research*, vol 45, pp. 17-30.

Norton, R., Butler, M., Robinson, E., Lee-Joe, T. & Campbell, A.J. 2000, "Declines in physical functioning attributable to hip fracture among older people: a follow-up study of case-control participants", *Disability and Rehabilitation,* vol. 22, no. 8, pp. 345-351.

Nottidge, T., Akpanudo, E. & Akinbami, O. 2011, "Traditional versus orthodox fracture care in Uyo, Nigeria.", *Journal of the West African College of Surgeons,* vol. 1, no. 1, pp. 53-67.

Nurmi, I. & Luthje, P. 2002, "Incidence and costs of falls and fall injuries among elderly in institutional care", *Scandinavian Journal of Primary Health Care,* vol. 20, no. 2, pp. 118-122.

Nwadiaro, H.C., Ozoilo, K.N., Nwadiaro, P.O., Kidmas, A.T. & Oboiren, M. 2008, "Determinants of patronage of traditional bone setters in the middle belt of Nigeria.", *Nigerian Journal of Medicine : Journal of the National Association of Resident Doctors of Nigeria,* vol. 17, no. 3, pp. 356-9.

Nyberg, L., Gustafson, Y., Berggren, D., Brannstrom, B. & Bucht, G. 1996, "Falls leading to femoral neck fractures in lucid older people", *Journal of the American Geriatrics Society,* vol. 44, no. 2, pp. 156-160.

Oberkircher, L., Ruchholtz, S., Rommens, P. M., Hofmann, A., Bucking, B., & Kruger, A 2018. Osteoporotic Pelvic Fractures. *Deutsches Ärzteblatt International*, vol. 115, pp. 70-80.

Office of National Statistics (ONS) 2014, *Estimates of the very old (including Centenarians) : England and Wales, and United Kingdom, 2002 to 2014*, Statistical bulletin, London.

Office of National Statistics 2011, *Population Census*, UK Statistics Authority, Cardiff.

Office of Fair Trading 2005, *Care homes for older people in the UK; a market study*, Office for National Statistics, Cardiff.

Office of National Statistics (ONS) 2018, *2011 Census Population Bosto*n.
available: www.ons.gov.uk [2018, April/Wednesday].

Office of the Surgeon General (US) 2004, *Bone Health and Osteoporosis: A report of the Surgeon General*, Office of The Surgeon General (US), Rockville, USA.

Oleksik, A., Lips, P., Dawson, A., Minshall, M. E., & Shen, W. 2000, Health related quality of life in postmenopausal women with low BMD with or without prevalent veterbral fractures. *Journal of Bone and Mineral Research*, vol. 15, no. 7, pp. 1384-1392

Oliver D, 2014. Admission to a nursing home can never become a `never` event. *The King`s Fund (https;//www.kingsfund.org.uk/blog/2014/08/admission-nursing-home-can-never-bec…*

Oliver, D.P., Porock, D. & Zweig, S. 2005, "End-of-life care in U.S. nursing homes: a review of the evidence", *Journal of the American Medical Directors Association,* vol. 6, no. 3 Suppl., pp. S21-30.

Ooms, M.E., Vlasman, P., Lips, P., Nauta, J., Bouter, L.M. & Valkenburg, H.A. 1994, "The Incidence of Hip-Fractures in Independent and Institutionalized Elderly People", *Osteoporosis International,* vol. 4, no. 1, pp. 6-10.

Orimo, H., Nakamura,T., Hosoi. T., Iki., M., Uenishi., K., Endo., N, Ohta., H., Shiraki., M., Sugimoto., T., Suzuki., T., Soen., S., Nishizawa., Hagino., H,Fukunaga., M. & Fujiwara.,S 2012, Japanese 2011 guidelines for prevention and treatment of osteoporosis. *Archives of Osteoporosis,* vol. 7, pp. 3-20.

Oygard, S., Anderson, J., Sandvoll, A. & et al 2017, "Deficient reporting of falls in nursing homes", *Peer-Reviewed Research,*

Palacus, C., Gonzalez, L., 2014, Is vitamin D deficiency a major global health problem? *The Journal of Steroid Biochemistry and Molecular Biology,* pp. 138-145. doi 10.1016/j-jsbmb.2013.11.003

Palvanen, M., Kannus, P. & Parkkari, J. 2000, "Injury mechanisms of osteoporotic upper limb fractures." *Journal of Bone and Mineral Research,* vol. 15, pp. S539-S539.

Papaioannou, A., Kennedy, C.C., Ioannidis, G., Gao, Y., Sawka, A.M., Goltzman, D., Tenenhouse, A., Pickard, L., Olszynski, W.P., Davison, K.S., Kaiser, S., Josse, R.G., Kreiger, N., Hanley, D.A., Prior, J.C., Brown, J.P., Anastassiades, T., Adachi, J.D. & Camos Res Grp 2008, "The osteoporosis care gap in men with fragility fractures: the Canadian Multicentre Osteoporosis Study", *Osteoporosis International,* vol. 19, no. 4, pp. 581-587.

Park, S. 2017, "Tools for assessing fall risk in the elderly: a systematic review and meta-analysis", *Aging Clinical and Experimental Research*.

Parker, M.J., Gillespie, L.D. & Gillespie, W.J. 2000, "Hip protectors for preventing hip fractures in the elderly.", *Cochrane database of systematic reviews (Online),* , no. 2, pp. CD001255-CD001255.

Parkinson`s UK 2015, *Audit 2015: What did we find?,* Parkinson`s UK, London.

Pasco, J., Henry, M., Gaudry, T., Nicholson, G. & Kotowicz, M. 1999, "Identification of incident fractures: the Geelong Osteoporosis Study", *Australian and New Zealand Journal of Medicine,* vol. 29, no. 2, pp. 203-206.

Pearce, J. & Ferrier, S. 2000, "Evaluating the predictive performance of habitat models developed using logistic regression", *Ecological Modelling,* vol. 133, no. 3, pp. 225-245.

Peduzzi, P., Concato, J., Kemper, E., Holford, T.R. & Feinstein, A.R. 1996, "A simulation study of the number of events per variable in logistic regression analysis", *Journal of Clinical Epidemiology,* vol. 49, no. 12, pp. 1373-1379.

Pepe, M.S. 2000, "Receiver operating characteristic methodology", *Journal of the American Statistical Association,* vol. 95, no. 449, pp. 308-311.

Perell, K.L., Nelson, A., Goldman, R.L., Luther, S.L., Prieto-Lewis, N. & Rubenstein, L.Z. 2001, "Fall risk assessment measures: An analytic review", *Journals of Gerontology Series A-Biological Sciences and Medical Sciences,* vol. 56, no. 12, pp. M761-M766.

Perier, M.A., Gineyts, E., Munoz, F., Sornay-Rendu, E. & Delmas, P.D. 2007, "Homocysteine and fracture risk in postmenopausal women: the OFELY study", *Osteoporosis International,* vol. 18, no. 10, pp. 1329-1336.

Peterson, T. 2006, "Uses and requirements of ecological niche models and related distributional models." *Biodiversity Informatics,* vol. 3, pp. 59-72.

Petty, D.R. & Scrivener, G. 1998, "Prescribing patterns for patients in homes", *Prescriber,* vol. 9, pp. 103-106.

Pfeifer, M., Begerow, B., Minne, H.W., Schlotthauer, T., Pospeschill, M., Scholz, M., Lazarescu, A.D. & Pollahne, W. 2001, "Vitamin D status, trunk muscle strength, body sway, falls, and fractures among 237 postmenopausal women with osteoporosis", *Experimental & Clinical Endocrinology & Diabetes,* vol. 109, no. 2, pp. 87-92.

Pham,A.N; Datta, S.K; Weber,T.J; Walter,T.C & Colón-Emeric,C.S 2011. Cost-effectiveness of oral bisphosphonates for osteoporosis at different ages and levels of life expectancy. *Journal of the American Geriatrics Society* vol. 59, no. 9, pp. 1642 - 1649

Phillips, S., Fox, N., Jacobs, J. & Wright, W.E. 1988, "The Direct Medical Costs of Osteoporosis for American-Women Aged 45 and Older, 1986", *Bone,* vol. 9, no. 5, pp. 271-279.

Pitfield, C., Shahriyarmolki, K. & Livingston, G. 2011, "A systematic review of stress in staff caring for people with dementia living in 24-hour care settings", *International Psychogeriatrics,* vol. 23, no. 1, pp. 4-9.

Pleschberger, S. 2007, "Dignity and the challenge of dying in nursing homes: the residents' view", *Age and Ageing,* vol. 36, no. 2, pp. 197-202.

Pluijm, S.M.F., Koes, B., de Laet, C., Van Schoor, N.M., Kuchuk, N.O., Rivadeneira, F., Mackenbach, J.P., Lips, P., Pols, H.A. & Steyerberg, E.W. 2009, "Simple Risk Score for the Assessment of Absolute Fracture Risk in General Practice Based on Two Longitudinal Studies", *Journal of Bone and Mineral Research,* vol. 24, no. 5, pp. 768-774.

Pluijm, S.M.F., Tromp, A.M., Smit, J.H., Deeg, D.J.H. & Lips, P. 2000, "Consequences of vertebral deformities in older men and women", *Journal of Bone and Mineral Research,* vol. 15, no. 8, pp. 1564-1572.

Podsiadlo, D. & Richardson, S. 1991, "The Timed Up and Go - a Test of Basic Functional Mobility for Frail Elderly Persons", *Journal of the American Geriatrics Society,* vol. 39, no. 2, pp. 142-148.

Polder, J.J., Meerding, W.J., Koopmanschap, M.A., Bonneux, L. & van der Maas, P.J. 1998, "[The cost of sickness in the Netherlands in 1994; the main determinants were advanced age and disabling conditions].", *Nederlands tijdschrift voor geneeskunde,* vol. 142, no. 28, pp. 1607-11.

Polit, D.F., Beck, C.T. & Hungler, B.P. 2001, *Essentials of Nursing Research: Methods, appraisal and Utilization,* 5th edn. Lippincott Williams & Wilkins, Philadelphia.

Pontius, R.G. & Schneider, L.C. 2001, "Land-cover change model validation by an ROC method for the Ipswich watershed, Massachusetts, USA", *Agriculture Ecosystems & Environment,* vol. 85, no. 1-3, pp. 239-248.

Population cancer screening in Canada 2002, *Strategic priorities,* Population cancer screening in Canada, Ottawa.

Port, L., Center, J., Briffa, N. & et al 2003, "Osteoporotic fracture: missed opportunity for intervention", *Osteoporosis International,* vol. 14, no. 9, pp. 780-784.

Porter, R.W., Miller, C.G., Grainger, D. & Palmer, S.B. 1990, "Prediction of hip fracture in elderly women: A prospective study", *British Medical Journal,* vol. 301, no. 6753, pp. 638-641.

Provost, E. & Fawcett, T. 2001, "Robust classification for imprecise environments", *Machine Learning,* vol. 42, pp. 203-231.

Prudham, D. & Evans, J.G. 1981, "Factors associated with falls in the elderly: a community study." *Age and Ageing,* vol. 10, no. 3, pp. 141-6.

Querfurth, H.W. & LaFerla, F.M. 2010, "MECHANISMS OF DISEASE Alzheimer's Disease", *New England Journal of Medicine,* vol. 362, no. 4, pp. 329-344.

Random.org 2018, *Random Sequence Generator*. Available: www.random.org [2015, March/Monday].

Rapp, K., Becker, C., Lamb, S.E., Icks, A. & Klenk, J. 2008, "Hip Fractures in Institutionalized Elderly People: Incidence Rates and Excess Mortality", *Journal of Bone and Mineral Research,* vol. 23, no. 11, pp. 1825-1831.

Ray, N.F., Chan, J.K., Thamer, M. & Melton, L.J. 1997, "Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: Report from the national osteoporosis foundation", *Journal of Bone and Mineral Research,* vol. 12, no. 1, pp. 24-35.

Ray, S., Laur, C. & Golubic, R. 2014, "Malnutrition in healthcare institutions: A review of the prevalence of under-nutrition in hospitals and care homes since 1994 in England", *Clinical Nutrition,* vol. 33, no. 5, pp. 829-835.

Ravindrarajah, R., Hazra, N.C., Charlton, J., Jackson, S. H. D., Dregan, A., & Gulliford, M. C. 2017, Incidence and mortality of fractures by frailty level over 80 years of age: cohort study using UK electronic health records. *Geriatric Medicine Research,* vol 8, no. 1

Royal College of Physicians (RCP) 2016, *National Hip Fracture Database Annual Report 2016*, Royal College of Physicians, London.

Royal College of Physicians (RCP), 2017, National Audit of Inpatient falls Audit report, Audit report 2017

Recker, R., Lappe, J., Davies, K.M. & Heaney, R. 2004, "Bone remodelling increases substantially in the years after menopause and remains increased in older osteoporosis patients", *Journal of Bone and Mineral Research,* vol. 19, no. 10, pp. 1628-1633.

Redondo, N. & Lloyd-Sherlock 2009, *Institutional Care for Older People in Developing Countries: Repressing Rights or Promoting autonomy? The Case of Buenos Aires, Argentina.* University of East Anglia, Norwich, United Kingdom.

Redmond, J., Jarjou, L. M. A., Zhon, B., Prentice, A., & Schoenmakers, I, 2014. Ethnic differences in calcium, phosphate and bone metabolism. *Proceedings of the Nutrition Society,* vol. 73, pp. 340-351.

Rizzoli, R. Bonjour, J.P 1999, Malnutrition and osteoporosis. *Zeitschrift fur Gerontuwgie und Geriatrie* vol. 32 suppl. 1. Pp 131-137

Robbins, J., Aragaki, A.K., Kooperberg, C., Watts, N., Wactawski-Wende, J., Jackson, R.D., LeBoff, M.S., Lewis, C.E., Chen, Z., Stefanick, M.L. & Cauley, J. 2007, "Factors associated with 5-year risk of hip fracture in postmenopausal women", *JAMA-Journal of the American Medical Association,* vol. 298, no. 20, pp. 2389-2398.

Robertson, R., Gregory, S. & Jabbal, J. 2014, *The social care and health systems of nine countries*, The King`s Fund.

Robinovitch, S.N., Hayes, W.C. & Mcmahon, T.A. 1991, "Prediction of Femoral Impact Forces in Falls on the Hip", *Journal of Biomechanical Engineering-Transactions of the Asme,* vol. 113, no. 4, pp. 366-374.

Rodondi, A., Chevalley, T. & Rizzoli, R. 2012, "Prevalence of vertebral fracture in oldest old nursing home residents", *Osteoporosis International,* vol. 23, no. 11, pp. 2601-2606.

Rommens, P.M., Wagner, D., & Hofmann, A 2017. Fragility fractures of the pelvis. *Journal of Bone and Joint Surgery Reviews* vol. 5. pp. 1 – 13.

Ronald, L.A., McGregor, M.J., McGrail, K.M., Tate, R.B. & Broemling, A. 2008, "Hospitalization rates of nursing home residents and community-dwelling seniors in British Columbia", *Canadian Journal on Aging-Revue Canadienne Du Vieillissement,* vol. 27, no. 1, pp. 109-115.

Ross, P.D., Davis, J.W., Vogel, J.M. & Wasnich, R.D. 1990, "A Critical-Review of Bone Mass and the Risk of Fractures in Osteoporosis", *Calcified Tissue International*, vol. 46, no. 3, pp. 149-161.

Ross, P.D., Norimatsu, H., Davis, J.W., Yano, K., Wasnich, R.D., Fujiwara, S., Hosoda, Y. & Melton, L.J. 1991, "A Comparison of Hip Fracture Incidence among Native Japanese, Japanese-Americans, and American Caucasians", *American Journal of Epidemiology*, vol. 133, no. 8, pp. 801-809.

Rossi, I.A., Rousson, V. & Paccaud, F. 2013, "The contribution of rectangularization to the secular increase of life expectancy: an empirical study", *International Journal of Epidemiology*, vol. 42, no. 1, pp. 250-258.

Rothman, K.J. 2008, "BMI-related errors in the measurement of obesity", *International Journal of Obesity*, vol. 32, pp. S56-S59.

Roux, C., Garnero, P., Thomas, T., Sabatier, J.P., Orcel, P., Audran, M. & Comite Scientifique GRIO 2005, "Recommendations for monitoring antiresorptive therapies in postmenopausal osteoporosis", *Joint Bone Spine*, vol. 72, no. 1, pp. 26-31.

Royal College of Physicians (RCP) 2017b, , *The National Hip Fracture Database. 2017 Annual Report*. Available: http://www.nhfd.co.uk [2018, May/Saturday].

Royal College of Physicians 1989, *Fractured neck of femur*, Royal College of Physicians, London.

Royal College of Physicians 1992, *Standardised Assessment Scales for Elderly People*, Royal College of Physicians, London.

Rubenstein, L.Z. 1997, "Preventing falls in the nursing home", *JAMA-Journal of the American Medical Association*, vol. 278, no. 7, pp. 595-596.

Rubenstein, L.Z; Josephson, K.R; Osterwell, D 1996. Falls and fall prevention in the nursing home. *Clinics in Geriatric Medicine.* vol. 12, pp. 881 - 902

Rubenstein, L.Z., Josephson, K.R. & Robbins, A.S. 1994, "Falls in the Nursing-Home", *Annals of Internal Medicine*, vol. 121, no. 6, pp. 442-451.

Rubenstein, L.Z., Josephson, K.R. & Robbins, A.S. 1994, "Falls in the Nursing-Home", *Annals of Internal Medicine*, vol. 121, no. 6, pp. 442-451.

Rubenstein, L.Z., Robbins, A.S., Josephson, K.R., Schulman, B.L. & Osterweil, D. 1990, "The Value of Assessing Falls in an Elderly Population - a Randomized Clinical-Trial", *Annals of Internal Medicine*, vol. 113, no. 4, pp. 308-316.

Rubenstein, L.Z., Robbins, A.S., Schulman, B.L., Rosado, J., Osterweil, D. & Josephson, K.R. 1988, "Falls and Instability in the Elderly", *Journal of the American Geriatrics Society*, vol. 36, no. 3, pp. 266-278.

Rubin, K.H., Abrahamsen, B., Hermann, A.P., Bech, M., Gram, J. & Brixen, K. 2011, "Prevalence of risk factors for fractures and use of DXA scanning in Danish women. A

regional population-based study", *Osteoporosis International,* vol. 22, no. 5, pp. 1401-1409.

Rubin, K.H., Friis-Holmberg, T., Hermann, A.P., Abrahamsen, B. & Brixen, K. 2013, "Risk assessment tools to identify women with increased risk of osteoporotic fracture: Complexity or simplicity? A systematic review", *Journal of Bone and Mineral Research,* vol. 28, no. 8, pp. 1701-1717.

Rud, B., Hilden, J., Hyldstrup, L. & Hrobjartsson, A. 2007, "Performance of the osteoporosis self-assessment tool in ruling out low bone mineral density in postmenopausal women: A systematic review", *Osteoporosis International,* vol. 18, no. 9, pp. 1177-1187.

Rudman, I.W. & Rudman, D. 1989, "High-Rate of Fractures for Men in Nursing-Homes", *American Journal of Physical Medicine & Rehabilitation,* vol. 68, no. 1, pp. 2-5.

Russell, A. & Elia, M. 2011, *Nutrition screening survey in the UK and Republic of Ireland in 2011*, British Association for Parenteral and Enteral Nutrition (BAPEN), Redditch, England.

Saag, K.G. & Geusens, P. 2009, "Progress in osteoporosis and fracture prevention: focus on postmenopausal women", *Arthritis Research & Therapy,* vol. 11, no. 5, pp. 251.

Shah,S.M; Carey,I.M; harris,T; DeWilde,S; Hubbard, S.L & Cook,D.G 2010. “Identifying the clinical characteristics of older people living in care homes using a novel approach in a primary care database”. *Age and Ageing* vol. 39, pp. 617- 623

Sallin, U., Mellstrom, D. & Eggertsen, R. 2005, "Osteoporosis in a nursing home, determined by the DEXA technique", *Medical Science Monitor,* vol. 11, no. 2, pp. CR67-CR70.

Sambrook, P.N., Flahive, J., Hooven, F.H., Boonen, S., Chapurlat, R., Lindsay, R., Nguyen, T.V., Diez-Perez, A., Pfeilschifter, J., Greenspan, S.L., Hosmer, D., Netelenbos, J.C., Adachi, J.D., Watts, N.B., Cooper, C., Roux, C., Rossini, M., Siris, E.S., Silverman, S., Saag, K.G., Compston, J.E., LaCroix, A. & Gehlbach, S. 2011, "Predicting Fractures in an International Cohort Using Risk Factor Algorithms Without BMD", *Journal of Bone and Mineral Research,* vol. 26, no. 11, pp. 2770-2777.

Sanford, A.M., Orrell, M, Tolson, D., Abbatecola, A.M., Arai, H., Bauer, J.M., Cruz-Jentoft, A.J., Dong, B., Ga, H., Goel, A., Hajjar, R., Holmerova, I., Katz, P.R., Koopmans, R.T.C.M., Rolland, Y., Visvanathan, R., Woo, J., Morley, J.E., & Vellas, B 2015. An International Definition for “Nursing Home” *The Journal of Post-Acute and Long-Term Care Medicine,* vol. 16, pp. 181 – 184.

Sarkar, S., Mitlak, B.H., Wong, M.M., Stock, J.L., Black, D.M. & Harper, K.D. 2002, "Relationships between bone mineral density and incident vertebral fracture risk with raloxifene therapy", *Journal of Bone and Mineral Research,* vol. 17, no. 1, pp. 1-10.

Schuit, S.C.E., van der Klift, M., Weel, A.E.A.M., de Laet, C.E.D.H., Burger, H., Seeman, E., Hofman, A., Uitterlinden, A.G., van Leeuwen, J.P.T.M. & Pols, H.A.P. 2006, "Fracture incidence and association with bone mineral density in elderly men and women: The Rotterdam Study (vol 34, p 195, 2004)", *Bone,* vol. 38, no. 4, pp. 603-603.

Scottish Intercollegiate Guidelines Network (SIGN) 2015, *SIGN 142. Management of osteoporosis and the prevention of fragility fracture*s, Scottish Intercollegiate Guideline Network, Edinburgh.

Seeley, D.G., Browner, W.S., Nevitt, M.C., Genant, H.K., Scott, J.C. & Cummings, S.R. 1991, "Which Fractures are Associated with Low Appendicular Bone Mass in Elderly Women", *Annals of Internal Medicine,* vol. 115, no. 11, pp. 837-842.

Seeliger, C., Karpinski, K., Haug,A.T., Vester, H., Schmitt, A., Bauer, J.S., & van Griensven, M., 2015, Five freely circulating miRNAs and bone tissue miRNAs are associated with osteoporotic fractures, *Journal of Bone and Mineral Research,*vol. 30, no. 1, pp. 195-196.

Seeman, E. 1997, "From density to structure: Growing up and growing old on the surfaces of bone", *Journal of Bone and Mineral Research,* vol. 12, no. 4, pp. 509-521.

Shah, S.M., Carey, I.M., Harris, T., DeWilde, S. & Cook, D.G. 2013, "Mortality in older care home residents in England and Wales", *Age and Ageing,* vol. 42, no. 2, pp. 209-215.

Sharabiani, M.T.A., Aylin, P. & Bottle, A. 2012, "Systematic Review of Comorbidity Indices for Administrative Data", *Medical care,* vol. 50, no. 12, pp. 1109-1118.

Shepard,D.S, Gold,M.R, Siegel, L.B, Russell, M.C, Weinstein M.C (Eds.), 1999, Cost-effectiveness in Health and Medicine, *The Journal of Mental Health Policy and Economics,* vol. 2, *Oxford University Press, New York 1996,* pp.91-92

Shepperd, S., Doll, H., & Angus, R.M 2008. Hospital at home admission avoidance, *Cochrane Database for systematic Reviews.* Article No.: CD007491.DOI:10.1002/14651858.CD007491

Silverman SL, C.A. 2010, "The utility and limitations of FRAX: A US perspective.", *Current Osteoporosis Reports,* vol. 8, no. 4, pp. 192-197.

Silverman, S.L., Delmas, P.D., Kulkarni, P.M., Stock, J.L., Wong, M. & Plouffe, L.,Jr 2004, "Comparison of fracture, cardiovascular event, and breast cancer rates at 3 years in postmenopausal women with osteoporosis", *Journal of the American Geriatrics Society,* vol. 52, no. 9, pp. 1543-1549.

Siminoski, K., Leslie, W.D., Frame, H., Hodsman, A., Josse, R.G., Khan, A., Lentle, B.C., Levesque, J., Lyons, D.J., Tarulli, G. & Brown, J.P. 2007, "Recommendations for bone mineral density reporting in Canada: A shift to absolute fracture risk assessment", *Journal of Clinical Densitometry,* vol. 10, no. 2, pp. 120-123.

Simpson, J., Worsfold, C., Reilly, E. & et al 2002, "A Standard Procedure for Using TURN 180: Testing dynamic postural stability among elderly people Contributions", *Physiotherapy,* vol. 88, no. 6, pp. 342-353.

Sinclair, A.J., Gadsby, R., Penfold, S., Croxson, S.C.M. & Bayer, A.J. 2001, "Prevalence of diabetes in care home residents", *Diabetes Care,* vol. 24, no. 6, pp. 1066-1068.

Singer, A., Exudides, A., Spangler, L., Johnson, K., Colby, C., Baker, J., & Kagan, R. 2015, Burden of illness for osteoporotic fractures compared with other serious diseases among postmenopausal women in the USA. *Mayo Clinic Proceedings*

Siqueira, F.V., Facchini, L.A. & Hallal, P.C. 2005, "The burden of fractures in Brazil: A population-based study", *Bone,* vol. 37, no. 2, pp. 261-266.

Siris, E. & Delmas, P.D. 2008, "Assessment of 10-year absolute fracture risk: a new paradigm with worldwide application", *Osteoporosis International,* vol. 19, no. 4, pp. 383-384.

Siris, E.S., Brenneman, S.K., Barrett-Connor, E., Miller, P.D., Sajjan, S., Berger, M.L. & Chen, Y.T. 2006, "The effect of age and bone mineral density on the absolute, excess, and relative risk of fracture in postmenopausal women aged 50-99: results from the National Osteoporosis Risk Assessment (NORA)", *Osteoporosis International,* vol. 17, no. 4, pp. 565-574.

Siris, E.S., Brenneman, S.K., Miller, P.D., Barrett-Connor, E., Chen, Y.T., Sherwood, L.M. & Abbott, T.A. 2004, "Predictive value of low BMD for 1-year fracture outcomes is similar for postmenopausal women ages 50-64 and 65 and older: Results from the National Osteoporosis Risk Assessment (NORA)", *Journal of Bone and Mineral Research,* vol. 19, no. 8, pp. 1215-1220.

Skelton, D. 2009, *Greater Glasgow and Clyde Strategy for Osteoporosis and Falls Prevention 2006-2010. An evaluation 2007-200*9, Greater Glasgow and Clyde NHS, Glasgow.

Sloan, F.A., Bethel, M.A., Ruiz, D.,Jr., Shea, A.H. & Feinglos, M.N. 2008, "The growing burden of diabetes mellitus in the US elderly population", *Archives of Internal Medicine,* vol. 168, no. 2, pp. 192-199.

Smith S, *Nutritional assessment in practice-current & future*. Available: https://www.peng.org.uk/pdfs/presentations/nutritional-assessment.sara.smith.pdf [2018, July/Monday].

Sousa, R.M., Ferri, C.P., Acosta, D., Albanese, E., Guerra, M., Huang, Y., Jacob, K.S., Jotheeswaran, A.T., Llibre Rodriguez, J.J., Rodriguez Pichardo, G., Calvo Rodriguez, M., Salas, A., Luisa Sosa, A., Williams, J., Zuniga, T. & Prince, M. 2009, "Contribution of chronic diseases to disability in elderly people in countries with low and middle incomes: a 10/66 Dementia Research Group population-based survey", *Lancet,* vol. 374, no. 9704, pp. 1821-1830.

Sowers, M.R., Clark, M.K., Hollis, B., Wallace, R.B. & Jannausch, M. 1992, "Radial Bone-Mineral Density in Premenopausal and Perimenopausal Women - a Prospective-Study of Rates and Risk-Factors for Loss", *Journal of Bone and Mineral Research,* vol. 7, no. 6, pp. 647-657.

Sowers, M.R., Clark, M.K., Jannausch, M.L. & Wallace, R.B. 1991, "A Prospective-Study of Bone-Mineral Content and Fracture in Communities with Differential Fluoride Exposure", *American Journal of Epidemiology,* vol. 133, no. 7, pp. 649-660.

Stauber, M. & Muller, R. 2006, "Age-related changes in trabecular bone microstructures: global and local morphometry", *Osteoporosis International,* vol. 17, no. 4, pp. 616-626.

Stefanacci, R.G 2018. “Direct Admissions to Skilled Nursing Facilities – Are You Ready”? *Annals of Long-Term Care* vol. 26, no. 7

Stephanie, G 2014, Statistics How To.
https;//www.statisticshowto.datasciencecentral.com/sensitivity-vsspecificity-statisticcal/

Steiger, P., Cummings, S.R., Black, D.M., Spencer, N.E. & Genant, H.K. 1992, "Age-Related Decrements in Bone-Mineral Density in Women Over 65", *Journal of Bone and Mineral Research,* vol. 7, no. 6, pp. 625-632.

Steiger, P., Genant, H.K., Grman, M.E., Hangartner, T., Hanson, J., Kalender, W.A., Mazess, R., Morita, R., Schiessl, H., Stein, J. & Tamegai, T. 1995, "Standardization of Spine Bmd Measurements", *Journal of Bone and Mineral Research,* vol. 10, no. 10, pp. 1602-1603.

Sterke, C.S., Verhagen, A.P., Van Beeck, E.F. & van der Cammen, T.J.M. 2008, "The influence of drug use on fall incidents among nursing home residents: a systematic review", *International Psychogeriatrics,* vol. 20, no. 5, pp. 890-910.

Steurer, J., Haller, C., Haeuselmann, H., Brunner, F. & Bachmann, L.M. 2011, "Clinical Value of Prognostic Instruments to Identify Patients with an Increased Risk for Osteoporotic Fractures: Systematic Review", *Plos One,* vol. 6, no. 5, pp. e19994.

Stevens, J.A. & Rudd, R.A. 2013, "The impact of decreasing U.S. hip fracture rates on future hip fracture estimates", *Osteoporosis International,* vol. 24, no. 10, pp. 2725-2728.

Stephenson, J 2015 Manutrition remains significant problem in care homes. *Nursing Times. https://www.nursingtimes.net/clinical-archive/nutrition/malnutrition-remains-signific..*

Stone, K.L., Seeley, D.G., Lui, L.Y., Cauley, J.A., Ensrud, K., Browner, W., Nevitt, M.C., Cummings, S.R. & Osteoporotic Fractures Research 2003, "BMD at multiple sites and risk of fracture of multiple types: Long-term results from the study of osteoporotic fractures", *Journal of Bone and Mineral Research,* vol. 18, no. 11, pp. 1947-1954.

Strom, O., Borgstrom, F., Kanis, J.A., Compston, J., Cooper, C., McCloskey, E.V. & Jonsson, B. 2011, "Osteoporosis: burden, health care provision and opportunities in the EU: a report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA).", *Archives of Osteoporosis,* vol. 6, pp. 59-155.

Sullivan, M.P., Balwin, K.D., Donegan, D.J., Mehta, S.& Ahn,.J 2014. “Geriatric fractures about the hip: divergent patterns in the proximal femur, acetabulum, and pelvis”. *Orthopedics,* vol. 37, pp. 151 – 157.

Takele, Y., Adem, E., Getahun, M., Tajebe, F., Kiflie, A., Hailu, A., Raynes, J., Mengesha, B., Ayele, T.A., Shkedy, Z., Lemma, M., Diro, E., Toulza, F., Modolell, M., Munder, M., Mueller, I. & Kropf, P. 2016, "Malnutrition in Healthy Individuals Results in Increased Mixed Cytokine Profiles, Altered Neutrophil Subsets and Function", *Plos One,* vol. 11, no. 8, pp. e0157919.

Tamura, B.K., Bell, C.L., Masaki, K.H. & Amella, E.J. 2013, "Factors Associated With Weight Loss, Low BMI, and Malnutrition Among Nursing Home Patients: A Systematic

Review of the Literature", *Journal of the American Medical Directors Association,* vol. 14, no. 9, pp. 649-655.

Tan, B.-., Price, R.I., Briffa, N.K., Dhaliwal, S.S., Day, R.E. & Singer, K.P. 2008, "Assessment of osteoporotic fracture risk in community settings: a study of post-menopausal women in Australia", *Health & Social Care in the Community,* vol. 16, no. 6, pp. 621-628.

Tanaka, S., Kuroda, T., Saito, M. & Shiraki, M. 2013, "Overweight/obesity and underweight are both risk factors for osteoporotic fractures at different sites in Japanese postmenopausal women (vol 24, p 69, 2013)", *Osteoporosis International,* vol. 24, no. 3, pp. 1143-1144.

Tanaka, S., Yoshimura, N., Kuroda, T., Hosoi, T., Saito, M. & Shiraki, M. 2010, "The Fracture and Immobilization Score (FRISC) for risk assessment of osteoporotic fracture and immobilization in postmenopausal women-A joint analysis of the Nagano, Miyama, and Taiji Cohorts", *Bone,* vol. 47, no. 6, pp. 1064-1070.

Teede, H.J., Jayasuriya, I.A. & Gilfillan, C.P. 2007, "Fracture prevention strategies in patients presenting to Australian hospitals with minimal-trauma fractures: a major treatment gap", *Internal Medicine Journal,* vol. 37, no. 10, pp. 674-679.

Termansen, M., Collin, J. & McClean, C. 2006, "The use of generic algorithm and Bayesian classification to model species distributions", *Ecological Modelling,* vol. 192, no. 3-4, pp. 410-424.

Thabane, L., Ma, J., Chu, R., Cheng, J., Ismaila, A., Rios, L.P., Robson, R., Thabane, M., Giangregorio, L. & Goldsmith, C.H. 2010, "A tutorial on pilot studies: the what, why and how", *BMC Medical Research Methodology,* vol. 10, pp. 1.

Thapa, P.B., Brockman, K.G., Gideon, P., Fought, R.L. & Ray, W.A. 1996, "Injurious falls in non-ambulatory nursing home residents: A comparative study of circumstances, incidence, and risk factors", Jo*urnal of the American Geriatrics Society,* vol. 44, no. 3, pp. 273-278.

*The care of patients with fragility fractures*2007, British Orthopaedic Association.

The Gold Standard Framework (GSF) Team 2018, *The Gold standards framework*. Available: www.goldstandardsframework.org.uk/ [2018, May/Monday].

The National Falls Prevention Coordination Group (NFPCG) 2017, *Falls and fracture consensus statement Supporting commissioning for prevention*, Public Health England, London.

The Royal College of Physicians of London and The British Geriatrics Society 1992, *A report of joint workshops of the Research Unit of the Royal College of Physicians and British Geriatrics Society: STANDARDISED ASSESSMENT SCALES FOR ELDERLY PEOPLE*, The Royal College of Physicians of London and The British Geriatrics Society, London.

Thornton, H. 1993, "Clinical trials: a "ladyplan" for trial recruitment? - everyone`s business!", *Lancet,* vol. 341, pp. 795-796.

Tinetti, M.E. & Speechley, M. 1989, "Prevention of Falls in the Elderly - Reply", *New England Journal of Medicine,* vol. 321, no. 23, pp. 1614-1615.

Tinetti, M.E. & Williams, C.S. 1997, "Falls, injuries due to falls, and the risk of admission to a nursing home", *New England Journal of Medicine,* vol. 337, no. 18, pp. 1279-1284.

Tinetti, M.E. 1986, "Performance-Oriented Assessment of Mobility Problems in Elderly Patients", *Journal of the American Geriatrics Society,* vol. 34, no. 2, pp. 119-126.

Tinetti, M.E., Speechley, M. & Ginter, S.F. 1988, "Risk-Factors for Falls among Elderly Persons Living in the Community", *New England Journal of Medicine,* vol. 319, no. 26, pp. 1701-1707.

Tobias, J.H., Hutchinson, A.P., Hunt, L.P., McCloskey, E.V., Stone, M.D., Martin, J.C., Thompson, P.W., Palferman, T.G. & Bhalla, A.K. 2007, "Use of clinical risk factors to identify postmenopausal women with vertebral fractures", *Osteoporosis International,* vol. 18, no. 1, pp. 35-43.

Todd, C.J., Palmer, C., Camilleriferrante, C., Freeman, C.J., Laxton, C.E., Parker, M.J., Payne, B.V. & Rushton, N. 1995, "Differences in Mortality After Fracture of Hip", *British Medical Journal,* vol. 311, no. 7011, pp. 1025-1025.

Toofanny, N., Maddens, M.E., Voytas, J. & Kowalski, D. 2004, "Low bone mass and postfall fracture risk among elderly nursing home men", *Journal of the American Medical Directors Association,* vol. 5, no. 6, pp. 367-70.

Torgerson, D.J. & Dolan, P. 2000, "The cost of treating osteoporotic fractures in the United Kingdom female population - The author replies", *Osteoporosis International,* vol. 11, no. 6, pp. 551-552.

Torgerson, D.J., Gosden, T. & Reid, D.M. 1997, "The economics of osteoporosis prevention", *Trends in Endocrinology and Metabolism,* vol. 8, no. 6, pp. 236-239.

Treece, E. & Treece, W. 1982, *Elements of research in nursing,* 3rd ed., Mosby.

Trefethen, N. 2013, *BMI exaggerates thinness in short people and fatness in tall people* [2018, May/Monday].

Turner, C.H. 2002, "Biomechanics of bone: Determinants of skeletal fragility and bone quality", *Osteoporosis International,* vol. 13, no. 2, pp. 97-104.

Turner, L.W., Faile, P.A. & Tomlinson, R., Jr 1999, "Osteoporosis diagnosis and fracture", *Orthopaedic Nursing,* vol. 18, no. 5, pp. 21-28.

UK Metric Association 2013, *Adult weight and height*, UK Metric Association.

United Lincolnshire Hospitals NHS Trust (ULHT) 2017, *Annual Report and Financial Accounts 2016-17. United Lincolnshire Hospitals NHS Trust*. Available: https://www.ulh.nhs.uk [2018, May/Sunday].

United Lincolnshire Hospitals NHS Trust (ULHT) 2017, *Mortality Report 2017*, Trust Mortality Reduction Action Group (MORAG), Lincoln.

United Lincolnshire Hospitals NHS Trust (ULHT) 2018, *Trust Mortality Report 2018*, Quality Governance Unit, ULHT, Lincoln.

United Nations (Department of Economic and Social Affairs) 2017. World population projected to reach 9.8 billion in 2050, and 11.2 billion in 2100. (HTTPS://WWW.UN.ORG/DEVELOPMENT/DESA/E)

United Nations 2019. *Levels and trends in population Ageing.* https://www.un.org/en/sections/issues-depth/ageing/

United States Centers for Disease Control and Prevention (CDC) 2012, *Falls in Nursing Homes*, Centers for Disease Control and Prevention, Atlanta, USA.

US Department of Health and Human Services. 2004, *Bone health and osteoporosis: a report of the Surgeon General.*, US Department of Health and Human Services, Office of the Surgeon General, Rockville, MD, USA.

US Food and Drug Administration (FDA) 2013, *CLIA Categorization Criteria.* Available: www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124208.htm [2018, October/Friday].

van Belle, G. 2002, *Statistical rules of thumb*, John Wiley, New York.

van de Pol,Marjolein Helena Johanna, Fluit, C.R.M.G., Lagro, J., Niessen, D., Rikkert, M.G.M.O. & Lagro-Janssen, A.L.M. 2015, "Quality care provision for older people: an interview study with patients and primary healthcare professionals", *British Journal of General Practice*, vol. 65, no. 637, pp. E500-E507.

van der Voort, D.J.M., Geusens, P.P. & Dinant, G.J. 2001, "Risk factors for osteoporosis related to their outcome: Fractures", *Osteoporosis International*, vol. 12, no. 8, pp. 630-638.

van Schooten, K., Yang, Y., Feldman, F. & et al 2017, "The association between fall frequency, injury risk and characteristics of falls in older residents of long-term care: do recurrent fallers fall more safely?", *The Journals of Gerontology. Series A, Biological sciences and medical sciences*, .

Van Staa, T.P., Dennison, E.M., Leufkens, H.G.M. & Cooper, C. 2001, "Epidemiology of fractures in England and Wales", *Bone*, vol. 29, no. 6, pp. 517-522.

van Staa, T.P., Geusens, P., Kanis, J.A., Leufkens, H.G.M., Gehlbach, S. & Cooper, C. 2006, "A simple clinical score for estimating the long-term risk of fracture in post-menopausal women", *QJM-an International Journal of Medicine*, vol. 99, no. 10, pp. 673-682.

van Staa, T.P., Leufkens, H.G.M. & Cooper, C. 2002a, "The epidemiology of corticosteroid-induced osteoporosis: A meta-analysis", *Osteoporosis International*, vol. 13, no. 10, pp. 777-787.

van Staa, T.P., Leufkens, H.G.M. & Cooper, C. 2002b, "Utility of medical and drug history in fracture risk prediction among men and women", *Bone*, vol. 31, no. 4, pp. 508-514.

Vandijk, P.T.M., Meulenberg, O.G.R.M., Vandesande, H.J. & Habbema, J.D.F. 1993, "Falls in Dementia Patients", *Gerontologist,* vol. 33, no. 2, pp. 200-204.

Vanlint, S., 2013, Vitamin D and Obesity. *Nutients* vol. 5 no. 3 pp. 949-956.

Vaughan, I.P. & Ormerod, S.J. 2005, "The continuing challenges of testing species distribution models", *Journal of Applied Ecology,* vol. 42, no. 4, pp. 720-730.

Vaugier B 2018 , *Charlson Index Online Calculator* [2018, May/Monday].

Verbeek- Qudijk, D 2017, Older persons in nursing and care homes. National summary of their life situation. The Netherlands Institute for Social Research. The Hague, Sept. 2017

Vergouwe, Y., Steyerberg, E.W.,Eijkemans, M.J.C. & Habbema, J.D.F. 2005, "Substantial effective sample sizes were required for external validation studies of predictive logistic regression models", *Journal of Clinical Epidemiology,* vol. 58, no. 5, pp. 475-483.

Visentin, P., Ciravegna, R., Uscello, L., Molaschi, M. & Fabris, F. 1995, "Site-Specific Relative Risk of Fractures in the Institutionalized Elderly", *Gerontology,* vol. 41, no. 5, pp. 273-279.

Viswanathan, M; Reddy,S; Berkman, N; Cullen,K; Cook Middleton, J; Nicholson,W.K; & Kahwati,l.C 2018. Screening to prevent osteoporotic fractures: updated evidence report and systematic review for the US Preventive Services Task Force. *Journal of the American Medical Association,* vol. 319,no.24, pp. 2532 – 2551.

Wahid, F., Khan, T., Kim, Y. Y., 2014. MicroRNA and diseases: therapeutic potential as new generation of drugs; 104, pp12-26. doi: 10.1016/j.biochi.2014.05.004

Wahigren, T; Levitt, S; Kowaiski, J; Nilsson, S; & Brandberg, Y 2011. Use of the Charlson Combined Index To Predict Postradiotherapy Quality of Life for Prostate Cancer Patients.*Radiation Oncology,* vol.81, no.4, pp. 997 – 1004.

Wainwright, S.A., Marshall, L.M., Ensrud, K.E., Cauley, J.A., Black, D.M., Hillier, T.A., Hochberg, M.C., Vogt, M.T. & Orwoll, E.S. 2005, "Hip fracture in women without osteoporosis", *Journal of Clinical Endocrinology and Metabolism,* vol. 90, no. 5, pp. 2787-2793.

Walters, S.J., Henriques-Cadby, I.B.D.A., Bortolami, O., Flight, L., Hind, D., Jacques, R.M., Knox, C., Nadin, B., Rothwell, J., Surtees, M. & Julious, S.A. 2017, "Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme", *BMJ Open,* vol. 7, no. 3, pp. e015276.

Walter, E., Dellago,. H., Hackl, M., Grillari, J. & Dimai, H.P., 2018, Cost-utility analysis of fracture-risk assessment using MicroRNAs compared to standard tools and no-monitoring in the austrain female population, *Bone,* vol. 108, pp. 44-54

Wang, H., Hung, C., Lin, S., Tai, Y., Lu, K., Liliang, P., Lin, C., Lee, Y., Fang, P., Chang, L. & Li, Y. 2014, "Increased risk of hip fractures in patients with dementia: a nationwide population-based study", *BMC Neurology*, vol. 14, pp. 175.

Wang, X., Shen, X., Li, X. & Agrawal, C.M. 2002, "Age-related changes in the collagen network and toughness of bone", *Bone*, vol. 31, no. 1, pp. 1-7.

Watts, N.B., Ettinger, B. & LeBoff, M.S. 2009, "FRAX Facts", *Journal of Bone and Mineral Research*, vol. 24, no. 6, pp. 975-979.

Wells, G.A; Cranney, A; Peterson, J; Boucher, M; Shea, B; Robinson, V; Coyle, D & Tugwell, P 2008. Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. *Cochrane Database of Systematic Reviews* doi: 10.1002/14651858.CD001155.pub2

Westert, G. & Wammes, J. 2013, *The Dutch health care system, 2013 in Thompson S, Osborn R, Squires D and Jun MI (ed.), International profiles of health care systems, 2013, New York, US: The Commonwealth Fund.* .

WHO Regional Office for Europe 2017, *Data and Statistics; The Challenge of Diabetes*, World Regional Office for Europe UN City, Copenhagen, Denmark.

WHO 2018, Ageing and Health; Key Facts. https://www.who.int>Newsroom>Fact shhets>

Wichman, A. & Sandler, A. 1997, "Research involving critically ill subjects in emergency circumstances: new regulation, new challenges. ", *Neurology*, vol. 48, pp. 1151-1155.

Wickham, C., Cooper, C., Margetts, B.M. & Barker, D.J.P. 1989, "Muscle Strength, Activity, Housing and the Risk of Falls in Elderly People", *Age and Ageing*, vol. 18, no. 1, pp. 47-51.

Willig, R., Luukinen, H. & Jalovaara, P. 2003, "Factors related to occurrence of hip fracture during a fall on the hip", *Public Health*, vol. 117, no. 1, pp. 25-30.

Wilson, C.B. 2009, "Developing community in care homes through a relationship-centred approach", *Health & Social Care in the Community*, vol. 17, no. 2, pp. 177-186.

Wilson, J. & Jungner, G. 1968, *Principles and practice of screening for disease*, World Health Organisation (WHO), Geneva, Switzerland.

Winblad, B., Kilander, L., Eriksson, S. & Severe Alzheimer's Dis Study Grp 2006, "Donepezil in patients with severe Alzheimer's disease: double-blind, parallel-group, placebo-controlled study (vol 367, p 1057, 2006)", *Lancet*, vol. 368, no. 9548, pp. 1650-1650.

Winner, S.J., Morgan, C.A. & Evans, J.G. 1989, "Premenopausal Risk of Falling and Incidence of Distal Forearm Fracture", *British Medical Journal*, vol. 298, no. 6686, pp. 1486-1488.

WMA, W.M.A. 2013, "Declaration of Helsinki", *Journal of the American Medical Association*, vol. 227, pp. 925-926.

Wootton, R., Brereton, P.J., Clark, M.B., Hesp, R., Hodkinson, H.M., Klenerman, L., Reeve, J., Slavin, G. & Tellezyudilevich, M. 1979, "Fractured Neck of Femur in the Elderly - Attempt to Identify Patients at Risk", *Clinical Science,* vol. 57, no. 1, pp. 93-101.

World Health Organization (WHO) 2014, *WHO methods for life expectancy and healthy life expectancy. Global Health Estimates Technical Paper WHO/HIS/HIS/GHE*, The World Health Organisation (WHO), Switzerland, Geneva.

Xiang, B., Huang, W., Zhou, G., Hu, N., Chen, H. & Chen, C. 2017, "Body mass index and the risk of low bone mass-related fractures in women compared with men: a PRISMA-compliant meta-analysis of prospective cohort studies", *Medicine,* vol. 96, no. 12, pp. e5290.

Youn, J., Okuma, O., Hwang, M., Kim, D. & Cho, J.W. 2017, "Falling Direction can Predict the Mechanism of Recurrent Falls in Advanced Parkinson`s Disease", *Scientific Reports,* vol. 7.

Ytterstad, B. 1999, "The Harstad injury prevention study: the characteristics and distribution of fractures amongst elders--an eight year study.", *International Journal of Circumpolar Health,* vol. 58, no. 2, pp. 84-95.

Zanchetta, J. 2012, *The LATIN AMERICA REGIONAL AUDIT. Epidemiology, costs & burden of osteoporosis in 2012*, International Osteoporosis Foundation, Buenos Aires, Argentina.

Zarowitz, B.J., Cheng, L., Allen, C., O'Shea, T. & Stolshek, B. 2015, "Osteoporosis Prevalence and Characteristics of Treated and Untreated Nursing Home Residents With Osteoporosis", *Journal of the American Medical Directors Association,* vol. 16, no. 4, pp. 341-348.

Zebaze, R.M.D. & Seeman, E. 2003, "Epidemiology of hip and wrist fractures in Cameroon, Africa", *Osteoporosis International,* vol. 14, no. 4, pp. 301-305.

Zermansky, A.G., Alldred, D.P., Petty, D.R. & Raynor, D.K. 2007, "Striving to recruit: the difficulties of conducting clinical research on elderly care home residents", *Journal of the Royal Society of Medicine,* vol. 100, no. 6, pp. 258-261.

Zimmerman, S.I., Girman, C.J., Buie, V.C., Chandler, J., Hawkes, W., Martin, A., Holder, L., Hebel, J.R., Sloane, P.D. & Magaziner, J. 1999, "The prevalence of osteoporosis in nursing home residents", *Osteoporosis International,* vol. 9, no. 2, pp. 151-157.

Appendices

Appendix A IRAS approval

Health Research Authority

NRES Committee East Midlands - Nottingham 1

Royal Standard Place
Nottingham
NG1 6FS

Telephone: 0115 8839428

09 January 2015

Dr Felix Ihama
Department of Medicine
Pilgrim Hospital, Sibsey Road, Boston
PE21 9QS

Dear Dr Ihama

Study title:	**A feasibility study evaluating the performance of three fragility risk assessment tools in predicting falls in older people; A prospective study of older care home residents in the UK**
REC reference:	**14/EM/1225**
Protocol number:	**1**
IRAS project ID:	**59238**

Thank you for your letter of 06 January 2015, responding to the Committee's request for further information on the above research and submitting revised documentation. The further information has been considered on behalf of the Committee by the Vice-Chair. We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager, Ms Penelope Gregory, NRESCommittee.EastMidlands-Nottingham1@nhs.net. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion
On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Mental Capacity Act 2005
I confirm that the committee has approved this research project for the purposes of the Mental Capacity Act 2005. The committee is satisfied that the requirements of section 31 of the Act will be met in relation to research carried out as part of this project on, or in relation to, a person who lacks capacity to consent to taking part in the project.

Conditions of the favourable opinion
The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from NRES. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites
NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Approved documents
The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Other – Individual research recommendation details document		
Covering letter on headed paper		20 September
GP/consultant information sheets or letters		
Other – Introduction to Good Clinical Practice certificate – Felix		24 June 2011
Other – Certificate – e-learning course – Manual Handling – Felix		17 October 2013
IRAS Checklist XML [Checklist_06012015]		06 January 2015
IRAS Checklist XML [Checklist_08012015]		08 January 2015
Letter from sponsor		
Letter from statistician		
Non-validated questionnaire		
Non-validated questionnaire		
Other [CV - Anand D Pandyan]		
Other [CV - Dr F Lally]		
Other [CV - Christine Roffe]		
Other [Consent form]	2.0	06 January 2015
Other [Consultee form]	2.0	06 January 2015
Other [Consultee information sheet]	1.0	05 January 2015
Other [Letter of invitation]	2.0	05 January 2015
Other [Consultee invitation letter]	2.0	05 January 2015
Other [Participant information sheet]	3.0	08 January 2015
REC Application Form [REC_Form_22102014]		22 October 2014
Referee's report or other scientific critique report		
Research protocol or project proposal		
Response to Request for Further Information [Documents uploaded to HARP]		06 January 2015
Summary CV for Chief Investigator (CI)		
Summary CV for student		
Validated questionnaire		
Validated questionnaire		

Statement of compliance
The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review
Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback
The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training
We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

14/EM/1225 **Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project. Yours sincerely

Dr Carl Edwards
Chair

Email:NRESCommittee.EastMidlands-Nottingham1@nhs.net

Enclosures: "After ethical review – guidance for researchers" *[SL-AR2]*

Copy to: *Professor Christine Roffe*
Dr T Ahmed, United Lincolnshire NHS Trust

Appendix B IRAS approval for minor amendments

Health Research Authority

NRES Committee East Midlands - Nottingham 1
Royal Standard Place Nottingham NG1 6FS
Tel: 0115 883 9428

10 March 2015

Professor Christine Roffe
Stroke Research Network
North Staffs Combined Healthcare NHS Trust, Holly Lodge, 62 Queens Road
Hartshill, Stoke-on-Trent
ST4 7LH

Dear Professor Roffe

Study title:	**A feasibility study evaluating the performance of three fragility risk assessment tools in predicting falls in older people; A prospective study of older care home residents in the UK**
REC reference:	**14/EM/1225**
Protocol number:	**1**
Amendment number:	**SA1**
Amendment date:	**06 February 2015**
IRAS project ID:	**59238**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Notice of Substantial Amendment (non-CTIMP)		06 February 2015

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval
ll investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

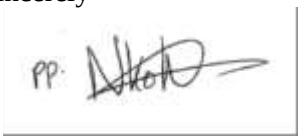
Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

14/EM/1225: Please quote this number on all correspondence

Yours sincerely



Reverend Keith Lackenby
Chair

E-mail: NRESCommittee.EastMidlands-Nottingham1@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Dr T Ahmed, United Lincolnshire NHS Trust*

*Dr Felix Ihama***NRES Committee East Midlands - Nottingham 1**

Attendance at Sub-Committee of the REC meeting on 10 March 2015

Committee Members:

Name	*Profession*	*Present*	*Notes*
Professor Cris Constantinescu	Professor of Clinical	Yes	
Reverend Keith Lackenby (Chairing)	Lay member	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Nicola Kohut	REC Assistant

Appendix C Research and Development approval

United Lincolnshire Hospitals NHS
NHS Trust

RESEARCH & DEVELOPMENT DEPARTMENT

Contact: Helen Ayre
(Research Governance & Quality Manager)
T: 01522 512512 Ext 2552
F: 01522 597845 Email: Helen.Ayre@ULH.NHS.UK

Lincoln County Hospital
Greetwell Road
Lincoln
LN2 5QY

Dr Felix Ihama
Consultant Physician / Care of the Elderly
Pilgrim Hospital
Sibsey Road
Boston, PB21 9QS

Date: 11th March 2015
R&D Ref: 141014Ihama
REC Ref: 14/EM/1225

Dear Dr Ihama,

Re: A feasibility study evaluating the performance of three fragility risk assessment tools in predicting falls in older people; A prospective study of older care home residents in the UK

Thank you for submitting the above project for local research governance approval. I am pleased to inform you that the Research and Development department has no objection.

- **United Lincolnshire Hospitals NHS Trust – Pilgrim Hospital**

The final list of documents reviewed and approved are as follows:

Document	*Version*	*Date*
NHS R&D Form	**59238/683848/14/75**	**03/10/2014**
Research Proposal	**Unversioned**	**May 2014**
REC Favourable Opinion Letter	**-**	**09/01/2015**
REC Favourable Opinion Letter (REISSUE)	**-**	**20/01/2015**
Consultee Invitation	**2.1**	**19/01/2015**
Letter of invitation	**2.1**	**19/01/2015**
Participant Information Sheet	**3.0**	**08/01/2015**
Consultee Information sheet	**1.0**	**05/01/2015**
Participant Consent Form	**2.0**	**06/02/2015**
Consultee Declaration Form	**2.0**	**06/01/2015**
Letter to GP	**1.0**	**19/01/2015**

Please notify the R&D department of any future amendments to the approved study and/or documents along with a copy of any Research Ethics Committee correspondence/approval.

Conditions of Approval:

- All researchers involved in Clinical Research must have up to date GCP training – See LCRF Training SOP09 for further details. Available at http://www.ulh.nhs.uk/for_staff/lincolnshire_crf/documents/sop/SOP09_Training_Record.pdf
- You must ensure that any reports on the progress and/or outcome of your research requested by R&D are produced on time and to an acceptable standard, in accordance with your responsibilities under section 3.6.3 of the Research Governance Framework, 2nd Edition (DOH, 2005). As a minimum, this will include completion of the ULHT R&D annual progress report.
- Please note that the Trust audits 10% of ULH non-sponsored studies and we anticipate auditing 100% of ULHT sponsored projects approved, on an annual basis.
- Please note that should a Suspected Unexpected Serious Adverse Reaction (SUSAR) or complaint arise from this research, the Research & Development department must be informed within 24 hours of identification.
- Please note that should a Serious Adverse Event (SAE) arise from this research, the Research Sponsor must be informed within 24 hours of identification. In the case of ULHT Sponsored studies, the Research & Development department must be informed as the Sponsors representative.
- The project is subject to the Research Governance Framework for Health and Social Care, 2nd Edition (DOH 2005) and if a CTIMP trial, The Clinical Trials Regulations and its subsequent amendments.
- Please ensure that you are familiar with all ULHT Lincolnshire Clinical Research Facility SOP's and comply with those relevant to your project. All current SOP's are available at: http://www.ulh.nhs.uk/for_staff/lincolnshire_crf/sop.asp

Please note that this Trust approval applies only to the documents listed above. Any changes to the protocol and/or study documents can only be initiated following notification to and approval by all relevant parties, such as the MHRA, Research Ethics Committee, R&D. All correspondence to the Ethics committee must be copied to Research & Development in order to maintain your Trusts Research & Development approval and indemnity status.

Please contact Helen Ayre (Research Governance & Quality Manager), if you require any further information.

On behalf of the Trust, I wish you every success with the study.

Yours sincerely

Dr Tanweer Ahmed
Head of Research & Development, Director of LCRF & IP Lead

CC: Ms Nicola Leighton (Sponsor R&D Office)
Professor Christine Roffe (Sponsor Contact)

Appendix D Letter of invitation to participants

United Lincolnshire Hospitals NHS
NHS Trust

Dr F Ihama, Consultant Physician Care of the Elderly
Department of Care of the Elderly
Secretary : 01205 445305
Office: 01205 445477
Email: felix.ihama@ulh.nhs.uk

Pilgrim Hospital
Sibsey Road
Boston
Lincolnshire
PE21 9QS

Tel: 01205 364801
Fax: 01205 354395

www.ulh.nhs.uk

Monday, 05 January 2015
Version 2.0

Dear Sir/Madam,

Invitation to participate in a research

You are invited to take part in a study which is seeking to evaluate the performance of three common fracture risk assessment tools in care home residents in Boston. Before you decide to join, it is important to understand why the research is being done and what it will involve for you. Dr Ihama, the Chief Investigator will go through the information sheet with you and answer any questions you have. This will take about 10 minutes.

So please consider the information leaflet carefully. Talk to your family, friends, GP or Nurse if you want to. If any information is unclear or if you would like more information, please contact Dr F E Ihama. Contact details can be found at the bottom of the participant information sheet. If you do not want to take part, I would like to assure you that your current medical care will not be compromised in any way and would like to thank you for giving me some of your time.

The purpose of this study and the details of how the study will be carried out has been presented in summary (part 1) and more detailed versions (part 2). Many thanks.

Yours sincerely,

Dr F Ihama
Principal Investigator

Appendix E Participant information sheet

United Lincolnshire Hospitals NHS
NHS Trust

Pilgrim Hospital
Sibsey Road
Boston
Lincolnshire
LN2 5QY

Tel: 01205 364801
www.ulhnhs.uk

Department of Medicine, Elderly Care Unit, Pilgrim Hospital, Boston. Lincolnshire. PE21 9QS

Title of study; A feasibility study evaluating three fragility risk tools

Participant Information sheet
Version 3.0

You are invited to take part in the above study which is seeking to evaluate the performance of three common fracture risk assessment tools in care home residents in Boston. Before you decide, it is important to understand why the research is being done and what it will involve for you. So please consider this leaflet carefully, talk to your family, friends, GP or Nurse if you want to.

If any information is unclear or if you would like more information, please contact Dr F E Ihama who will go through it with you, it will take about 10 minutes. Contact details can be found at the bottom of this document. If you do not want to take part, I would like to assure you that your current medical care will not be compromised in any way and will like to thank you for giving me some of your time. Part 1 is a summary of the information; Part 2 is the more detailed version.

Part 1

Aim; A feasibility study evaluating the performance of three fracture risk assessment tools in Boston.

WHY; Fractures are very common in care home residents. Some of these can be prevented if high risk care home residents are identified early enough.

WHY HAVE I BEEN INVITED: Because you are a care home resident and meet the requirements for this study. 200 care home residents including yourself will be needed for this research.

DO I HAVE TO TAKE PART; No, this is entirely voluntary.

WHAT WILL HAPPEN IF I DO DECIDE TO TAKE PART;

1. You will be requested to sign a consent form.
2. The nursing staff and myself will weigh you.
3. I will take measurement of your forearm with a tape measure.
4. I will request you to walk a distance of 10 feet in-doors (if you can), turn around and sit down. This will happen thrice after a test run.
5. I will access your medical noted for relevant details.

WHAT WILL I HAVE TO DO;

1. Answer a few questions for about 20 minutes relating to fractures and falls.
2. You will be weighed
3. I will take measurement of your forearm with a tape measure.
4. I will request you to walk a distance of 10 feet in-doors (if you can), turn around and sit down. This will happen thrice after a test run.

WHAT ARE THE POSSIBLE DISADVANTAGES; None apart from the inconveniences of answering a few questions, been weighed, your forearm measured and walking.

WHAT ARE THE POSSIBLE BENEFITS; None to you but this research may help others like yourself in future.

WILL ANYONE ELSE KNOW I AM DOING THIS: Your identity will be kept secret and only those who need to know will be informed for example, your GP who you could contact for an independent opinion whether to participate in this study or not.

WHO IS ORGANISING AND FUNDING THIS RESEARCH
I am doing this as my research project in the University of Keele. This research is privately funded entirely and there is no incentive.

WHO HAS REVIEWED THE STUDY: The appointed Agency of the Government of the UK, `Nottingham 1 REC` and the University of Keele Research Authority.

WHAT HAPPENS IF I DON`T WANT TO PARTICIPATE IN THE RESEARCH ANYMORE. Fine but please inform your nurse or GP who will contact me.

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?
The results will be published but your identity will not be revealed.

Thank you very much for your time.

Part 2

Aim; A feasibility study evaluating the performance of three fragility risk assessment risk tools to predict falls in care home residents in Boston.

Why is this research important?
Fractures due to brittle bone disease are common in the elderly. They are even more common in care home residents many of whom are very frail due to various diseases. Risk assessment can be used to identify those residents who are likely to fall and sustain these fractures. Risk assessment tools consist of some questions. For fractures, I have identified three from review of previous studies but these were developed from research which involved healthy elderly in the community. Secondly, these three tools I have identified assess the risk of fractures over a 5 year or 10 year period. It is therefore not clear if these same tools can be useful in care home residents. The aim of this study is to compare the performance of these three tools in care home residents and determine the best which can predict fracture risk over a shorter period of 12 months.

Why have I been invited to take part?

You have been invited to take part because you are a care home resident and you meet with the requirements for this study. This project will involve 200 care home residents including you. This study has not been done before.

Do I have to take part?

Participation in this study is entirely voluntary therefore you are not obliged to support or participate in this study. If you do decide to take part, you will be requested to sign a consent form. If you decide to take part, you are still free to withdraw from the study at any time without giving any reasons. Your decision to withdraw will not affect the standard of care which you receive. You may have someone present with you if you wish during the interview and measurements required for this study and your nurse will always be present.

What will happen if I decide to take part?

If you decide to take part, I will need access to your medical records and it may be necessary to contact your GP for some clarifications. I will then enter the relevant details of your records into my computer which is secured as I alone have the password to it. Dr F E Ihama will ask the questions and record them on a sheet of paper. The questions that I shall be asking will relate to falls, brittle bones and fractures. You will also need to be weighed by the nursing staff and myself on the usual electronic weighing scale with you wearing light clothing and usual shoes. I will take a measurement of your arm with a tape measure using the left forearm preferably. From these measurements I will be able to estimate your height and body mass index. I will request you to walk a distance of 10 feet in-doors (if you can) turn around then sit down. This will happen thrice after a test run. These done, I will telephone the care staffs from time to time to see if you have had any falls or sustained any fractures. This research will not affect your usual treatment in any way.

What will I have to do?

You will be required to answer some questions regarding your fall and fracture condition then you will be weighed on the usual electronic weighing scale and I will take measurement of your forearm with a tape measure and request you to walk indoors.

What are the possible disadvantages?

The questions may take about 20 minutes of your time, the weighing will take a few minutes and the measurement of your forearm will take a couple of minutes and the walking test will take a few minutes.

What are the possible benefits of taking part?

You may not benefit from this study but the result may enable me identify the best risk assessment tool to recommend for use in care home residents to prevent falls and fractures in future.

Will anyone else know I am taking part in this Research Project?

If you decide to take part in this study, your identity will be kept secret and will not be given to any person except only those who have the need to know. I will only send out information that has your name and address removed. All information collected during the study will be stored in a computer secured by a password. I will however need to inform your GP about your participation in this study. You may wish to contact your GP for an independent opinion about whether to take part or not.

Who is organising and funding the research project

I am doing this as my research project in the University of Keele where I am a student. The research is entirely privately funded and there is no incentive.

Who has reviewed the research project

Before any research like this is conducted, it has to be reviewed by the Research Ethics Committee, the designated arm of the Government of the UK, they make sure that the research is appropriate.

What happens if I don`t want to do the research anymore

If at any time you don`t want to continue with the research, please inform the nurse or GP. They will inform me and I will not be offended.

What will happen to the results of the study

At the end of the study, I will analyse the result to determine the best of the three fracture risk tools and then recommend it for use in care home residents. This will then form part of the initial assessment when anybody is admitted to the care home in

much the same way blood pressure, pulse rate and temperature are assessed on admission.

I will also publish my result in medical journals as well as presenting it in conferences so that others might benefit from my study. If you are interested and want to be informed of the results, do let me know by ticking the relevant section in the consent form and I will make a simplified summary available to you by post.

The result from this research may be used to support other research in this area in future but it will not be possible to specifically identify you as one of the participants.

What if there is a problem in the Research process

If you have any concerns about any aspect of this study, you should ask to speak to Dr Ihama who will do his best to answer your questions. If you remain unhappy and wish to complain formally, you can do so by contacting the Complaint Department through the Research and Development Department, ULHT.

I will like to thank you for taking time to read this information about this study. If you have further questions, please contact me through the details giving below and I will be happy to answer them. If you wish to support this study could you please sign the consent form. If however you have decided not to participate, I will like to thank you for taking the time to find out about this study.

Thank you very much.

Dr F E Ihama
Department of Medicine, Pilgrim Hospital,
Boston. Lincolnshire. PE219QS
Telephone; 01205 364 801 bleep 506

Appendix F Letter of invitation to Consultee

United Lincolnshire Hospitals NHS
NHS Trust

Pilgrim Hospital
Sibsey Road
Boston
Lincolnshire
PE21 9QS

Tel: 01205 364801
Fax: 01205 354395

www.ulh.nhs.uk

Tuesday, 06 January 2015
Version 2.0

Dear Sir/Madam,

Invitation to participate in a research

Your relative/friend is invited in a study which is seeking to evaluate the performance of three common fracture risk assessment tools in care home residents in Boston. I feel your relative/friend is unable to decide for himself/herself whether to participate in this research.

To help decide if he/she should participate in this study, I wish to ask your opinion whether or not they would want to be involved. I will like you to consider what you know of his/her wishes and feelings, and to consider his/her interests. Please let me know of any advance decisions he/she may have made about participating in research. These should take precedence. The information sheet is enclosed and is similar to what would have been provided to your relative/friend.

If you decide your relative/friend would have no objection to taking part, may I request you to read and sign the consultee declaration form enclosed. I will then give you a copy to keep. I will keep you fully informed during the study so that you can let me know if you have any concerns or you think your relative/friend should be withdrawn.

If you decide that your relative/friend would not wish to take part, it will not affect the standard of care he/she receives in any way. If you are unsure about taking the role of consultee you may seek independent advice. I will understand if you do not want to take on the responsibility. Many thanks

Yours Sincerely,

Dr F E Ihama
Principal Investigator

Appendix G Consultee information sheet

United Lincolnshire Hospitals NHS
NHS Trust

Pilgrim Hospital
Sibsey Road
Boston
Lincolnshire
PE21 9QS

Tel: 01205 364801
Fax: 01205 354395

www.ulh.nhs.uk

Title of study; A feasibility study evaluating three fragility risk assessment tools

Consultee Information sheet
Version 1.0

Your relative/friend is being invited to take part in the above study which is seeking to evaluate the performance of three common fracture risk assessment tools in care home residents in Boston. As his/her consultee, before you decide, it is important to understand why the research is being undertaken and what it will involve so please read this leaflet carefully, talk to your family, friends, his/her GP or nurse if you want to. If any information is unclear or if you would like more information, please contact Dr F E Ihama through the contact details at the bottom of this document. If you do not want him/her to take part , I would like to assure your that his/her current medical care will not be compromised in any way and would like to thank you for giving me some of your time. The document has been presented in two parts; the summary version (part 1) and a more detailed version (part 2).

Part 1

Aim; A feasibility study evaluating the performance of three fracture risk assessment tools in Boston

Why?; Fractures are very common in care home residents. Some of these fractures can be prevented if high risk care home residents are identified early enough.

Why has your relative/friend been invited? Your relative/friend is a care home resident and meet the requirements for enrolment in the study. 200 care home residents including him/her will be needed for this research.

Does he/she need to take part? No, this is entirely voluntary.

What will happen if he/she decides to take part?

1. The nursing staff/Dr Ihama will take his/her weight
2. Dr Ihama will take measurement of his/her forearm using a tape measure
3. Dr Ihama will request him/her to walk (if he/she can) 10 feet indoors, turn around walk back to an armed chair then sit down. This will happen thrice after a test run. This is the walking test
4. I will request access to his/her medical case file for relevant information
5. I will request you to sign a consultee form; one copy will be put in her file, you will have a copy and I will have a copy
6. Periodically, I will contact his/her care home to find out if he/she has had a fall or fracture

What will your relative/friend need to do?

1. Answer a few questions for about 20 minutes
2. Your relative/friend will be weighed
3. Dr Ihama will take measurement of her forearm
4. He/she will be requested to do the walking test if he/she can

What are the possible disadvantages?; None apart from the inconveniences of answering a few questions, being weighed, taking the forearm measurement and doing the walking test.

What are the possible benefits?
None to your relative/friend but this research may benefit others in future.

Will anyone else know about the identity of your relative/friend?
His/her identity will be kept secret and only those who need to know will be informed; for example his/her GP who you could contact for an independent opinion.

Who is organising and funding this research?
It is a research project in the University of Keele. It is privately funded and there are no incentives

Who has revised this study?
It has been reviewed and approved by the UK Government appointed Agency; IRAS and the University of Keele.

What happens if you wish to withdraw assent?; Fine but please inform his/her nurse and GP or you may wish to contact me.

What will happen to the results of the research?
The results will be published but the identity of your relative/friend will not be revealed.

Part 2

Aim; A feasibility study to evaluate the performance of three fragility risk assessment tools in predicting falls in care home residents in Boston

Why?
Fractures due to brittle bone disease are common in the elderly. They are especially common in care home residents many of whom are frail due to various diseases. Risk assessment can be used to identify those residents who are likely to fall and sustain fractures. Risk assessment tools consist of some questions. For fractures, I have identified three but these were developed from research which involved healthy elderly in the community.

Secondly, these tools I have identified assess the fracture risk over a 5-year or 10-year period. It is therefore not clear if these same tools can be useful in care home residents. The aim of this study is to compare the performances of these three tools in care home residents and determine the best which can predict fracture risk over a shorter period of 12 months.

Why has your relative/friend been invited to take part?
He/she has been invited to take part in this study because he/she meets with the requirements. This research will enrol 200 participants including your relative/friend.

Does he/she need to take part?
Participation in this study is entirely voluntary. If you decide to give assent, you will be requested to sign a consultee form and you are free to withdraw it at any time without giving any reason, this will not affect the standard of care he/she receives. You may wish to be present during the interview and the measurements required and her care nurse will always be present.

What will happen if he/she takes part?
If you give assent, by signing the consultee form, I will need to assess his/her medical notes and it may be necessary to contact his/her GP for some clarification. The information obtained will be entered into my computer which is secured as it is password protected. I will then ask him/her some questions relating to falls and fractures; this will take about 20 minutes.

He/she will be weighed on the usual electronic scale with the resident wearing light clothing and usual shoes. I will take measurement of the forearm with a tape measure and from the weight and forearm length I will be able to estimate the body mass index which is a measure of the state of nutrition. I will request him/her to walk (if he/she can) 10-feet indoors, turn around, walk back to an armed chair and sit down. This will happen three times after a test run. This is the walking test. These done, I will telephone the care home nurse periodically to find out if a fall or fracture has occurred. This research will not affect his/her usual treatment in any way.

What will he/she need to do?
He/she will be requested to answer some questions regarding fall and fractures. He/she will be weighed on the usual weighing scale, measurement of the forearm will be taken using a tape measure and she will be requested to undertake the walking test if he/she can.

What are the possible disadvantages of taking part?
The questioning takes about 20 minutes, the weighing, forearm measurement and walking test take a few minutes.

What are the possible benefits in taking part?
He/she will not benefit from this study but the result may enable me to identify the best fracture risk assessment tool to recommend for use in care home residents.

Will anyone else know he/she is taking part in the study?
His/her identity will be kept secret and will not be given to any person except those who need to know. I will only send out information that has his/her name, and address removed. All information collected will be stored in a computer which is secured as it is password protected. I will inform his/her GP of participation. You may wish to contact his/her GP for an independent opinion about participation in this study.

Who is organising and funding this research?
This research is part of my project in the University of Keele. It is entirely privately funded and there is no incentive.

Who has reviewed this research project?
Before any research of this type is conducted in the UK, it must be reviewed by the Government Agency called IRAS to determine if the project is appropriate. This study has been approved by IRAS as well as the University of Keele.

What happens if you do wish to withdraw assent?
If at any time you do not want him/her to continue with the study, please you can contact me, the nurse or GP, I will not be offended.

What will happen to the results of this study?
At the end of the study, I will analyse the information and determine the best of the three tools to recommend for use in care homes. This will then form part of the initial assessment when anybody is admitted to a care home in much the same way blood pressure, temperature, pulse rate are assessed on admission.

I will publish my findings as well as presenting it in conferences so that others might benefit from my study. If you are interested and want to be informed of the results do let me know by ticking the relevant box in the consultee form and I will make a simplified summary available to you by post. The result from this study may be used to support other research of this type in future but it will not be possible to specifically identify him/her as one of the participants.

What if there is a problem in the research process?
If you have any concerns about any aspect of this research, you may request to speak to me and I will do my best to answer your questions. If you are not satisfied and wish to complain formally, you can do so by contacting the Compliant Department through the Research and Development Department, ULHT.

I will like to thank you for taking time to read this information leaflet. If you have further questions, please contact me through the details at the bottom of this document. If you wish to support this study, could you please sign the consultee form enclosed. If you have decided not to sign I will like to thank you for taking the time to find out about this study.

Thank you very much

Dr F E Ihama
Department of Medicine,
Pilgrim Hospital,

Boston.
Lincolnshire
PE21 9QS
Telephone; 01205 364 801, bleep 506

Appendix H Consent form

United Lincolnshire Hospitals NHS
NHS Trust

Pilgrim Hospital
Sibsey Road
Boston
Lincolnshire
LN2 5QY

Tel: 01205 364801
www.ulhnhs.uk

Study Number:

Patient Identification Number for this study:

CONSENT FORM
VERSION 2.0

Title of Project: A feasibility study evaluating the efficacy of three fragility risk assessment tools to predict falls and fractures in care home residents

Name of Researcher: Dr F E Ihama

Please initial all boxes

I confirm that I have read and understand the information sheet dated (DATE) version number X for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily. ☐

I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my care or legal rights being affected. ☐

I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from the University of Keele, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals and Dr Ihama to have ☐

access to my medical records for research purposes

I agree to my GP being informed of my participation in the study. ☐

I agree to take part in the above study. ☐

I will like to be informed of the outcome of this research ☐

I agree to my data being used in future research if it is necessary ☐

_____	_____	_____
Name of Participant	**Date**	**Signature**
_____	_____	_____
Name of Witness	**Date**	**Signature**
_____	_____	_____
Name of Person Taking consent	**Date**	**Signature**

When completed 1 for participant, 1 for researcher site file, 1 (original) to be kept in medical notes

Appendix I Consultee form

United Lincolnshire Hospitals NHS
NHS Trust

Pilgrim Hospital
Sibsey Road
Boston
Lincolnshire
LN2 5QY

Tel: 01205 364801
www.ulhnhs.uk

Study Number:

Patient Identification Number for this study:

CONSULTEE DECLARATION FORM
(Participant`s representative)
Version 2.0

Title of Project: A feasibility study evaluating the efficacy of three fragility fracture risk tools to predict falls and fractures in care home residents

Name of Researcher: Dr F E Ihama

Please initial all boxes

I (name of consultee) have been consulted about (name of potential participant)`s participation in this research project. I have had the opportunity to ask questions about the study and understand what is involved. ☐

In my opinion he/she would have no objection to taking part in the study ☐

I understand that I can request he/she is withdrawn from the study at any time without giving any reason and without his/her care or legal rights being affected. ☐

I understand that the relevant sections of his/her care record and data collected during the study may be looked at by responsible individuals from the University of Keele and the United Lincolnshire Hospital NHS Trust or from regulatory authorities, where it is relevant to their taking part in this research. ☐

I agree to his/her GP being informed of participation in the study. ☐

I will like to be informed of the outcome of this research ☐

I agree to his/her data being used in future research if it is necessary ☐

_____	_____	_____
Name of Consultee	**Date**	**Signature**

Relationship to participant:

_____	_____	_____
Researcher	**Date**	**Signature**

When completed: 1 (original) to be kept in care record, 1 for consultee; 1 for researcher site file

Appendix J Letter to the General Practitioner

United Lincolnshire Hospitals NHS
NHS Trust

Pilgrim Hospital
Sibsey Road
Boston
Lincolnshire
LN2 5QY

Tel: 01205 364801
www.ulhnhs.uk

Department of Medicine, Elderly Care Unit, Pilgrim Hospital, Boston. Lincolnshire. PE21 9QS

Letter to the General Practitioner
Version; 1.0

Title of Study; A feasibility study evaluating the efficacy of three fragility risk assessment tools to predict falls and fractures in care home residents

Date;

Dear Dr

I am conducting a research on the above subject. It is a prospective observational cohort study. I have the written signed informed consent of your patient (name of patient, NHS number;) to contact you for clarification of some details. I have enclosed a photo copy of the signed consent form and the participant information sheets.

Many thanks.

Yours Sincerely,

Dr F E Ihama

Appendix K Research pathway

Research pathway

OPTION A - Identified by Care home manager as having mental capacity

(VISIT 1) To be completed by Care Home Manager:

Care home _____

Telephone number of care home _____

Principal investigator _____

Information Sheet given? Y / N (Date_____)

Permission given for contact by Dr Ihama? Y / N *(If 'no' record initials/DOB only)*

Name / Initials _____

Date of birth _____ *(Dr Ihama to record pt on screening log)*

(VISIT 2) To be completed by Dr Ihama:

Date referral received: _____

Date of first approach: _____

Time of first approach: _____

Information sheet received previously? Yes / No

Discussion of study? Yes / No

Witness (name) _____

Any questions following discussion? Yes / No Outcome of first visit:

- ☐ Written Consent Yes / No *(Only applicable if PIL given >24 hours previously)*
- ☐ Will consider participating
- ☐ Not interested in participating *(record on screening log)*

(VISIT 3) To be completed by Dr Ihama:

Date _____

Time _____

Remains happy to participate? Yes / No

Witness present? (Name) _____

Continuing Mental capacity? Yes / No (if no for consultee: see pathway 2 below)

Written Consent obtained? Yes / No *(Only if not previously obtained)*

Activity checklist *(See completed questionnaire for full detail):*

- ☐ Questionnaire
- ☐ Weight
- ☐ Ulnar Length
- ☐ Timed Get up and Go Test

OPTION B - Identified by Care home manager as not having full mental capacity

(VISIT 1) - To be completed by Care Home Manager:

Care home _____

Telephone number of care home _____

Principal investigator _____

Name _____

Date of birth _____

Consultee name _____

Relationship _____

Telephone number _____

Contact address _____

_____

Date information leaflet and contact detail form given/posted to consultee

_____

Date consultee form returned _____ ***(Please forward completed form to Dr Ihama)***

(VISIT 2) – To be completed by Dr Ihama

Date of notification from care home manager / referral received: _____

Date of discussion with consultee _____

Information sheet received previously? Yes / No

Discussion of study? Yes / No

Any questions following discussion? Yes / No

Outcome of first visit:

- ☐ Written assent given? Yes / No *(Only applicable if Information Leaflet given >24 hours previously)*
- ☐ Will consider
- ☐ Not interested in participating *(record on screening log)*

(VISIT 3) To be completed by Dr Ihama:

Date _____

Time _____

Remains happy to provide assent for participation? **Yes / No**

Written Assent obtained? **Yes / No** *(Only if not previously obtained)*

Activity checklist *(See completed questionnaire for full detail):*

- ☐ Questionnaire
- ☐ Weight
- ☐ Ulnar Length
- ☐ Timed Get up and Go Test

NOTES
Incidents Yes/No
Type
End of study date
Total duration of recruitment process
Any other comments

Appendix L Screening log template

Screening Log

Primary Investigator Name	Centre Name	Centre No:

Patient initials/DOB	Date Screened	Eligible Y/N	Recruited Y/N	Date of recruit/fail	Reasons/Comments

_____ of _____

Appendix M Scoring in the composite questionnaire

The table shows the scoring system of the composite questionnaire. Categorical variables were assigned numerical values and the actual values were recorded for the continuous variables.

FRAX

Identity			
Variable	**Participant`s response**	**Scoring system for EXCEL**	**Score**
Age (ys.)	Actual age record		
Date of Birth (Year Month Day)	Actual record		
Sex (Male, Female)		Male=1, Female=0	
Weight (kg)	Actual weight record	Actual weight record	
Height (cm)	Actual height record	Actual height record	
Previous fracture (No, Yes)		No=0, Yes=1	
Parental Fractures Hip (No, Yes)		No=0, Yes=1	
Current smoking (No, Yes)		No=0, Yes=1	
Glucocorticoids (No, Yes)		No=0, Yes=1	
Rheumatoid arthritis (No,, Yes)		No=0, Yes=1	
Secondary osteoporosis (No, yes)		No=0, Yes=1	
Alcohol 3 or more units/day (No, Yes)		No=0, Yes=1	
10 year absolute fracture probability	Actual score	Actual score record	
Time to complete FRAX in minutes	Actual record	Actual record	

Appendix M Scoring system of the composite questionnaire (continued)

QFractureScores

Variable	**Participant`s response**	**Scoring system for EXCEL**	**Score**
Age (30-99 ys.)	Actual age record		
Sex (Male, Female)		Male=1, Female=0	
Ethnicity (White, Indian, Pakistani, Bangladeshi, Other Asian, Black Caribbean, Black African, Chinese, Other Ethnic group)		White=0, Indian=1, Pakistani=2, Bangladeshi=3, Other Asian=4, Black Caribbean=5, Black African=6, Chinese=7,Other Ethnic group=8)	
Smoking (non-smoker, ex-smoker, light smoker ;less than 10), moderate smoker;10-19), heavy smoker;20 or over)		Non-smoker=0, Ex-smoker=1, Light smoker; less than 10=2, Moderate smoker;10-19=3, Heavy smoker ;20 or over=4	
Alcohol status (None, <1 unit per day, 1-2 units per day, 3-6 units per day, 7-9 units per day, >9 units per day)		None=0,<1 unit/day=1, 1-2 units/day=2, 3-6 units/day=3, 7-9 units/day=4, >9units/day=5	
Diabetes (None, Type1, Type 2)		None=0, Type 1=1, Type2=2	
Do either your parents have osteoporosis/hip fracture? (No, Yes)		No=0 Yes=1	
Do you live in a nursing or care home? (No, Yes)		No=0 Yes=1	
Have you had a wrist, spine, hip or shoulder fracture? (No, Yes)		No=0 Yes=1	
History of fall/ (No, Yes)		No=0 Yes=1	
Dementia? (No, Yes)		No=0 Yes=1	
Cancer (No, Yes)		No=0 Yes=1	

Appendix M Scoring system of the composite questionnaire (continued)

Asthma? (No, Yes)		No=0 Yes=1	
Heart attack, angina, stroke or TIA? (No, Yes)		No=0 Yes=1	
Chronic liver disease? (No, Yes)		No=0 Yes=1	
Chronic kidney disease? (No, Yes)		No=0 Yes=1	
Parkinson`s disease? (No, Yes)		No=0 Yes=1	
Rheumatoid disease? (No, Yes)		No=0 Yes=1	
Malabsorption e.g. Crohn`s disease, ulcerative colitis, Coeliac disease, steatorrhoea or blind loop syndrome? (No, Yes)		No=0 Yes=1	
Endocrine problems e.g. Thyrotoxicosis, hyperthyroidism, Cushing`s syndrome?		No=0 Yes=1	
Epilepsy or taking anticonvulsants? (No, Yes)		No=0 Yes=1	
Taking antidepressants? (No, Yes)		No=0 Yes=1	
Taking steroid tablets regularly? (No, Yes)		No=0 Yes=1	
Taking oestrogen only HRT? (No, Yes)		No=0 Yes=1	
Body mass index	Actual record	Actual record	
Height (cm)	Actual record	Actual record	
Weight (kg)	Actual record	Actual record	
10 year absolute fracture probability	Actual record	Actual record	
Time to complete QFractureScore in minutes	Actual record	Actual record	

Appendix M Scoring system of the composite questionnaire (continued)

Garvan nomogram

Variable	**Participant`s response**	**Scoring system for EXCEL**	**Score**
Sex (Male, Female)		Male=1, Female-0	
Age	Actual age record		
Fracture since age of 50 years (Excluding major trauma e.g. car accidents) (0, 1, 2, 3 or more)		0=0 1=1 2=2 3 or more =3	
Falls over last 12 months (0, 1, 2 3 or more)		0=0 1=1 2=2 3 or more=3	
Weight (kg)	Actual record	Actual record	
10 year absolute fracture probability	Actual record	Actual record	
Time to complete Garvan nomogram in minutes	Actual record	Actual record	

Timed Up & Go Test (TUGT)

Variable	**Participant`s response**	**Scoring system for EXCEL**	**Score**
Time to complete TUGT (< 10 seconds= freely mobile, <20 seconds Mostly independent, 20-29 seconds variable mobility, > 30 seconds impaired mobility)	Actual record First attempt Second attempt Third attempt Average=	≤ 10 seconds=0 11- 19 seconds=1 20-29 seconds=2 ≥30 seconds= 3	
Participant unable to undertake task	Participant unable to undertake task	4	
TUGT	With walking aids=1 Without walking aids=0		
Time to complete TUGT in minutes(including preparation)	Actual record		

Appendix M Scoring system of the composite questionnaire (continued)

Other variables

Variables	**Participant`s response**	**Scoring system for EXCEL**	**Score**
Number of comorbidities	Actual number record		
Charlson`s comorbidity index in 1yr	Actual record		
Duration in days to complete questionnaire including consenting	Actual record		
Falls in study (No, Yes)		No=0 Yes=1	
Fractures in study (No, Yes)		No=0 Yes=1	
Radiologically verified fractures		No=0 Yes=1	
Falls and Fractures in study (No, Yes)		No=0 Yes=1	
Outcome of participant at end of study (Alive, Dead)		Alive =0 Dead=1	
Name of Care Home	Actual record	Actual record	
Type of Care Home (RH, NH, MIH)		RH=0 NH=1 MIH=2	
Telephone number of Care Home	Actual record	Actual record	
GP of Participant	Actual record	Actual record	
Telephone number of Participant`s GP	Actual record	Actual record	
Next of Kin (NOK)	Actual record	Actual record	
Telephone number of NOK	Actual record	Actual record	
Date of recruitment of participant	Actual record	Actual record	
Proposed termination date	Actual record	Actual record	

Appendix N Definitions of terms

For this research, the following terms were defined thus:

Age: Defined as the number of years since the last birthday.

*Date of birth***:** Defined as the date of birth in the participant`s case file.

Adult: A person who has attained the age of legal majority (18 years for most purposes).

Older person: In high resourced countries older age is defined in relation to retirement from paid employment and receipt of a pension at 60 or 65 year (WHO 2012).

Sex: Defined as the sex recorded in the participants care home case file.

Ethnicity: Defined as the state of belonging to a social group that has a common natural or cultural tradition and recorded in the casefile.

Body weight: Defined as the weight in kilograms measured by SECA sit-in electronic weighing scale with the participant weighed sitting in the scale, wearing normal clothing, light shoes and feet off the ground.

Body mass index (BMI): Calculated from baseline objective weight and height measurements, as weight in kilograms divided by height in squared meters (kg/m^2).

Smoking status: Defined as smoking status recorded in the participant`s case file.

Alcohol status: Defined as alcohol consumption recorded in the participant`s case file.

Co-morbidities: Defined as the past medical history recorded in the participant`s case file.

Medications: Defined as medications recorded on the participant's treatment sheet.

Use of walking aid: Defined as the current use of a walking frame, stick, crutches or wheelchair irrespective of the frequency of use.

History of previous fall: Defined as history of fall prior to recruitment.

Number of previous falls: Defined as the number of previous falls prior to recruitment.

Previous Fragility Fractures: Defined as any previous fragility fractures in the past.

Parental history of hip fractures/osteoporosis: Defined as a history of hip fractures and osteoporosis obtained from the participant, Next of kin (NOK) or GP.

Secondary osteoporosis: Defined as osteoporosis with identified causes.

Outcome at the end of 12 months of study: Defined as the status of the participant at the end study, dead or alive.

Date of recruitment of participant: Defined as the date the participant was enrolled in this study.

Termination date: Defined as the date of termination of follow-up (12 months after recruitment).

Crude incidence rate: The number of new cases occurring in a specified population in a year.

Person-centred care; the experience (to the extent the informed individual patient desires it) of transparency, individualization, recognition, respect, dignity, and choice in all matters, without exception, related to one`s person, circumstances, and relationships in health care (Berwick DM et al 2009).

Statistical power: Defined as the probability that the test will reject a false null hypothesis. In plain English, statistical power is the likelihood that a study will detect an effect when there is an effect there to be detected (Ellis P.D 2010).

Appendix O The QUADAS tool

The tool is structured as a list of 14 questions which should each be answered "yes", "no", or "unclear".

Item		Yes	No	Unclear
1.	Was the spectrum of patients representative of the patients who will receive the test in practice?	( )	( )	( )
2.	Were selection criteria clearly described?	( )	( )	( )
3.	Is the reference standard likely to correctly classify the target condition?	( )	( )	( )
4.	Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?	( )	( )	( )
5.	Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?	( )	( )	( )
6.	Did patients receive the same reference standard regardless of the index test result?	( )	( )	( )
7.	Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?	( )	( )	( )
8.	Was the execution of the index test described in sufficient detail to permit replication of the test?	( )	( )	( )
9.	Was the execution of the reference standard described in sufficient detail to permit its replication?	( )	( )	( )
10.	Were the index test results interpreted without knowledge of the results of the reference standard?	( )	( )	( )
11.	Were the reference standard results interpreted without knowledge of the results of the index test?	( )	( )	( )
12.	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	( )	( )	( )
13.	Were uninterpretable/ intermediate test results reported?	( )	( )	( )
14.	Were withdrawals from the study explained?	( )	( )	( )

Appendix P Order of selection of the care homes

1. Log on google using www.google.co.uk *then*
2. Enter online random generation *then*
3. Assess random org-true random number services *then*
4. Locate number selection section and locate sequence generator *then*
5. Enter the number 1 for smallest and the number 18 (number of care homes in Boston) for largest and the number 1 for format *then*

   enter the `Get sequence` button.

Appendix Q Power calculation

Contents from the abstract

In the observational study, 217 (35%) participants out of 618 residents in the 18 care homes were enrolled. Out of the 217 participants, 147 (68%) had mental capacity and only 70 (32%) did not. This was because there was difficulty in obtaining informed consent from the consultees in residents without mental capacity. The odds ratios for the prediction of the outcomes were as follows: FRAX falls 1.003 (p=0.813), fractures 1.027 (p=0.267), combined falls and fractures 1.027 (p=0.267); QFractureScores falls 1.007 (p=.160), fractures 1.024 (p=0.036), combined falls and fractures 1.024 (p=0.036); Garvan nomogram fall, 1.010 (p=0.054), fractures 1.021 (p=0.0620, combined falls and fractures 1.021 (p=0.062); BMI falls 0.952 (p=0.015), fractures 0.868 (p=0.024), combined falls and fractures 0.868 (p=0.024); TUGT: falls 0.999 (p=0.013), fractures 1.000 (p=0.829), combined falls and fractures 1.000 (p=0.829).

Power analysis and sample size computations

The purpose of this project was to determine the minimum sample size needed for each tool (FRAX, QFractureScore, Garvan, BMI, and TUGT) under each circumstance (fall, fractures, and combined falls and fractures), based on a two-tailed test and an alpha level of 0.05, to give 80% power to detect an odd ratio of 2 (small to medium effect) for each tool in the prediction of falls and fractures.

A priori power analysis was conducted based on binary logistic regression (for binary response variable, i.e., falls vs. no falls; fractures vs. no fractures; combined falls and fractures vs. neither) to determine the minimum sample size required for this study for each tool (FRAX, QFractureScore, Garyan, BMI, and TUGT) under each circumstance (fall, fractures, and combined falls and fractures) using Gpower version 3.1.9.2 (Faul, Erdfelder, Buchner, and Lang, 2009). During the process of sample size computation for each tool, the following assumptions were made: 1) the predictor of interest is a categorical variable with two levels (above the threshold vs. not above the threshold), and 2) a medium effect size (odds ratio = 2) (Haddock, Rindskopf, & Shadish, 1998). Additionally, the probability of event happening if the score of a tool is above the threshold (ex: probability of falls given FRAX score above a threshold) is computed based on the observed odds in the pilot study (see Table 1).

The results of the power analysis are presented in Table 1. For a two-sided test with a significance level of 0.05, medium effect size (odds ratio = 2), and a power of 0.8 to show a significant effect of the predictor, the minimum sample size needed (N_{total}) for each tool under each circumstance in the study ranged from 271 (for BMI) to 277 (for FRAX).

Furthermore, in the pilot study, 68% of the participants had mental capacity and 32% did not. Hence, we assumed the sample would contain 70% patients with mental capacity and 30% patients without metal capacity. The required number of samples from each group (with mental capacity vs. without mental capacity) for each tool under each circumstance is presented in Table 1.

Also from the pilot study, we learned that only 21% of patients without mental capacity would give consents and 57% of patients with mental capacity would give consents for the study.

To obtain enough patients without mental capacity (N_{total_nm}), the researcher would need to sample N_{nm} (= N_{total_nm} /0.21) residents without mental capacity; to obtain enough patients with mental capacity (N_{total_m}), the researcher would need to sample N_m (= N_{total_m} /0.57) residents with mental capacity, see Table 1.

For example, according to the results presented in Table 1, for tool = “FRAX” and circumstance = “Falls”, the minimum sample required (N_{total}) is 276, in which, 193 (N_{total_m}) is expected to have mental capacity and 83

(N_{total_nm}) is expected to have no mental capacity. Furthermore, based on the consent rate of the pilot study, to ensure enough residents would participate in the study, 339 patients with mental capacity (N_m) should be sampled and 395 patients without mental capacity (N_{nm}) should be sampled.

Table 1: Results of Power Analysis

Tool	Outcome	Observed odds ratio	Observed probability = odds ratio/(1+odds ratio)	N_{total}	N_{total_m}	N_{total_nm}	N_m	N_{nm}
FRAX	Falls	1.003	0.501	276	193	83	339	395
	Fractures	1.027	0.507	277	194	83	340	395
	Combined falls and fractures	1.027	0.507	277	194	83	340	395
QFractureScores	Falls	1.007	0.502	276	193	83	339	395
	Fractures	1.024	0.506	277	194	83	340	395
	Combined falls and fractures	1.024	0.506	277	194	83	340	395
Garvan	Falls	1.010	0.502	276	193	83	339	395
	Fractures	1.021	0.505	277	194	83	340	395
	Combined falls and fractures	1.021	0.505	277	194	83	340	395
BMI	Falls	0.952	0.488	274	192	82	337	390
	Fractures	0.868	0.465	271	190	81	333	386
	Combined falls and fractures	0.868	0.465	271	190	81	333	386
TUGT	Falls	0.999	0.500	276	193	83	339	395
	Fractures	1.000	0.500	276	193	83	339	395
	Combined falls and fractures	1.000	0.500	276	193	83	339	395

Note: N_{total} = minimum sample size required. N_{total_m} = minimum sample size required for patients with mental capacity = 70% of total N. N_{total_nm} = minimum sample size required for patients without mental capacity = 30% of total N. $N_m = N_{total_m} /0.57$ = number of residents with mental capacity that need to be sampled. $N_{nm} = N_{total_nm} /0.21$ = number of residents without mental capacity that need to be sampled.

This power calculation was done by Dr Y Su, Consultant Statistician in Hawaii, USA.

Appendix R Data extraction template of the systematic literature review

1. Number of authors
2. Year of publication
3. Type of study; Review/meta-analysis/original
4. Title of article
5. Country of study
6. Mean age in years of the participants
7. Sex; male/female
8. Ethnicity
9. Setting; community/care home/mixed
10. Design of the study
11. Number of participants
12. Type of assessment
13. Site of primary outcome measure
14. Method of fracture verification; self-report/radiologist/case note review
15. Duration of follow-up
16. Method of statistical analysis
17. Conflict of interest declared; yes/no
18. Ethical approval; yes/no
19. Performance characteristics
20. Internal validation; yes/no
21. External validation; yes/no
22. Internal and external validation; yes/no
23. Tool calibration; yes/no
24. Authors involved in calibration; yes/no
25. Output of tools
26. No of risk factors
27. Missing data reported; yes/no
28. Loss to follow-up reported; yes/no

Appendix S Pilgrim Hospital named best hospital in the UK for Hip Fracture management

Boston Standard

Hip op hooray! Pilgrim named top in country

The winners - The hip fracture team with (third from left) Theo Joachim.

Published: 21:15
Wednesday 11 February 2015

Share this article

Pilgrim Hospital has been named the best in the country for the way it treats patients with hip fractures – bagging the title for the second year in a row.

The National Hip Fracture Database has said that the Pilgrim is best of all 182 hospitals for ensuring all patients are operated on quickly.

The figures also say Boston's hospital was the number one in the country for achieving best practice criteria in the National Hip Fracture Database reports in 2013.

The average length of stay for patients is also one of the lowest in the country at 12.7 days compared to a national average of 15.3 days.

The team at the hospital, led by Theo Joachim, orthopaedic surgeon, said it had recognised the need to improve standards and care for patients admitted to hospital with hip fractures.

To address the issues the team says it 'revolutionised' the care of patients who have hip fractures, by improving assessment, the speed at which patients are taken to theatre for surgery and after care.

They say that improvements have been achieved by changing the way clinical teams work, ensuring such cases are treated as a priority, and using operating theatre time smartly to reduce delays.

Speaking of their national success as a result of the changes, Mr Joachim said: "The project has been a fantastic success in helping to shape the healthcare delivered at the trust.

"Most hip fractures are suffered by frail elderly patients, for whom the injury is life-threatening.