**Effective communication and the osteoporosis care gap**

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**Abstract**

Many pharmacological treatments are now available to prevent the occurrence of fragility fractures in patients with osteoporosis. Despite this there are persisting concerns that many individuals who might benefit from osteoporosis treatment do not receive it – the so called “osteoporosis treatment gap”. The underlying reasons for this gap are diverse and include those who are not identified as being eligible for treatment as well as those who intentionally choose not to take medications because of uncertainty, unanswered questions or inability to understand or do what is being asked of them. In this perspective article we highlight the importance of providing information on the causes and consequences of osteoporosis during encounters when treatment is being discussed as well as what osteoporosis treatment can achieve and what it cannot. We also review the importance of communicating the benefits and risks of treatment in absolute terms so that patients can understand what taking treatment will mean for them and discuss the utility of decision aids to assist in these conversations. We suggest it is not the treatment gap which is the problem but the *care* gap. This language acknowledges the importance of healthcare providers identifying those likely to benefit from treatment and increasing the quality of clinical conversations to promote patient engagement and involvement, while respecting that treatment is not suitable or wanted by all.

There has been a concern for many years that many individuals who might benefit from osteoporosis treatment do not receive it – this has been referred to as the “osteoporosis treatment gap” (1) . In this perspective we have analysed individual components of the treatment gap and put forward potential solutions, focusing primarily on the importance of providing patients with accurate information on the balance between absolute benefits and absolute risks of treatment, giving the patient an accurate diagnosis by dual-x-ray energy absorptiometry (DXA) and ensuring that physicians respect shared decision making when advising on medical treatments for osteoporosis. We also suggest that the term “treatment gap” should be replaced by “osteoporosis care gap” to take account of the fact that not all patients want to take drug treatment having been fully informed of the risks and benefits.

**What is the osteoporosis treatment gap?**

Various definitions of the treatment gap have been put forward but in a recent review by Fuggle and colleagues it was defined as the difference between the number of individuals who *require* osteoporosis treatment and the number that receive it (2). The authors did not define what they meant by “require” but our assumption was that these are individuals who would benefit from receiving such treatment in terms of a reduction in fracture risk. Other definitions of the treatment gap have also been put forward; in a recent publication by McCloskey and colleagues based on a cross-sectional study of 3798 postmenopausal women aged 70 and over in eight European countries the definition was widened to include individuals who were not being treated who had suffered a major osteoporotic fracture over the age of 50; those with osteoporosis diagnosed by DXA or those with a “high fracture risk”. This was defined as a 10-year major osteoporotic fracture risk above country specific cut-offs (3) which ranged between 10% in Poland to 25% in Sweden and Switzerland.

**What benefit can the patient expect from treatment?**

Since osteoporosis is clinically silent until a fracture occurs, the treatments that physicians prescribed to prevent future fractures don’t provide any immediate symptomatic benefit. Accordingly, when discussing treatment options, it is important to ensure that the patient is aware of what benefits they might expect, and what side effects might occur. Some individuals in the “treatment gap” as defined by McCloskey (3) such as those who have had a fragility fracture aged over 50 and those with a high fracture risk may not derive benefit from drug treatment for osteoporosis. We say this because there is no evidence that the commonly used drug treatments for osteoporosis reduce the risk of fractures in *all* individuals who have experienced a fracture above the age of 50, or because they have a 10-year fracture risk over a certain threshold. It is probable that some of these individuals will benefit in terms of fracture prevention but the magnitude of benefit for the individual is uncertain and information on to what degree the patient may benefit is crucial to shared decision making.

Of relevance to the issue of fracture prevention in those at high fracture risk, the UK based SCOOP trial looked at the effectiveness of a population-based screening strategy for high fracture risk in women age greater than 70 linked to an offer of DXA which was used to refine the fracture risk calculation (4). Disappointingly, this study showed no overall reduction in major osteoporotic fractures in the screened population although there was a reduction in hip fractures in the screened population. In both groups, the proportion of patients who were treated for osteoporosis was low (14% in the screened group and 4% in the control group). Although all participants in SCOOP would lie within the treatment gap as defined by high fracture risk, the strategy was not effective in reducing the overall fracture burden. With the exception of HRT, the strongest evidence base for fracture prevention using the most widely used treatments for osteoporosis are based on their use when there is DEXA proven osteoporosis (T-score <-2.5) and/or vertebral fractures (5) or in the case of zoledronic acid, osteopenia (T-score between -1.0 and -2.5) (6). Consequently, we believe that it is important to perform DXA in people with high fracture risk to give a more precise estimate of fracture risk; to evaluate the effect size of the likely benefit; and to maximize acceptance of treatment.

**The importance of diagnosing osteoporosis**

Over recent years there has been a move away from treating osteoporosis simply because the BMD T-score is less than -2.5 to a model where absolute fracture risk is also considered. In the UK for example, the current iteration of the NOGG guidelines (7) suggest that drug treatment for osteoporosis should be initiated in people with a high fracture risk whether or not BMD measurements have been performed. Although some patients with very high fracture risk will benefit from treatment, we believe that measurement of BMD is a key component of the treatment pathway not least because the diagnosis of osteoporosis is highly influential in the likelihood of a patient accepting treatment. The “Common Sense” Model of disease tells us that a diagnostic label helps patients understand their condition and that this in turn helps to guide their coping strategies actions (8). Empirical research evidence also supports this, since in the McCloskey study cited previously (3) the “treatment gap” in those with a DXA diagnosis of osteoporosis was only 30.9% compared with 94.2% in those without a diagnosis. A systematic review also demonstrated that prior BMD measurements before starting osteoporosis medication is associated with higher persistence and adherence compared to non-testing (9). Finally, in the SCOOP trial adherence to osteoporosis treatment was better in patients who had assessment of fracture risk followed by a BMD assessment as compared to those allocated to usual care which did not consistently use DXA scanning before treatment start (4). This indicates that a diagnostic label, whether it be “osteoporosis” or “osteopenia” as demonstrated by BMD measurements helps patients make sense of their susceptibility to fracture, and the likely benefit of treatment.

**Problems with the term treatment gap**

Several subgroups of individuals can be identified in the so called “treatment gap”. There are those who are likely to benefit from treatment but have not been offered it and there are other individuals who have been offered treatment who have decided not to take or continue it. Proponents of the term ’treatment gap’ suggest that 100% of patients in whom treatment is thought to be clinically indicated should be taking medicine. This is a paternalistic standpoint and does not take account of the individual patient’s situation or preferences. For example, there are individuals who have been identified as benefiting from treatment but who have decided against proceeding having been fully informed about the risks or benefits. Arguably patients who have made an informed choice are not non-adherent. Furthermore, individuals living with frailty and limited life expectancy who may not value or significantly benefit from a preventative treatment and may decide in partnership with their treating clinician that treatment is not appropriate.

**Person-centered medicine**

Providing accurate information is at the core of person-centered medicine (10) which aims to put the patient at the centre of decisions made about their care. This represents a movement away from decision making on the appropriateness of treatment being based solely on a cut-off point above or below a somewhat arbitrary threshold. For example, the current UK NOGG guideline (accessible via the FRAX UK calculator) presents clinicians with options of “treat” or “don’t treat” above a certain level of fracture risk (7). A footnote to this algorithm states that “these thresholds are for guidance only and the final decision to assess BMD or to initiate therapeutic intervention lies with the *individual clinician*”. While we acknowledge that a ‘threshold’ approach may make it easier for non-specialists to identify those in whom treatment may be offered, the wording implies that the decision to initiate treatment lies with the clinician whereas in fact, treatment decisions need to be considered both by the clinician and the patient taking into account the wider clinical context.

To improve outcomes for people with osteoporosis, healthcare professionals must play a much more pro-active role in providing information to facilitate shared decision making. The information should be presented in a way that is understandable, should address concerns about adverse effects or uncertainties as well as offering alternative modes of treatment– such as intravenous therapy - for patients who lack capacity or find the burden of oral treatments too high (Figure 1). Health care professionals should not only explain the range of possible treatment options available but also should include the option of not being treated. It is crucial to consider the wider clinical context and preferences of the patient, including co-morbidities, frailty, polypharmacy, and life expectancy, particularly in the frail elderly population. A preventative treatment which has no effect on symptoms may not be attractive or appropriate to the patient who prioritizes symptom control and a low treatment burden, or who has a limited life expectancy.

**Effective communication and shared decision making**

Effective communication is crucial in person-centered medicine. The way in which osteoporosis is framed and the risks and benefits of treatment are presented can have a major influence on the patient’s decision making. Before treatment is even discussed, the healthcare professional must establish the patient’s baseline understanding about osteoporosis and fracture reducing medications. Exploring patient beliefs might reveal misunderstandings about what osteoporosis is, what the causes and consequences of osteoporosis are and what treatment can achieve. Qualitative research has indicated that patients decide not to initiate or continue osteoporosis medicine if they hold beliefs that osteoporosis is a normal part of ageing for which treatment is futile, if they do not believe they are personally at risk, or if they do not consider the consequences of osteoporosis as important. (11-13) Furthermore, treatment discontinuation may be associated with unrealistic treatment expectations, such as anticipating stronger bones will result in improvements in physical function or believing medicine will help symptoms of joint pain (11). One of the barriers to shared decision making is the assumption by clinicians that they ‘are already doing it’, yet observational studies show that in clinical practice, it is unusual for patient concerns, beliefs and preferences to be addressed (14). Once patient beliefs and knowledge have been established, the clinician can share information about osteoporosis, ‘filling in the gaps’ and address any misinformation to help patients make sense of osteoporosis, it is important to explain what it is, describe particular risk factors, explain the physical, social and psychological consequences of fracture and emphasize that the condition is treatable (15,16). Another issue which may erode patients’ confidence in understanding the diagnosis and treatment advice may be competing health conditions such as poor dental health and conflicting messages on the risks of treatment by different healthcare professionals (17,18). This highlights the importance of education of all healthcare professionals involved in the patient’s care so that similar advice can be given to the patient by healthcare professionals from different specialties. An approach of informed and shared decision making is suitable for all patients, although the extent of this can be flexible dependent on patient preferences. For example, patients who have established long-term trust in their physician, might want to be told what the physician feels is the best thing to do. Even for patients who prefer to be guided in their decision making, using the principles of shared decision making helps the clinician to make decisions in the patient’s best interest and improves the quality of communication and understanding.

Recent systematic reviews have shown mixed results regarding the use of patient education alone to improve adherence to osteoporosis treatment (19). This is not surprising because it is well established that knowledge alone is insufficient to achieve behaviour change. By using the principles of shared decision making, patient beliefs are elicited, information giving is more targeted and perceptions of illness and treatment are more likely to change. This explains why shared decision-making interventions have shown promise in increasing uptake of preventative medicines such as vaccines and stroke prevention (20) .

**Decision aids for effective communication**

Patients make decisions about whether to take medication based on their perceptions of need for that medicine, balanced with concerns about side effects and risks, as well as practical considerations around medication administration (21). However, existing patient information about osteoporosis medicines contains much more focus on harms than benefits, (14,22) such that both patients and primary care clinicians consider the benefits of osteoporosis medicines to be ambiguous and vague (13). In simple terms, osteoporosis medicines strengthen bone and reduce fracture risk (15). However, how reduction in fracture risk is communicated can influence patient perceptions and intentions. The use of relative risk is not recommended as this can lead to over-estimation of treatment benefit than when the same information is presented using a personalised absolute risk format (23). In osteoporosis, a recently published study emphasized the difference between expressing benefit in terms of an absolute risk reduction versus relative risk reduction when applied as part of routine care in a secondary care setting in the UK (24). This study showed that patients were less likely to accept treatment when benefits were presented as an absolute rather than relative risk reduction and revealed that approximately 25% declined treatment after the absolute benefit was explained, when they would have accepted treatment when presented with a relative risk reduction. Further analysis showed that the two main factors which influenced the patients’ decision to decline treatment were the low absolute fracture risk and increasing age. Although paradoxically this could lead to a decline in treatment uptake, we feel this represents informed decision making and as such, is not widening the care gap. Based on this study, the authors developed an application termed Osteoporosis Risk Benefit Calculator (ORB) (25) which allows clinicians to enter the patients’ risk of a major osteoporotic fracture (MOF) over given time period and estimate the absolute risk reduction for commonly used treatments on any major osteoporotic fracture, hip fracture, vertebral fracture and non-vertebral, non-hip fractures. Entering data into the App takes only 2-3 minutes and the results can be reviewed with the patient in numerical form or by using a visual aid in which the total number of fractures with or without treatment is displayed. A decision aid tool has also been developed at the Mayo Clinic (26), but this only considers the effects of bisphosphonates and does not allow calculation of the risk of individual fracture types. Furthermore, the Mayo tool may over-estimate the benefit of bisphosphonates which are assumed to reduce MOF fracture risk by 40%, whereas in reality, the reduction is lower particularly with non-vertebral non-hip fractures and varies with type of bisphosphonate (27). The iFraP tool incorporates a pictorial presentation of individualized major and hip fracture risk, with and without treatment alongside information about risk factors and bone density, an explanation of why bone health matters including animations and information about treatment benefits, side effects and practical issues (28). A clinical trial to evaluate the implementation iFraP and the associated shared decision-making training package, within routine clinical practice is currently in progress, with a nested process evaluation and economic analysis. The iFRAP tool is not yet publicly available but will be published on the study website when the trial has been completed.

Although these decision aids are available, it is important to emphasize that these tools do not meet international patient decision aids standards (29)nor have they been shown to improve clinical outcome, Nonetheless, we have all have encountered patients who are terrified about the risks of very rare adverse effects such as osteonecrosis of the jaw or atypical femoral fractures and a decision aid that could put these risks in context and side-by side with potential benefits of therapy in terms of fractures prevented would be helpful. This has been achieved in other areas of medicine and was used to good effect by the MHRA (Medicines and Health Care Regulatory Authority in the UK) to communicate the benefits of the Astra-Zeneca Covid-19 vaccine, in relation to the very rare occurrence of cerebral thrombosis (30).

Healthcare professionals will need to help guide patients through using the most appropriate resources to assist with decision making, particularly in the frail and elderly population. Patient access to online resources including the previously described decision aids is increasing, however remains limited in the older age group. There has been a growth in internet use among older adults in the UK, however in 2019 only 47% of those age 75 and over had accessed the internet in the previous 3 months, with 29% of those over 65 having never accessed the internet. Interestingly, in the UK men have been shown to be more frequent internet users, with 54% of men aged over 75 being recent internet users compared to 41% of women, which is relevant for the osteoporosis patient population (31).

**Closing the osteoporosis care gap**

We suggest it is not the treatment gap which is the problem but the osteoporosis *care* gap (Figure 1). This language acknowledges the importance of healthcare providers identifying those likely to benefit from treatment and increasing the quality of clinical conversations to promote patient engagement and involvement, while respecting that treatment is not suitable or wanted by all. A previous perspective article in the JBMR focused on solutions to addressing the ‘crisis’ in the treatment of osteoporosis and one of those was to enhance patient-engagement strategies (32). We agree that engagement is essential to ensure that patients are on board with the treatment on offer and are aware of the risks and benefits to them as an individual. Clinicians should be aware that the use of tools which present information on absolute benefit may result in a reduction in the proportion of patients who accept treatment but ultimately this is the patient’s decision, even though it may negatively impact on fracture occurrence at a population level. It could be that the wider introduction of anabolic treatments followed by antiresorptive therapy, using a “gain and maintain approach” might increase acceptance rates due to the greater efficacy as compared with oral bisphosphonates (33,34), which have been the mainstay of managing osteoporosis over the past three decades. In the meantime, clinicians might reflect on the extent to which their services and individual practice enables patients to feel involved, informed and respects their autonomy.

**Figure 1. Reasons and solutions to address the osteoporosis care gap**



**References**

1. Khosla S, Shane E. A Crisis in the Treatment of Osteoporosis. J Bone Miner Res. Aug 2016;31(8):1485-7. Epub 2016/06/24.

2. Fuggle NR, Curtis B, Clynes M, Zhang J, Ward K, Javaid MK, et al. The treatment gap: The missed opportunities for osteoporosis therapy. Bone. Mar 2021;144:115833. Epub 2020/12/29.

3. McCloskey E, Rathi J, Heijmans S, Blagden M, Cortet B, Czerwinski E, et al. The osteoporosis treatment gap in patients at risk of fracture in European primary care: a multi-country cross-sectional observational study. Osteoporos Int. Feb 2021;32(2):251-9. Epub 2020/08/24.

4. Parsons CM, Harvey N, Shepstone L, Kanis JA, Lenaghan E, Clarke S, et al. Systematic screening using FRAX((R)) leads to increased use of, and adherence to, anti-osteoporosis medications: an analysis of the UK SCOOP trial. Osteoporos Int. Jan 2020;31(1):67-75. Epub 20191012.

5. Management of osteoporosis and prevention of fragility fractures. <https://www.sign.ac.uk/our-guidelines/management-of-osteoporosis-and-the-prevention-of-fragility-fractures/>: SIGN; 2021.

6. Reid IR, Horne AM, Mihov B, Stewart A, Garratt E, Wong S, et al. Fracture Prevention with Zoledronate in Older Women with Osteopenia. N Engl J Med. Dec 20 2018;379(25):2407-16. Epub 2018/12/24.

7. Gregson CL, Armstrong DJ, Bowden J, Cooper C, Edwards J, Gittoes NJL, et al. UK clinical guideline for the prevention and treatment of osteoporosis. Arch Osteoporos. Apr 5 2022;17(1):58. Epub 2022/04/06.

8. Hale ED, Treharne GJ, Kitas GD. The common-sense model of self-regulation of health and illness: how can we use it to understand and respond to our patients' needs? Rheumatology (Oxford). Jun 2007;46(6):904-6. Epub 2007/04/24.

9. Fatoye F, Smith P, Gebrye T, Yeowell G. Real-world persistence and adherence with oral bisphosphonates for osteoporosis: a systematic review. BMJ Open. Apr 14 2019;9(4):e027049. Epub 20190414.

10. Realistic Medicine. <https://www.realisticmedicine.scot/about/>: Scottish Government; 2021.

11. Salter C, McDaid L, Bhattacharya D, Holland R, Marshall T, Howe A. Abandoned acid? Understanding adherence to bisphosphonate medications for the prevention of osteoporosis among older women: a qualitative longitudinal study. PLoS One. 2014;9(1):e83552. Epub 2014/01/07.

12. Hawarden A, Jinks C, Mahmood W, Bullock L, Blackburn S, Gwilym S, et al. Public priorities for osteoporosis and fracture research: results from a focus group study. Arch Osteoporos. Jun 16 2020;15(1):89. Epub 2020/06/18.

13. Paskins Z, Crawford-Manning F, Cottrell E, Corp N, Wright J, Jinks C, et al. Acceptability of bisphosphonates among patients, clinicians and managers: a systematic review and framework synthesis. BMJ Open. Nov 3 2020;10(11):e040634. Epub 2020/11/06.

14. Pieterse AH, Jager NA, Smets EM, Henselmans I. Lay understanding of common medical terminology in oncology. Psychooncology. May 2013;22(5):1186-91. Epub 2012/05/11.

15. Bullock L, Crawford-Manning F, Cottrell E, Fleming J, Leyland S, Edwards J, et al. Developing a model Fracture Liaison Service consultation with patients, carers and clinicians: a Delphi survey to inform content of the iFraP complex consultation intervention. Arch Osteoporos. Mar 24 2021;16(1):58. Epub 2021/03/25.

16. Leventhal H, Benyamini Y, Brownlee S, Diefenbach M, Leventhal EA. llness representations: theoretical foundation. In: Petrie KJ, Weinman JA, editors. Perceptions of health and illness: current research and application. 1. Amsterdam: Harwood Academic Publisher; 1997. p. 19-46.

17. Cramer JA, Silverman S. Persistence with bisphosphonate treatment for osteoporosis: finding the root of the problem. Am J Med. Apr 2006;119(4 Suppl 1):S12-7.

18. Beaton DE, Sujic R, McIlroy Beaton K, Sale J, Elliot-Gibson V, Bogoch ER. Patient perceptions of the path to osteoporosis care following a fragility fracture. Qual Health Res. Dec 2012;22(12):1647-58. Epub 20120824.

19. Rubaek M, Hitz MF, Holmberg T, Schonwandt BMT, Andersen S. Effectiveness of patient education for patients with osteoporosis: a systematic review. Osteoporos Int. May 2022;33(5):959-77. Epub 2021/11/14.

20. Stacey D, Legare F, Lewis K, Barry MJ, Bennett CL, Eden KB, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. Apr 12 2017;4:CD001431. Epub 2017/04/13.

21. Horne R, Cooper V, Wileman V, Chan A. Supporting adherence to medicines for long-term conditions: A perceptions and practicalities approach based on an extended common-sense model. 2019;24:82-96.

22. Crawford-Manning F, Greenall C, Hawarden A, Bullock L, Leyland S, Jinks C, et al. Evaluation of quality and readability of online patient information on osteoporosis and osteoporosis drug treatment and recommendations for improvement. Osteoporos Int. Aug 2021;32(8):1567-84. Epub 2021/01/28.

23. Fischhof B, Brewer NT, Downs JS. Communicating Risks and Benefits: An Evidence-Based User's Guide. Silver Spring, MD: Food and Drug Administration; 2011.

24. Ralston KAP, Phillips J, Krause A, Hauser B, Ralston SH. Communicating Absolute Fracture Risk Reduction and the Acceptance of Treatment for Osteoporosis. Calcif Tissue Int. Feb 13 2022. Epub 2022/02/14.

25. Osteoporosis Risk Benefit Calculator (ORB). <https://webapps.igmm.ed.ac.uk/world/research/rheumatological/ORBCalculator/>: University of Edinburgh; 2021.

26. Osteoporosis decision aid. <https://osteoporosisdecisionaid.mayoclinic.org/index.php/osteo/index>: Mayo Clinic; 2020.

27. Barrionuevo P, Kapoor E, Asi N, Alahdab F, Mohammed K, Benkhadra K, et al. Efficacy of Pharmacological Therapies for the Prevention of Fractures in Postmenopausal Women: A Network Meta-Analysis. J Clin Endocrinol Metab. May 1 2019;104(5):1623-30. Epub 2019/03/26.

28. Paskins Z, Bullock L, Crawford-Manning F, Cottrell E, Fleming J, Leyland S, et al. Improving uptake of Fracture Prevention drug treatments: a protocol for Development of a consultation intervention (iFraP-D). BMJ Open. Aug 18 2021;11(8):e048811. Epub 2021/08/20.

29. Paskins Z, Torres Roldan VD, Hawarden AW, Bullock L, Meritxell Urtecho S, Torres GF, et al. Quality and effectiveness of osteoporosis treatment decision aids: a systematic review and environmental scan. Osteoporos Int. Oct 2020;31(10):1837-51. Epub 2020/06/06.

30. Communicating the potential benefits and harms of the AstraZeneca COVID-19 Vaccine. <https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/976877/CovidStats_07-04-21-final.pdf>: MHRA; 2021.

31. Statistics OoN. Internet users, UK: 2020. London: Office of National Statistics; 2020. p. Internet use in the UK; annual estimates by age, sex, disability and geographical location.

32. Khosla S, Cauley JA, Compston J, Kiel DP, Rosen C, Saag KG, et al. Addressing the Crisis in the Treatment of Osteoporosis: A Path Forward. J Bone Miner Res. Mar 2017;32(3):424-30. Epub 2017/01/19.

33. Saag KG, Petersen J, Brandi ML, Karaplis AC, Lorentzon M, Thomas T, et al. Romosozumab or Alendronate for Fracture Prevention in Women with Osteoporosis. N Engl J Med. Sep 11 2017;377(15):1417-27. Epub 2017/09/12.

34. Kendler DL, Marin F, Zerbini CAF, Russo LA, Greenspan SL, Zikan V, et al. Effects of teriparatide and risedronate on new fractures in post-menopausal women with severe osteoporosis (VERO): a multicentre, double-blind, double-dummy, randomised controlled trial. Lancet. Nov 9 2017. Epub 2017/11/14.

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**Conflicts of interest**

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