**Temporal Changes in Comorbidity Burden in Patients Having Percutaneous Coronary Intervention and Impact on Prognosis**

Running title: Comorbidity burden in PCI and impact on prognosis

Jessica Potts MSca, Chun Shing Kwok MBBS, MSca, Joie Ensor PhDa, Muhammad Rashid MBBSa, Umesh Kadam PhDb, Tim Kinnaird MDc, Nicholas Curzen BM PhDd, Samir B. Pancholy MDe, Danielle Van der Windt PhDa, Richard D. Riley PhDa, Rodrigo Bagur MD PhDf, Mamas A. Mamas BM BCh DPhila

a. Keele Cardiovascular Research Group, Centre for Prognosis Research, Institute of Primary Care and Health Sciences, Keele University, UK

b. Diabetes Research Centre, Department of Health Sciences, Leicester University, UK

c. University Hospital of Wales, Cardiff, UK

d. University Hospital Southampton and Faculty of Medicine, University of Southampton, UK

e. The Commonwealth Medical College, Scranton, PA, USA

f. Division of Cardiology, London Health Sciences Centre, Department of Medicine,

and Epidemiology & Biostatistics, Western University, London, Ontario, Canada

Corresponding author:

Mamas A Mamas

Keele Cardiovascular Research Group,

Centre for Prognosis Research, Institute for Primary Care and Health Sciences,

Keele University, Stoke-on-Trent

ST4 7QB UK

Tel: +44 (0)1782 671654 Fax: +44 (0)1782 674467

Email: mamasmamas1@yahoo.co.uk

**List of Supports/Grants Information:** The study was supported by a grant from the Research and Development Department at the Royal Stoke Hospital.

**Acknowledgement:** The data used in this project can from HCUP Nationwide Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP). 2004-2011. Agency for Healthcare Research and Quality, Rockville, MD. [www.hcup-us.ahrq.gov/nisoverview.jsp](https://www.hcup-us.ahrq.gov/nisoverview.jsp) and HCUP National Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP). 2012-2014. Agency for Healthcare Research and Quality, Rockville, MD. [www.hcup-us.ahrq.gov/nisoverview.jsp](https://www.hcup-us.ahrq.gov/nisoverview.jsp). A full list of participating states can be found at [www.hcup-us.ahrq.gov/hcupdatapartners.jsp](https://www.hcup-us.ahrq.gov/db/hcupdatapartners.jsp)

**Conflict of interest disclosure:** The authors have no conflicts of interest to declare.

**Abstract**

This study aims to evaluate the impact of comorbidity burden on outcomes among patients who undergo percutaneous coronary intervention (PCI). We used the Nationwide Inpatient Sample to identify all PCI procedures undertaken in the United States between 2004 – 2014. We then determined comorbidity burden for each patient record based on the Charlson Comorbidity Score. Multivariable logistic regression models were used to examine the association between comorbidity burden and in-hospital mortality other in-hospital complications. A total of 6,601,526 PCI procedures were included in the analysis. Overall comorbidity burden increased over time, with severe comorbidity burden (defined as a CCI score ≥3) increasing from 5.3% in 2004 to 14.2% in 2014 (P<0.0001). After adjustment for confounding factors increasing comorbidity burden was independently associated with increased odds of in-hospital mortality, complications, length of hospital stay and total cost of hospitalisation post PCI. A CCI score of 1 was independently associated with an increase in the odds of in hospital mortality (OR 1.19 (95% CI 1.15-1.25)), a score of 2 associated with an almost 1.5-fold increase (OR 1.41 (95% CI 1.34-1.48)) and a score of ≥3 a 2-fold increase (OR 1.96 (95% CI 1.86-2.07)) compared to no comorbid burden (CCI score of 0). In conclusion, our results show that comorbid burden is independently associated with increased risk of in-hospital mortality, in-hospital complications, length of stay and healthcare costs.

**Keywords:** comorbidity; percutaneous coronary intervention; prognosis

**Introduction**

Boththe average age of patients undergoing percutaneous coronary intervention (PCI) in contemporary practice and the complexity of the disease being tackled has increased over time.1 This aging population inevitably has an increasing burden of comorbid conditions, with registry studies suggesting that at least 75% of patients undergoing PCI have at least 1 comorbid condition.2 Previous studies on comorbidity in patients undergoing PCI have mainly focused on individual cardiovascular comorbid conditions and their impact on prognosis, even though patients with CVD often have a broad spectrum of both cardiovascular and non-cardiovascular comorbidities3,4 that may influence outcomes synergistically rather than in isolation. The Charlson comorbidity index (CCI) is a measure of comorbidity burden and provides a means of quantifying the prognostic impact of 22 comorbid conditions on the basis of their number and their individual impact by means of a score that was developed as a prognostic indicator for patients with a variety of medical conditions.3,5 Whilst previous reports have studied comorbid burden in highly selected small single centre or registry studies, there have been no previous reports of neither the prevalence, nature, clinical outcomes nor healthcare costs associated with comorbid disease in patients undergoing PCI from a national perspective, nor how comorbid burden has changed over time in this population. Therefore, we aimed to study the prevalence, type and temporal trends of comorbid conditions (defined by CCI) and their impact on clinical outcomes and healthcare costs through analysis of over 6 million PCI procedures undertaken over a decade in the United States.

**Methods**

The data comes from the National Inpatient Sample (NIS) for hospital discharges in the United States between 2004 and 2014. The NIS is the largest all – payer inpatient health care database in the United States and was developed by the Healthcare Cost and Utilization Project (HCUP), which is sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS dataset contains within hospital information on between 7 and 8 million hospital discharges per year from 2004 onwards. The sampling strategy has changed over time in order to produce more generalizable estimates by reducing sampling bias. Before 2012 the NIS retained all discharges, but only from a sample of hospitals. Since the redesign the NIS now samples discharges from all hospitals participating in HUCP, approximating a 20% stratified sample of all discharges from US community hospitals.

We identified all individuals who had undergone a PCI between January 2004 and December 2014 by identifying all eligible discharges with an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure code of 00.66 (*Percutaneous Transluminal Coronary Angioplasty),*36.06 (*Insertion of non-drug-eluting coronary artery stent(s))* or 36.07 (*Insertion of a drug-eluting coronary artery stent(s))*. Before a revision of the codes in 2005 the codes 36.01 (*Single vessel percutaneous transluminal coronary angioplasty or coronary atherectomy without mention of thrombolytic agent),* 36.02 (*Single vessel percutaneous transluminal coronary angioplasty or coronary atherectomy with mention of thrombolytic agent)* and 36.05 (*Multiple vessel percutaneous transluminal coronary angioplasty [PTCA] or coronary atherectomy performed during the same operation, with or without mention of thrombolytic agent)* were also used and so these codes were also included when identifying procedures in discharges from 2004 and 2005.

All records were eligible for inclusion as long as the discharge record showed that the patient had undergone a PCI procedure during their hospital stay and was over the age of 18. Information of patient demographics is recorded for each hospital discharge including data regarding age, gender, race, admission type (elective or emergent), admission day (weekday or weekend), median household income according to ZIP code and patient comorbidity conditions using Deyo modification of the CCI. The comorbidities defined by Charlson et al5 use a point system with each weighted by a value depending on the prognostic impact of comorbid condition on mortality in the original cohort, ranging from 1 to 6 points (Supplementary Table 1). The scores are summated to calculate a CCI, with a range of possible scores 0, 1, 2, ≥3, that correspond to no, mild, moderate and severe comorbid burden respectively.

 The ICD-9-CM codes used to identify each of the conditions included in the CCI are given in supplementary Table 1.9 Each discharge record had information on up to 30 diagnoses that the patient had been given (15 between 2004 and 2008, 25 between 2009 and 2013 and 30 in 2014), and it was these diagnosis codes that were used to identify each of the comorbidity conditions present in the record in order to calculate the CCI at the time of hospitalisation. These codes were also used to identify whether the patient had a primary diagnosis of an acute myocardial infarction and also whether the individual had been diagnosed with cardiogenic shock.

Finally, information about the PCI procedure was determined from the procedure codes, including whether the PCI was a multi vessel, single vessel and whether it involved bifurcation stenting. The use of adjunctive devices including intracoronary pressure wire, intravascular ultrasound and an assist device (such as an intra-aortic balloon pump) were also recorded. Where available from the procedure codes we also included the stent type deployed (bare metal, drug-eluting).

In-hospital clinical outcomes and complications were identified. The main outcomes chosen included: (a) in-hospital mortality, (b) and in-hospital complication or (c) a composite of any of the in-hospital complications considered. The length of stay and the total charge of hospitalisation were also considered. The total charge given in the dataset represents the amount that hospital billed for the services, but is not representative of the hospital services actually cost. Therefore, a charge to cost conversion ratio was used in order to covert the reported charges into the actual cost for the payer.

Procedural complications were also identified using ICD-9-CM codes and patient safety indicators including: post-operative haemorrhage requiring transfusion, vascular injuries, cardiac complications including iatrogenic and pericardial complications, whether an individual required bail out or emergency coronary artery bypass grafting and post-operative stroke or transient ischaemic attack. Finally, bleeding complications were identified, including gastrointestinal, retroperitoneal, intracranial, intracerebral haemorrhage, unspecified haemorrhage, and whether a blood transfusion was required. Complications were identified by ICD-9-CM codes in any secondary diagnosis field (Supplementary Table 2).10

Statistical analysis was performed on Stata/MP version 14.0. Descriptive statistics are provided by each of the 12-month yearly data included from the NIS. Continuous variables are presented as median and interquartile range, and categorical data are presented as number and percentage. Multiple imputations with chained equations were used to account for missing data, where the covariate had more than 10% missing data. Where missing data was less than 10% of the covariate data, the observations with missing data were removed. Data was assumed to be missing at random. Using the *mi impute chained* function in Stata we generated 10 complete datasets with any missing covariate data imputed. Only ethnicity had more than 10% missing data and so was the only covariate imputed. All outcomes were included in the imputation model, but not themselves imputed.11 Other covariates used for the imputation were age, gender, median ZIP income, elective admission and year of hospitalisation. The imputed datasets are used to produce estimates from the fitted models, which are then combined together using Rubin’s Rules.12

For all analyses, the survey estimation commands were used (by using the svy prefix in analyses conducted in Stata), this followed the recommendations from AHRQ for analysis of survey data to account for the complex survey design of the NIS database. As records were not sampled individually but by hospital number, clustering of records within hospitals was taken into account in the survey estimation. This was done by defining each hospital to be the primary sampling unit. For calculation of national estimates and correct variances, sampling weights for each individual discharge that were provided by the AHRQ were used. The use of sampling weights are required because the design of the study means that different observations may have different probabilities of selection. Due to the redesign of the NIS data and the alternative sampling strategy used before 2012, these weights needed to be updated from the original sampling weights for 2004-2011 in order for the analysis to be conducted across all included years.

Multivariable analyses were conducted for the association of comorbidity burden on (a) in-hospital mortality, (b) any defined complication and (c) a composite of any considered complication. Logistic regression models were fitted using maximum likelihood estimation in order to investigate the association of comorbidity burden with odds of in-hospital death or an in-hospital complication, either post-operative bleeding, vascular complication, cardiac complication or a stroke/TIA. To assess the impact of comorbidity burden the multivariable analysis was adjusted for all potential confounders that were measured. These included age, gender, ethnicity, median income, elective admission, day of admission (weekend/weekday) primary diagnosis of MI, diagnosis of shock, hypertension, or hypercholesterolemia, patient smoking status, use of an assist device or IABP, use of a bare metal or drug eluting stent, bifurcation stenting, fractional flow reserve, single or multi-vessel PCI and year of hospitalisation, as well as accounting for the clustering of individuals by hospital. All confounders measured are presented in Table 1.

**Results**

 A total of 6,601,526 hospital episodes between 2004 and 2014 were recorded with a procedure code indicating that a PCI had been performed during hospitalisation. Discharges with greater than 10% missing data for included outcomes as well as covariates including age, gender and elective surgery indication were removed, Figure 1. In total approximately 7% of the original dataset was removed due to missing data, with approximately 50% of the missing data due to a missing cost charge ratio available for the hospital. The missing values of ethnicity were imputed as there was approximately 20% missing data in this covariate. The breakdown of the number of discharges with a PCI procedure performed across each of the years in the dataset is given in Supplementary Figure 1, with the numbers of PCI procedures decreasing from 747,129 in 2004 to 428,400 in 2014.

 Patient demographics for patients undergoing PCI for each year are presented in Table 1. The median age of included patients varied between 64 and 65 years. The proportion of males undergoing PCI increased over time, as did the proportion of patients undergoing PCI procedures in emergent situations. Specifically, there was an increase in the proportion of individuals who had a primary diagnosis of a myocardial infarction with their hospital admission from approximately 30% to over 60% over the 11-year time span. The prevalence of a number of cardiovascular risk factors such as diabetes, hypertension, hypercholesterolemia and smoking increased and the proportion of patients with severe comorbidity burden (defined as a CCI score ≥3) increased from 5.3% to 14.2%. The prevalence of both cardiovascular and non-cardiovascular comorbid conditions increased over time. Over time the median length of stay increased from 2 days to 3 days and hospital costs increased from $15,494 in 2004 to $19,048 in 2014.

 The distribution of comorbidity burden as defined by the CCI is presented in Supplemental Figure 2. Figure 2 shows how the burden of comorbidity (according to CCI category) has changed over time: the proportion of patients undergoing PCI with no comorbidities (CCI of 0) has declined from 40.6% to 34.2%, whilst those with severe comorbidity burden (CCI ≥3) has increased from 5.3% to 14.2%. The increasing comorbid burden is also seen when considering the mean CCI score each year, which is 1 in 2004, and steadily increases over time to 1.7 in 2014, Table 1.

 Table 2 presents patient demographics stratified by CCI category combined across all years in the study. It can be seen that those individuals with a higher CCI were older with a median age of 68, compared to between 62 and 65 for the other groups, and the proportion of females increased, with increasing comorbidity burden. As comorbidity burden increased, the indication for PCI was more likely to be emergent and involve haemodynamic instability, as evidenced by cardiogenic shock diagnosis or use of an assist device or an IABP.

 Table 3 describes crude event rates for in-hospital mortality and in-hospital complications including vascular and cardiac complications and a post-procedure stroke. In-hospital mortality and all other complications increased with increasing comorbidity burden; for example, crude in-hospital mortality increased from 1.0% in patients with no comorbid conditions to 3.2% in those patients with CCI score ≥3.

Multivariable analyses were conducted to examine the independent prognostic association of comorbidity burden on in-hospital mortality and post-procedure complications (Table 4). Increased comorbidity burden was independently associated with increased odds of in hospital mortality post PCI. A CCI score of 1 was independently associated with an increase in the odds of in hospital mortality (OR 1.19 (95% CI 1.15-1.25)), a score of 2 associated with an almost 1.5-fold increase (OR 1.41 (95% CI 1.34-1.48)) and a score of ≥3 a 2-fold increase (OR 1.96 (95% CI 1.86-2.07)) compared to no comorbid burden (CCI score of 0).

Table 4 also shows that, after adjustment for potential confounders, increased comorbidity is independently associated with increased odds of all other post procedure complications, except for cardiac complications. Supplemental table 3 reports the relationship between CCI (per unit increase) and post procedural complications and clinical outcomes. It can be seen that for all outcomes, each unit increase in CCI score is independently associated with increased risk with similar relationships reported to the main analysis. For example, each unit increase in CCI score is associated with a 18% increase in the odds of in-hospital mortality (OR 1.18 (95% CI 1.17, 1.19). Supplemental table 4 shows the prognostic impact of each individual component of the CCI score after multivariable analysis on both in hospital mortality and complications.

Increasing comorbidity burden was also associated with increasing length of stay (LOS): median LOS of 2 days, 2 days, 3 days and 4 days for a CCI of 0, 1, 2 and ≥3 respectively, seen in Figure 3. Supplementary Figure 3 shows variation in the LOS categorised by CCI score across the years studied. An increase in comorbid burden was associated with increasing healthcare costs. Specifically, patients with a CCI score of 0 had an average of $16,522 cost for their treatment, increasing to an average of $17,277 for those with a score of 1, $18,921 for those with a score of 2 and $21,625 for those with a score of ≥3, as shown in Figure 4. Supplementary Figure 4 shows the variation in the differences in the cost of hospitalisation total charge annually for each of the CCI scores.

**Discussion**

 Our study is the first to systematically study the prevalence, prognostic impact and healthcare costs associated with comorbidity burden in a national cohort of patients who underwent PCI. Our analysis of over 6 million PCI procedures undertaken in the United States has shown that comorbid burden in patients has increased significantly over the past decade, with 60% of the patients undergoing PCI in contemporary practice having at least 1 comorbid condition and nearly 10% of patients classed as severely comorbid (CCI ≥ 3). Furthermore, comorbid burden is independently associated with an increased risk of in hospital mortality, in hospital complications, length of stay and healthcare costs. Thus, after adjustment for other variables, patients with the greatest comorbid burden (CCI≥3) have 2-fold independent increased odds of in-hospital mortality, as well as a 2-day increased length of stay and an additional $5,000 average healthcare costs compared to patients without comorbidities undergoing PCI.

 The average age and comorbid burden of patients undergoing PCI has increased over time and increasingly complex disease is being tackled according to several national PCI analyses.8,13-16 Most contemporary studies only report changes in either cardiovascular comorbidities or cardiovascular risk factors when temporal trends in case mix have been examined and have, furthermore, treated individual comorbidities as isolated risk factors, rather than more holistically using global measures of comorbid burden. Non-cardiovascular conditions make an important contribution to overall comorbid burden and yet their association with outcomes after PCI has not been comprehensively studied. In fact, it is conceivable non-cardiovascular comorbid conditions may actually have a greater impact on prognosis and healthcare resource use than cardiovascular comorbidities. Our analysis suggests that comorbid burden and severity, as defined by CCI, has increased over time in patients undergoing PCI in the United States, in line with a previous study in Spain where the proportion of non-diabetic patients undergoing PCI with at least 1 comorbidity increased from 22.6% to >30% over a decade.8 Our findings suggest that both cardiovascular and non-cardiovascular comorbid conditions such as COPD, cancer and connective tissue diseases have increased in prevalence over the timeframe studied, and that they have an important impact on short-term clinical and health-economic outcomes in patients undergoing PCI. These changes may in part reflect referral bias and an increased willingness for interventional cardiologists to undertake increasingly complex cases in increasingly complex patients. As PCI outcomes have improved with improved stent technology, interventional equipment and more potent anti-thrombotic agents, interventional cardiologists are increasingly undertaking more complex comorbid PCI cases in multi-morbid patients with more extensive coronary disease that would have been managed medically, or surgically at earlier timepoints. A change from elective PCI to ACS where there is less scope for case selection towards lower risk cases will also contribute to the observed increases in comorbid burden. Finally, the prevalence of comorbid conditions such as diabetes, hypertension have increased over time, along with improvements in survival for a number of cardiovascular and non-cardiovascular diseases has meant that patients undergoing PCI are increasingly comorbid.

Our data demonstrate that CCI is independently associated with both in hospital mortality as well as a wide range of peri-procedural PCI complications, and with prolonged length of hospital stay and associated healthcare costs. This builds upon our previous findings that demonstrated that CCI was independently associated with cardiac death, major adverse cardiovascular events, major bleeding and stent thrombosis in a much smaller multicentre registry of patients undergoing PCI.6 Our current analysis is several orders of magnitude larger than this previous study (>6.0 million versus 3000 procedures) allowing us sufficient statistical power to study the impact of individual comorbid conditions in isolation with much greater granularity. Furthermore, our large sample size and unselected nature of our cohort allows the more precise estimate of the effect of comorbid burden in this population compared to studies derived from smaller more selective registries. Furthermore, our analysis for the first time provides insights into both the length of stay and health economic costs associated with comorbid burden that increase substantially with increasing comorbid burden.

 Our analysis suggests that many non-CV comorbidities such as liver disease, solid and haematological malignancies are much more strongly associated with procedural outcomes than many cardiovascular comorbid conditions. This is particularly important as whilst CV comorbid conditions such as diabetes, heart failure, chronic renal failure are important components of contemporary risk stratification tools in PCI17-19 measures of overall comorbid burden and non-CV comorbid conditions are not routinely collected in datasets from which such contemporary risk scores are derived and are therefore not included in the assessment of risk. The addition of global measures of comorbid burden such as CCI to contemporary PCI risk stratification scores has been shown to improve their performance. For example, addition of CCI to the Mayo Clinic Risk Score for PCI increased net re-classification index by 34% and improved the c-statistic for the model significantly.7 This is increasingly relevant as over the past 20 years the predominant cause of mortality following PCI has changed from cardiac to non-cardiac causes, with cardiac deaths only accounting for one third of deaths following PCI.20 Studies have reported that non-cardiac comorbidities at baseline are strongly predictive of future non-cardiac death, which is the commonest cause of mortality post PCI,20 and hence the ability to predict adverse outcomes using risk scores that do not include such non-cardiac comorbid conditions will be compromised. The performance of many risk models used in PCI has declined over time, in line with changes in practice, equipment and the clinical profile of patients undergoing these procedures, with several scores requiring an update to avoid calibration drift.17,18 Given the increasing comorbid burden of patients undergoing PCI in contemporary practice, and their important impact on outcomes, future risk scores should seek to incorporate more global measures of comorbid burden. Global measures of comorbid burden such as CCI can be used to identify patients at greatest risk of adverse outcomes and complications, enabling individualization of treatments for higher risk individuals. For example, our analysis suggests that patients with severe comorbid burden are at high risk of complications particularly major bleeding events, with patients with a CCI score of ≥3 having a 4-fold independent increase in odds of major bleeding complications. Bleeding avoidance strategies such as use of less aggressive antithrombotic regimes, stent platforms that require shorter DAPT duration21 and adoption of radial access22,23 may improve outcomes in such higher bleeding-risk patients groups. Better optimisation of comorbid conditions through a multi-speciality approach, particularly in elective cases where there is no urgency may contribute to better in-patient and outpatient outcomes. For example, recent work has reported that PCI patients with high comorbid burden are a high-risk group for unplanned readmissions.24 Targeted interventions that focus on management of comorbid conditions with discharge checklists has been shown to reduce such unplanned readmissions after PCI from 9.6% to 5.3%.25

 Our analysis has several strengths. Our analysis into the patterns of comorbidity, their prevalence, temporal trends and associated clinical outcomes in over 6 million PCI procedures in the United States undertaken over a decade is the largest to date by several orders of magnitude. Our analysis provides statistical power to study the prognostic impact of individual comorbid conditions, particularly non-cardiovascular conditions whose prognostic impact is greatest but where literature is most limited. Finally, our analysis is the first to study the health economic implications of comorbid burden in PCI in both the length of stay and healthcare costs.

 This work is subject to a number of limitations that are inherent to the *post hoc* analysis of large administrative databases. The lack of long-term follow up data limits our analysis to in-hospital endpoints, although our previous analysis derived from the Nobori-2 study suggests that comorbid burden may also impact on longer term outcomes, with CCI independently associated with cardiovascular death and major adverse cardiovascular events up to 5 years follow up.2 By only using in-hospital endpoints, there is a limit on the analyses that can be conducted. The limited follow up and lack of exact timing of events, means that time to event analyses specifically looking at death as a competing risk for length of stay are unable to be investigated as mortality after hospital discharge is unable to be considered. Furthermore, the prognostic impact of comorbid burden may be of even greater importance in this population in the longer term and has significant implications in the continued management of such patients in primary care. Secondly, NIS does not capture data about pharmacotherapy, or angiographic and procedural characteristics of the cohorts undergoing PCI and differences between groups may contribute in part to some of the relationships reported. Thirdly, as with any such administrative database, coding errors are always a potential source of bias and as is under-reporting of secondary and comorbid diagnoses. Finally, our imputation strategy meant that only data with greater than 10% missing data was imputed, meaning that 7% of the total number of records were discarded. In future a better method may be to impute all missing data. These limitations aside, the NIS offers the largest publicly available database in the world that enables analysis of real world outcomes of patients undergoing PCI, and allows the study of comorbid burden and clinical conditions that are not be routinely captured in large national PCI specific datasets.

 In conclusion, our analysis of over 6.5 million PCI procedures undertaken in the United States has shown that comorbid burden in patients has increased significantly over the past decade, with 10% of patients experiencing severe comorbid burden (CCI ≥ 3). Comorbid burden is independently associated with increased risk of in hospital mortality, in hospital complications, length of stay and healthcare costs. Patients with the greatest comorbid burden (CCI≥3) have a 2-fold independent increased risk of in hospital mortality, as well as a 2-day increased length of stay and an additional $5,000 average healthcare costs compared to patients without comorbidities undergoing PCI. Comorbid burden is an important predictor of poor outcomes after PCI and should be considered in decision-making processes particularly around patient risk stratification.

**References**

1. Singh M, Rihal CS, Gersh BJ, Lennon RJ, Prasad A, Sorajja P, Gullerud RE and Holmes DR, Jr. Twenty-five-year trends in in-hospital and long-term outcome after percutaneous coronary intervention: a single-institution experience. *Circulation* 2007;115:2835-2841.
2. Mamas MA, Fath-Ordoubadi F, Danzi GB, Spaepen E, Kwok CS, Buchan I, Peek N, de Belder MA, Ludman PF, Paunovic D and Urban P. Prevalence and Impact of Co-morbidity Burden as Defined by the Charlson Co-morbidity Index on 30-Day and 1- and 5-Year Outcomes After Coronary Stent Implantation (from the Nobori-2 Study). *Am J Cardiol* 2015;116:364-371.
3. Fraccaro P, Kontopantelis E, Sperrin M, Peek N, Mallen C, Urban P, Buchan IE and Mamas MA. Predicting mortality from change-over-time in the Charlson Comorbidity Index: A retrospective cohort study in a data-intensive UK health system. *Medicine* 2016;95:e4973.
4. Rashid M, Kwok CS, Gale CP, Doherty P, Olier I, Sperrin M, Kontopantelis E, Peat G, Mamas MA. Impact of Co-morbid burden on mortality in patients with coronary heart disease, heart failure and cerebrovascular accident: A systematic review and meta-analysis. *Eur Heart J Qual Care Clin Outcomes* 2017;3:20-36.
5. Charlson ME, Pompei P, Ales KL and MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-383.
6. Mamas MA, Fath-Ordoubadi F, Danzi GB, Spaepen E, Kwok CS, Buchan I, Peek N, de Belder MA, Ludman PF, Paunovic D and Urban P. Prevalence and Impact of Co-morbidity Burden as Defined by the Charlson Co-morbidity Index on 30-Day and 1- and 5-Year Outcomes After Coronary Stent Implantation (from the Nobori-2 Study). *Am J Cardiol* 2015;116:364-371.
7. Singh M, Rihal CS, Lennon RJ, Spertus JA, Nair KS and Roger VL. Influence of frailty and health status on outcomes in patients with coronary disease undergoing percutaneous revascularization. *Circ Cardiovasc Qual Outcomes* 2011;4:496-502.
8. Lopez-de-Andres A, Jimenez-Garcia R, Hernandez-Barrera V, Perez-Farinos N, de Miguel-Yanes JM, Mendez-Bailon M, Jimenez-Trujillo I, de Miguel AG, Pino CG and Carrasco-Garrido P. National trends in utilization and outcomes of coronary revascularization procedures among people with and without type 2 diabetes in Spain (2001-2011). *Cardiovasc Diabetol* 2014;13:3.
9. Badheka AO, Patel NJ, Grover P, Singh V, Patel N, Arora S, Chothani A, Mehta K, Deshmukh A, Savani GT, Patel A, Panaich SS, Shah N, Rathod A, Brown M, Mohamad T, Tamburrino FV, Kar S, Makkar R, O'Neill WW, De Marchena E, Schreiber T, Grines CL, Rihal CS and Cohen MG. Impact of annual operator and institutional volume on percutaneous coronary intervention outcomes: a 5-year United States experience (2005-2009). *Circulation* 2014;130:1392-1406.
10. Singh V, Patel NJ, Rodriguez AP, Shantha G, Arora S, Deshmukh A, Cohen MG, Grines C, De Marchena E, Badheka A and Ghatak A. Percutaneous Coronary Intervention in Patients With End-Stage Liver Disease. *Am J Cardiol* 2016;117:1729-1734.
11. Kontopantelis E, White IR, Sperrin M and Buchan I. Outcome-sensitive multiple imputation: a simulation study. *BMC Med Res Methodol* 2017;17:2.
12. Rubin, D. B. Multiple Imputation for Nonresponse in Surveys. New York: Wiley. 1987.
13. Blumenfeld O, Na'amnih W, Shapira-Daniels A, Lotan C, Shohat T and Shapira OM. Trends in Coronary Revascularization and Ischemic Heart Disease-Related Mortality in Israel. *J Am Heart Assoc* 2017;6 (2): e004734
14. Zheng X, Curtis JP, Hu S, Wang Y, Yang Y, Masoudi FA, Spertus JA, Li X, Li J, Dharmarajan K, Downing NS, Krumholz HM, Jiang L and China PCG. Coronary Catheterization and Percutaneous Coronary Intervention in China: 10-Year Results From the China PEACE-Retrospective CathPCI Study. *JAMA Intern Med* 2016;176:512-521.
15. Mamas MA, Nolan J, de Belder MA, Zaman A, Kinnaird T, Curzen N, Kwok CS, Buchan I, Ludman P, Kontopantelis E, British Cardiovascular Intervention S and the National Institute for Clinical Outcomes R. Changes in Arterial Access Site and Association With Mortality in the United Kingdom: Observations From a National Percutaneous Coronary Intervention Database. *Circulation* 2016;133:1655-1667.
16. Choi YJ, Kim JB, Cho SJ, Cho J, Sohn J, Cho SK, Ha KH and Kim C. Changes in the Practice of Coronary Revascularization between 2006 and 2010 in the Republic of Korea. *Yonsei Med J* 2015;56:895-903.
17. McAllister KS, Ludman PF, Hulme W, de Belder MA, Stables R, Chowdhary S, Mamas MA, Sperrin M, Buchan IE, British Cardiovascular Intervention S and the National Institute for Cardiovascular Outcomes R. A contemporary risk model for predicting 30-day mortality following percutaneous coronary intervention in England and Wales. *Int J Cardiol* 2016;210:125-132.
18. Brennan JM, Curtis JP, Dai D, Fitzgerald S, Khandelwal AK, Spertus JA, Rao SV, Singh M, Shaw RE, Ho KK, Krone RJ, Weintraub WS, Weaver WD, Peterson ED and National Cardiovascular Data R. Enhanced mortality risk prediction with a focus on high-risk percutaneous coronary intervention: results from 1,208,137 procedures in the NCDR (National Cardiovascular Data Registry). *JACC Cardiovasc Interv* 2013;6:790-799.
19. Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, Mintz GS, Lansky AJ, Moses JW, Stone GW, Leon MB and Dangas G. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. *J Am Coll Cardiol* 2004;44:1393-1399.
20. Spoon DB, Psaltis PJ, Singh M, Holmes DR, Jr., Gersh BJ, Rihal CS, Lennon RJ, Moussa ID, Simari RD and Gulati R. Trends in cause of death after percutaneous coronary intervention. *Circulation* 2014;129:1286-1294.
21. Urban P, Meredith IT, Abizaid A, Pocock SJ, Carrié D, Naber C, Lipiecki J, Richardt G, Iñiguez A, Brunel P, Valdes-Chavarri M, Garot P, Talwar S, Berland J, Abdellaoui M, Eberli F, Oldroyd K, Zambahari R, Gregson J, Greene S, Stoll HP, Morice MC; LEADERS FREE Investigators. Polymer-free Drug-Coated Coronary Stents in Patients at High Bleeding Risk. *N Engl J Med* 2015;373:2038-47.
22. Mamas MA, Nolan J, de Belder MA, Zaman A, Kinnaird T, Curzen N, Kwok CS, Buchan I, Ludman P, Kontopantelis E; British Cardiovascular Intervention Society (BCIS) and the National Institute for Clinical Outcomes Research (NICOR). Changes in Arterial Access Site and Association With Mortality in the United Kingdom: Observations From a National Percutaneous Coronary Intervention Database. Circulation. 2016;133:1655-1667.
23. Ratib K, Mamas MA, Anderson SG, Bhatia G, Routledge H, De Belder M, Ludman PF, Fraser D, Nolan J; British Cardiovascular Intervention Society and the National Institute for Cardiovascular Outcomes Research. Access site practice and procedural outcomes in relation to clinical presentation in 439,947 patients undergoing percutaneous coronary intervention in the United Kingdom. JACC Cardiovasc Interv. 2015;8:20-29.
24. Burden of 30-Day Readmissions After Percutaneous Coronary Intervention in 833,344 Patients in the United States: Predictors, Causes, and Cost: Insights From the Nationwide Readmission Database. Kwok CS, Rao SV, Potts JE, Kontopantelis E, Rashid M, Kinnaird T, Curzen N, Nolan J, Bagur R, Mamas MA. JACC Cardiovasc Interv. 2018;11:665-674.
25. Tanguturi VK, Temin E, Yeh RW, Thompson RW, Rao SK, Mallick A, Calvallo E, Ferris TG, Wasfy JH. Clinical interventions to reduce preventable hospital readmission after percutaneous coronary intervention. Circ Cardiovasc Interv 2016;9:600-604.

**Table 1:** Patient demographics for each year included in the study, from 2004 – 2014 including all years together.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | All years |
| Number of discharges with PCI procedure | 719,561 | 727,483 | 843,009 | 646,285 | 693,156 | 619,219 | 500,392 | 526,798 | 471,346 | 441,639 | 412,593 | 6,601,480 |
| Median Age, [IQR] (years) | 65 [56-74] | 65 [56-74] | 65 [56-74] | 65 [56-74] | 65 [56-74] | 65 [56-74] | 64 [55-74] | 65 [56-74] | 65 [56-74] | 65 [56-74] | 64 [56-74] | 65 [56-74] |
| Men |  65.7% |  66.5% |  66.0% |  66.1% |  66.1% |  65.9% |  66.9% |  66.3% |  66.6% |  67.0% |  67.5% | 66.4% |
| White | 57.3% | 59.2% | 60.5% | 58.7% | 61.3% | 65.9% | 66.1% | 68.1% | 72.2% | 72.0% | 72.3% | 64.9% |
| Black | 5.1% | 3.9% | 5.0% | 6.2% | 6.2% | 6.4% | 7.7% | 8.2% | 8.5% | 8.5% | 8.6% | 6.8% |
| Hispanic | 3.8% | 4.9% | 4.8% | 5.1% | 5.0% | 5.4% | 6.2% | 6.3% | 6.6% | 7.0% | 7.1% | 5.7% |
| Asian/Pacific Islander | 1.1% | 1.3% | 1.4% | 1.6% | 1.7% | 1.7% | 2.2% | 2.2% | 2.0% | 2.2% | 2.3% | 1.8% |
| Native American | 0.1% | 0.2% | 0.3% | 0.5% | 0.7% | 0.4% | 0.7% | 0.3% | 0.6% | 0.4% | 0.5% | 0.4% |
| Other | 2.0% | 2.6% | 2.4% | 2.5% | 3.3% | 2.9% | 2.4% | 3.5% | 3.9% | 3.5% | 3.4% | 3.0% |
| Missing Race | 30.6% | 27.9% | 25.8% | 25.4% | 21.8% | 17.2% | 14.8% | 11.4% | 6.3% | 6.4% | 5.8% | 17.6% |
| Admission types - Elective admission | 38.1% | 33.6% | 35.5% | 33.8% | 30.2% | 24.3% | 21.8% | 20.3% | 18.1% | 15.5% | 11.7% | 25.7% |
| Admission Day, Weekday | 87.6% | 87.3% | 87.5% | 86.3% | 85.2% | 83.9% | 81.1% | 80.5% | 80.1% | 78.4% | 76.9% | 83.2% |
| Median Length of stay,[IQR] (days) | 2 [1-4] | 2 [1-3] | 2 [1-3] | 2 [1-3] | 2 [1-3] | 2 [1-4] | 2 [1-4] | 2 [1-4] | 2 [1-4] | 2 [2-4] | 3 [2-4] | 2 [1-4] |
| Median total charge, [IQR] (dollars) | $15494 [$11518-$21508] | $16117 [$11811-$22447] | $16539 [$12135-$22880] | $16707 [$12276-$23239] | $17830[$13195-$24934] | $17827[$13134-$25038] | $19576[$14528-$27277] | $19374[$14397-$27023] | $17494[$13447-$23751] | $18569[$14174-$25598] | $19048[$14725-$26164] | $17455 [$12971-$24291] |
| Median ZIP income - 1st quartile | 24.6% | 25.8% | 23.6% | 26.8% | 26.7% | 26.9% | 27.3% | 28.1% | 30.6% | 29.2% | 28.7% | 27.1% |
| 2nd quartile | 26.6% | 25.2% | 26.5% | 25.6% | 29.0% | 28.3% | 27.1% | 25.5% | 26.4% | 27.5% | 29.2% | 27.0% |
| 3rd quartile | 24.0% | 26.0% | 25.9% | 24.0% | 23.5% | 24.6% | 24.8% | 26.2% | 23.4% | 23.9% | 23.1% | 24.5% |
| 4th quartile | 24.8% | 23.0% | 24.1% | 23.6% | 20.8% | 20.2% | 20.8% | 20.2% | 19.6% | 19.4% | 18.9% | 21.4% |
| Single vessel PCI | 82.1% | 76.6% | 66.8% | 67.5% | 67.8% | 72.8% | 69.3% | 75.4% | 77.1% | 77.4% | 76.1% | 73.5% |
| Multi-vessel PCI | 18.3% | 19.2% | 18.6% | 16.4% | 17.7% | 17.1% | 16.1% | 17.8% | 17.3% | 17.5% | 18.4% | 17.7% |
| Unknown vessel number | 0.4% | 3.8% | 12.9% | 14.0% | 13.3% | 7.9% | 15.2% | 6.5% | 6.1% | 5.5% | 5.7% | 8.3% |
| Bifurcation stenting | No Data | No Data |  0.4% | 1.7% | 2.3% | 2.9% | 2.5% | 2.5% | 2.6% | 2.8% | 2.7% | 2.3% |
| Use of assist devise or intra-aortic balloon pump | 2.6% | 2.5% | 2.5% | 2.8% | 3.2% | 3.4% | 3.9% | 4.0% | 4.2% | 4.2% | 4.6% | 3.5% |
| Shock | 1.6% | 1.7% | 1.8% | 2.1% | 2.5% | 2.8% | 3.5% | 3.8% | 3.9% | 4.3% | 5.1% | 3.0% |
| Primary diagnosis acute myocardial infarction | 31.2% | 31.3% | 30.6% | 34.7% | 35.6% | 40.4% | 47.8% | 48.9% | 53.3% | 57.1% | 62.8% | 43.1% |
| Fractional flow reserve | No Data | No Data | No Data | No Data |  0.01% |  0.6% | 0.8% | 1.2% | 2.0% | 2.5% | 2.8% | 1.4% |
| Intravascular ultrasound |  0.6% | 3.5% | 3.1% | 5.1% | 5.3% | 5.8% | 6.0% | 7.1% | 6.8% | 6.4% | 6.3% | 5.1% |
| Bare metal stent | 22.3% | 10.2% | 14.1% | 31.5% | 32.4% | 24.9% | 26.5% | 25.1% | 21.9% | 19.1% | 16.7% | 22.3% |
| Drug eluting stent | 73.4% | 86.7% | 82.7% | 64.4% | 63.2% | 69.7% | 67.6% | 68.7% | 71.8% | 74.3% | 76.4% | 72.6% |
| Unknown stent type | 7.1% | 5.3% | 5.9% | 7.3% | 7.3% | 7.2% | 7.7% | 7.7% | 7.4% | 7.6% | 7.9% | 7.1% |
| Both stent types used | 3.0% | 2.2% | 3.0% | 3.3% | 3.0% | 1.8% | 1.5% | 1.5% | 1.1% |  1.0% |  1.0% | 2.0% |
| Comorbidities - Charlson Comorbidity Index |  |  |  |  |  |  |  |  |  |  |  |  |
| 0 | 46.6% | 46.8% | 45.6% | 43.5% | 41.8% | 39.8% | 39.3% | 37.3% | 36.6% | 35.6% | 34.2% | 40.7% |
| 1 | 34.6% | 34.5% | 35.2% | 35.3% | 35.3% | 34.5% | 34.0% | 33.5% | 33.5% | 32.9% | 32.8% | 34.2% |
| 2 | 13.5% | 13.4% | 13.8% | 14.8% | 15.4% | 16.3% | 16.6% | 17.6% | 18.0% | 18.5% | 18.8% | 16.1% |
| ≥3 | 5.3% | 5.4% | 5.4% | 6.4% | 7.5% | 7.5% | 10.1% | 11.5% | 11.9% | 13.0% | 14.2% | 8.9% |
| Mean CCI (SD) | 1.0 (1.0) | 1.1 (1.1) | 1.1 (1.1) | 1.2 (1.1) | 1.2 (1.1) | 1.3 (1.2) | 1.4 (1.2) | 1.5 (1.2) | 1.5 (1.2) | 1.6 (1.3) | 1.7 (1.3) | 1.3 (1.2) |
| Previous myocardial infarction | 12.6% | 12.1% | 12.2% | 12.7% | 13.0% | 13.7% | 13.6% | 13.6% | 14.1% | 14.5% | 14.9% | 13.4% |
| Heart failure | 12.6% | 12.4% | 12.8% | 13.7% | 13.8% | 15.5% | 16.8% | 18.6% | 19.1% | 20.9% | 22.7% | 16.3% |
| Peripheral vascular disease | 1.1% | 1.0% | 1.2% | 1.3% | 1.4% | 1.6% | 1.4% | 1.4% | 1.4% | 1.5% | 1.5% | 1.4% |
| Previous stroke | 0.8% | 0.7% | 0.8% | 1.4% | 4.6% | 5.6% | 5.8% | 6.6% | 6.8% | 7.1% | 7.5% | 4.4% |
| Dementia | 0.1% | 0.1% |  0.1% |  0.1% |  0.2% |  0.2% |  0.2% |  0.2% |  0.2% |  0.2% |  0.2% | 0.2% |
| Chronic obstructive disease | 13.2% | 13.9% | 14.3% | 15.2% | 14.6% | 16.2% | 16.1% | 17.3% | 17.6% | 18.2% | 18.7% | 15.9% |
| Connective tissue disease | 1.3% | 1.3% | 1.4% | 1.5% | 1.6% | 1.7% | 1.8% | 2.0% | 2.0% | 2.0% | 2.1% | 1.7% |
| Peptic ulcer |  0.8% |  0.7% |  0.7% |  0.6% |  0.7% |  0.8% |  0.7% |  0.8% |  0.7% |  0.7% | 0.7% | 0.7% |
| Mild liver disease |  0.2% | 0.2% | 0.2% | 0.6% | 0.2% | 0.3% | 0.3% | 0.4% | 0.4% |  0.4% | 0.5% | 0.3% |
| Moderate-severe liver disease |  0.0% | 0.0% |  0.0% |  0.1% |  0.1% |  0.1% |  0.1% |  0.1% | 0.1% |  0.1% | 0.2% | 0.1% |
| Hemiplegia | 0.1% | 0.1% | 0.1% | 0.1% | 0.2% | 0.3% | 0.3% | 0.3% | 0.3% | 0.3% | 0.4% | 0.2% |
| Moderate-severe chronic kidney disease | 0.5% | 0.4% | 0.2% | 0.2% | 0.4% | 0.6% | 0.8% | 0.9% | 0.8% |  1.1% |  1.2% | 0.7% |
| Diabetes - controlled | 26.7% | 26.9% | 27.7% | 28.8% | 29.7% | 30.0% | 30.1% | 31.8% | 32.1% | 32.3% | 32.5% | 29.9% |
| Diabetes - uncontrolled | 2.4% | 2.5% | 2.4% | 2.8% | 2.8% | 3.3% | 3.7% | 4.3% | 4.4% | 4.6% | 5.2% | 3.5% |
| Leukaemia & lymphoma | 1.5% | 1.6% | 1.5% | 1.7% | 1.8% | 1.9% | 2.0% | 2.2% | 2.1% | 2.3% | 2.4% | 1.9% |
| Solid tumour + metastasis | 0.2% | 0.3% | 0.3% | 0.3% | 0.3% | 0.3% | 0.4% | 0.4% | 0.4% | 0.4% | 0.4% | 0.3% |
| AIDS | 0.1% | 0.1% | 0.1% | 0.1% | 0.1% | 0.1% | 0.1% | 0.1% | 0.1% | 0.1% | 0.1% | 0.1% |
| Hypertension | 63.3% | 64.2% | 67.0% | 68.1% | 70.5% | 71.2% | 71.8% | 73.3% | 74.0% | 74.4% | 75.1% | 69.5% |
| Hypercholesterolemia | 19.5% | 16.5% | 14.6% | 14.0% | 13.0% | 12.1% | 11.5% | 11.6% | 10.1% | 9.3% | 9.0% | 13.4% |
| Smoking | 26.5% | 29.1% | 30.5% | 32.2% | 34.6% | 36.5% | 38.2% | 39.7% | 42.0% | 43.4% | 46.4% | 35. 1% |

**Table 2:** Patient demographics stratified by categorised Charlson Index Score (CCI)

|  |  |
| --- | --- |
|  | Charlson Comorbidity Index Score |
| Variables | 0 | 1 | 2 | ≥ 3 |
| Discharges with PCI procedure | 41.5% | 34.4% | 15.7% | 8.5% |
| Median age, [IQR] (years) | 62 [54-72] | 65 [56-74] | 67 [58-76] | 68 [60-76] |
| Men | 70.9% | 65.0% | 60.9% | 59.4% |
| White | 64.5% | 62.0% | 62.5% | 63.1% |
| Black | 4.9% | 6.7% | 8.0% | 9.9% |
| Hispanic | 4.3% | 5.9% | 6.2% | 6.8% |
| Asian/Pacific Islander | 1.6% | 1.9% | 1.7% | 1.8% |
| Native American | 0.4% | 0.5% | 0.5% | 0.6% |
| Other | 2.8% | 3.0% | 2.7% | 2.7% |
| Missing Race | 21.5% | 20.0% | 18.4% | 15.3% |
| Admission types - Elective admission | 28.9% | 28.6% | 24.6% | 19.7% |
| Admission Day, Weekday | 84.3% | 84.6% | 83.2% | 81.4% |
| Median length of stay, [IQR] (days) | 2 [1-3] | 2 [1-4] | 3 [1-5] | 4 [2-7] |
| Median total charge, [IQR] (dollars) | $16522[$12455-$22288] | $17277[$12854-$24022] | $18921[$13801-$27211] | $21635[$15454-$32150] |
| Median ZIP income 1st quartile | 23.6% | 27.2% | 29.6% | 31.1% |
| 2nd quartile | 26.1% | 27.1% | 27.7% | 27.5% |
| 3rd quartile | 25.6% | 24.5% | 23.8% | 23.6% |
| 4th quartile | 24.7% | 21.2% | 18.8% | 17.8% |
| Single vessel PCI | 73.3% | 72.4% | 72.0% | 71.9% |
| Multi-vessel PCI | 16.8% | 18.1% | 18.9% | 20.3% |
| Unknown vessel number | 9.9% | 9.5% | 9.1% | 7.8% |
| Bifurcation stenting | 1.6% | 1.7% | 1.8% | 2.1% |
| Use of assist devise or intra-aortic balloon pump | 2.3% | 3.4% | 4.5% | 5.0% |
| Shock | 1.7% | 2.9% | 4.1% | 4.9% |
| Primary diagnosis acute myocardial infarction | 44.4% | 38.4% | 37.9% | 39.4% |
| Fractional flow reserve | 0.6% | 0.7% | 0.9% | 1.3% |
| Intravascular ultrasound | 4.7% | 4.9% | 5.0% | 5.5% |
| Bare Metal Stent | 21.1% | 21.5% | 23.4% | 26.7% |
| Drug Eluting Stent | 75.4% | 73.6% | 70.3% | 65.7% |
| Unknown Stent Type | 5.7% | 7.3% | 8.5% | 9.6% |
| Both stent types used | 2.2% | 2.2% | 2.2% | 2.0% |
| Hypertension | 62.6% | 73.8% | 76.0% | 76.3% |
| Hypercholesterolemia | 13.5% | 14.2% | 13.1% | 11.4% |
| Smoking | 35.6% | 34.9% | 35.5% | 35.7% |
| Charlson Index Components |  |  |  |  |
| Myocardial infarction | N/A | 15.9% | 29.1% | 37.4% |
| Heart failure | N/A | 13.1% | 37.6% | 61.6% |
| Peripheral vascular disease | N/A | 1.3% | 2.9% | 4.6% |
| Stroke | N/A | 2.8% | 8.6% | 17.7% |
| Dementia | N/A | 0.1% | 0.3% | 0.8% |
| Chronic obstructive disease | N/A | 16.8% | 35.8% | 50.0% |
| Connective tissue disease | N/A | 1.8% | 3.6% | 5.5% |
| Peptic ulcer | N/A | 0.7% | 1.6% | 2.8% |
| Mild liver disease | N/A | 0.2% | 0.6% | 1.6% |
| Moderate-severe liver disease | N/A | 0 | 0 | 0.9% |
| Hemiplegia | N/A | 0 | 0.4% | 1.7% |
| Moderate-severe chronic kidney disease | N/A | 0 | 0.6% | 5.9% |
| Diabetes – controlled | N/A | 47.3% | 56.1% | 53.1% |
| Diabetes – uncontrolled | N/A | 0 | 7.6% | 25.2% |
| Leukaemia & lymphoma | N/A | 0 | 3.4% | 13.9% |
| Solid tumour + metastasis | N/A | 0 | 0 | 3.7% |
| AIDS | N/A | 0 | 0 | 1.2% |

**Table 3:** Percentage of patients with in-hospital mortality and post procedural complications by Charlson score

|  |  |
| --- | --- |
|  | **Charlson Comorbidity Index Score** |
| **Variables** | **0** | **1** | **2**  | **≥3** |
| **Death** | 1.0% | 1.6% | 2.3% | 3.2% |
| **Any complications** | 6.0% | 8.0% | 11.3% | 16.5% |
| **Bleeding Complications** | 1.7% | 3.0% | 5.2% | 9.1% |
| **Vascular complications** | 1.0% | 1.1% | 1.2% | 2.0% |
| Post-op haemorrhage requiring transfusion | 0.1% | 0.1% | 0.1% | 0.1% |
| Vascular injury | 0.9% | 1.0% | 1.1% | 1.2% |
| **Cardiac complications** | 2.0% | 2.0% | 2.1% | 2.3% |
| Iatrogenic cardiac  | 1.9% | 1.9% | 1.9% | 2.1% |
| Pericardial complication | 0.1% | 0.1% | 0.1% | 0.1% |
| Requiring coronary artery bypass graft | 1.0% | 1.3% | 1.5% | 1.3% |
| **Post-op stroke/Transient ischemic attack** | 1.9% | 2.8% | 4.0% | 5.8% |

**Table 4:** Association between increasing comorbidity burden and in-hospital complications after PCI (odds ratio and 95% confidence intervals), adjusted for potential confounding

|  |  |
| --- | --- |
|  | Charlson Comorbidity Index Score  |
|  | 1 v 0 | 2 v 0 | ≥3 v 0 |
| In-hospital mortality | 1.19 (1.15,1.25) | 1.41 (1.34,1.48) | 1.96 (1.86,2.07) |
| Any complication | 1.23 (1.21,1.27) | 1.66 (1.61,1.70) | 2.47 (2.38,2.56) |
| Bleeding complication | 1.57 (1.52,1.61) | 2.47 (2.39, 2.56) | 4.26 (4.09, 4.42) |
| Vascular complication | 1.06 (1.02, 1.10) | 1.09 (1.03, 1.15) | 1.12 (1.05,1.20) |
| Cardiac complication | 0.94 (0.91, 0.97) | 0.94 (0.90, 0.99) | 1.00 (0.95, 1.04) |
| Stroke | 1.30 (1.26, 1.34) | 1.72 (1.67, 1.79) | 2.40 (2.30, 2.51) |

\*Adjustment for age, gender, ethnicity, median income, elective admission, day of admission (weekend/weekday) primary diagnosis of MI, diagnosis of shock, hypertension, or hypercholesterolemia, if the patient smokes, use of an assist device or intra-aortic balloon pump, use of a bare metal or drug eluting stent, bifurcation stenting, fractional flow reserve, single or multi-vessel PCI and year of hospitalisation

Figure 1: Flow diagram of included/excluded records

Age – 44 missing

Gender – 109 missing

Elective procedure – 4,360 missing

Length of Stay – 6 missing

Median Zip code income – 33,387 missing

Death – 282 missing

Total charge – 13,451 charge missing

 53, 368 Cost-Charge ratio missing

All records taken from NIS database from 2004 - 2014

Excluded records with covariate information that was greater than 10% missing data (n=1,379,384 – unweighted)

Unweighted 1,485,048 records were identified with PCI procedure

Restricted to Adult over the age of 18 (n=1,484,391 – unweighted)

Identified records with a PCI using ICD-9 codes including 0.66, 36.01, 36.02, 36.05, 36.06, 36.07

Records with a PCI procedure included in analysis (N= 6,601,526 - weighted)

Figure 2: The percentages of each category of the Charlson score for each PCI procedure by year

Figure 3: Association between increasing comorbidity burden and length of stay, median (IQR)

Figure 4: Association between increasing comorbidity burden and total cost of hospitalisation, median (IQR)

**Supplementary Table 1:** Deyo’s modification of Charlson’s co-morbidity index (CCI).

|  |  |  |
| --- | --- | --- |
| Reported ICD-9 codes | Condition | Charlson score |
| 412 | Previous Myocardial infarction | 1 |
| 428 – 428.9 | Congestive heart failure | 1 |
| 433.9, 441 – 441.9, 785.4 V43.4 | Peripheral vascular disease | 1 |
|  | Previous Cerebrovascular disease | 1 |
| 290 – 290.9 | Dementia | 1 |
| 490 – 496, 500 –505, 506.4 | Chronic pulmonary disease | 1 |
| 710.0, 710.1, 710.4, 714 – 714.2, 714.81, 725 | Rheumatologic disease | 1 |
| 531 – 534.9 | Peptic ulcer | 1 |
| 571.2, 571.5, 571.6, 571.4 –571.49 | Mild liver disease | 1 |
| 250 – 250.3, 250.7 | Diabetes | 1 |
| 250.4 – 250.6 | Diabetes with chronic complications | 2 |
| 344.1, 342 – 342.9 | Hemiplegia or paraplegia | 2 |
| 582 – 582.9, 583 – 583.7, 585, 586, 588 – 588.9 | Renal Disease | 2 |
| 140 – 172.9, 174 –195.8, 200 – 208.9 | Any malignancy including leukaemia and lymphoma | 2 |
| 572.2 – 572.8  | Moderate or severe liver disease | 3 |
| 196 – 199.1 | Metastatic solid tumour | 6 |
| 042 – 044.9 | AIDS | 6 |

**Supplementary Table 2:** ICD-9-CM codes for post procedural complications

|  |  |
| --- | --- |
| **Post-procedural Complication** | **ICD-9-CM codes** |
| **Bleeding complication** |  |
| Gastrointestinal | 578.9 |
| Unspecified haemorrhage | 459.0 |
| Retroperitoneal haemorrhage | 568.81 |
| Intracranial haemorrhage | 432.9 |
| Intracerebral haemorrhage | 431 |
| Blood transfusion | V58.2, 99.0x (procedure) |
| **Vascular complications** |  |
| Post-op haemorrhage requiring transfusion | 99.0 (procedure) |
| Vascular injury | 900-904, 998.2, 447, 868.04, 999.7 (diagnosis)39.31, 39.41, 39.49, 39.52, 39.53, 39.56 - 39.59 39.79 |
| **Cardiac complications** |  |
| Iatrogenic cardiac  | 997.1 |
| Pericardial comp | 423.0, 423.3, 47.0 |
| Requiring CABG | 36.1x, 36.2, 36.31, 36.32, 36.9x |
| **Post-op stroke/TIA** | 997.00-997.03, 435.9, 438.0, 4381.1, 4381.2, 4381.9, 4382.0, 4382.1, 4381.2, 4384.0, 4384.1 4384.2, 4385.0, 4385.1, 4385.2, 4385.3, 4388.1, 4388.2, 4388.9, 438.9 |

**Supplementary Figure 1:** Number of PCI procedures performed in each of the study years from 2004 – 2014

**Supplemental Figure 2:** Number of PCI discharges with each score of the Charlson Comorbidity index

**Supplementary Figure 3:** Average length of stay each year stratified by Charlson comorbidity index

**Supplementary Figure 4:** Average cost of stay each year stratified by Charlson comorbidity index

**Supplementary Table 3:** Impact of a 1-unit unit increase of CCI score on the odds of mortality and other complications after adjustment\*.

|  |  |
| --- | --- |
|  | Increase of 1 CCI score, OR (95% CI) |
| In hospital mortality | 1.18 (1.17, 1.19) |
| Any complication | 1.21 (1.20, 1.22) |
| Bleeding complication | 1.37 (1.36, 1.38) |
| Vascular complication | 1.03 (1.02, 1.05) |
| Cardiac complication | 1.00 (0.99, 1.02) |
| Stroke | 1.22 (1.21, 1.23) |

\*Adjustment for age, gender, ethnicity, median income, elective admission, day of admission (weekend/weekday) primary diagnosis of MI, diagnosis of shock, hypertension, or hypercholesterolemia, if the patient smokes, use of an assist device or IABP, use of a bare metal or drug eluting stent, bifurcation stenting, fractional flow reserve, single or multi-vessel PCI and year of hospitalisation

**Supplementary Table 4:** Association (OR, 95% CI) between individual Charlson components and clinical outcomes, after adjustment\* for each other and other covariates included in multivariate analysis

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Mortality | Any complication | Bleeding | Vascular complication | Cardiac complication | Post -op Stroke/TIA |
| Myocardial infarction | 0.78(0.74, 0.82) | 0.95(0.93, 0.98) | 0.96(0.92, 0.99) | 0.84(0.78, 0.89) | 0.82(0.79, 0.86) | 1.03(1.00, 1.07) |
| Heart failure | 1.42(1.36, 1.47) | 1.70(1.66, 1.75) | 2.50(2.43, 2.58) | 1.25(1.20, 1.31) | 1.11(1.07, 1.15) | 1.29(1.25, 1.32) |
| Peripheral vascular disease | 1.75(1.58, 1.93) | 1.88(1.80, 1.97) | 1.56(1.45, 1.68) | 2.25(2.02, 2.50) | 1.66(1.52, 1.81) | 2.10(1.98, 2.24) |
| Stroke | 1.18(1.10, 1.26) | 1.75(1.70, 1.80) | 1.25(1.20, 1.31) | 0.98(0.90, 1.07) | 0.96(0.90, 1.03) | 2.79(2.69, 2.89) |
| Dementia | 1.27(0.97, 1.65) | 6.11(5.29, 7.07) | 1.44(1.20, 1.74) | 1.00(0.69, 1.47) | 0.92(0.68, 1.24) | 14.5(12.5, 16.9) |
| Chronic obstructive disease | 1.30(1.25, 1.35) | 1.38(1.36, 1.41) | 1.69(1.65, 1.74) | 1.21(1.15, 1.26) | 1.06(1.02, 1.11) | 1.29(1.25, 1.33) |
| Connective tissue disease | 0.99(0.88, 1.11) | 1.21(1.15, 1.26) | 1.47(1.38, 1.56) | 0.98(0.87, 1.11) | 1.03(0.94, 1.13) | 1.06(0.98, 1.14) |
| Peptic ulcer | 1.11(0.96, 1.30) | 2.55(2.39, 2.72) | 4.55(4.13, 4.79) | 1.29(1.10, 1.53) | 1.14(1.00, 1.30) | 1.24(1.12, 1.38) |
| Mild liver disease | 2.59(2.15, 3.11) | 2.28(2.08, 2.51) | 4.15(3.72, 4.63) | 0.93(0.68, 1.27) | 0.99(0.79, 1.23) | 1.26(1.06, 1.50) |
| Moderate-severe liver disease | 6.19(4.77, 8.05) | 3.29(2.82, 3.83) | 6.21(5.20, 7.42) | 1.75(1.17, 2.62) | 1.10(0.79, 1.54) | 1.16(0.85, 1.58) |
| Hemiplegia | 3.78(3.08, 4.62) | 15.1(13.8, 16.5) | 3.00(2.64, 3.42) | 1.79(1.39, 2.31) | 1.65(1.37, 1.98) | 42.9(39.2, 47.1) |
| Moderate-severe chronic kidney disease | 2.16(1.87, 2.49) | 2.35(2.19, 2.50) | 3.76(3.48, 4.06) | 1.39(1.14, 1.68) | 0.93(0.79, 1.08) | 1.44(1.29, 1.62) |
| Diabetes – controlled | 0.99(0.96, 1.03) | 0.99(0.97, 1.00) | 1.08(1.06, 1.11) | 0.81(0.78, 0.85) | 0.78(0.76, 0.81) | 1.07(1.04, 1.09) |
| Diabetes – uncontrolled | 1.39(1.29, 1.50) | 1.95(1.89, 2.02) | 2.85(2.73, 2.97) | 1.08(0.99, 1.18) | 0.90(0.83, 0.97) | 1.68(1.60, 1.76) |
| Leukaemia & lymphoma | 1.79(1.65, 1.94) | 1.74(1.67, 1.81) | 2.61(2.48, 2.75) | 1.04(0.93, 1.18) | 1.61(1.50, 1.74) | 0.98(0.91, 1.05) |
| Solid tumour + metastasis | 3.15(2.71, 3.65) | 2.24(2.07, 2.43) | 3.35(3.04, 3.68) | 1.24(0.98, 1.57) | 1.82(1.57, 2.12) | 1.07(0.92, 1.25) |
| AIDS | 1.23(0.76, 1.98) | 1.14(0.92, 1.42) | 1.72(1.30, 2.28) | 1.10(0.63, 1.91) | 0.63(0.40, 1.00) | 0.71(0.43, 1.17) |

\*Adjustment for age, gender, ethnicity, median income, elective admission, day of admission (weekend/weekday) primary diagnosis of MI, diagnosis of shock, hypertension, or hypercholesterolemia, if the patient smokes, use of an assist device or IABP, use of a bare metal or drug eluting stent, bifurcation stenting, fractional flow reserve, single or multi-vessel PCI and year of