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Abstract

Background

The relationship between procedural volume and prognosis after percutaneous coronary intervention (PCI) remains uncertain, with some studies finding in favor of an inverse association and some against. This UK study provides a contemporary reassessment in one of the few countries in the world with a nationally representative PCI registry.

Methods and Results

A nationwide cohort study was carried out using the national British Cardiovascular Intervention Society registry. All adult patients undergoing PCI in 93 English and Welsh NHS hospitals between 2007 and 2013 were analyzed using hierarchical modeling with adjustment for patient risk. Of 427,467 (22.0% primary PCI) procedures in 93 hospitals, 30-day mortality was 1.9% (4.8% primary PCI). 87.1% of centers undertook between 200 and 2000 procedures annually. Case mix varied with center volume. In centers with 200-399 PCI cases per year, a smaller proportion were PCI for STEMI (8.4%) than in centers with 1500-1999 PCI cases per year (24.2%), but proportionally more were for STEMI with cardiogenic shock (8.4 vs. 4.3%). For the overall PCI cohort, after risk adjustment there was no significant evidence of worse, or better, outcomes in lower volume centers from our own study, or in combination with results from other studies. For primary PCI, there was also no evidence for increased or decreased mortality in lower volume centers.

Conclusions

Following adjustment for differences in case mix and clinical presentation, this study supports the conclusion of no trend for increased mortality in lower volume centers for PCI in the UK healthcare system.

Clinical Trials Registration: http://clinicaltrials.gov/show/NCT02184949

Keywords: angioplasty, percutaneous coronary intervention, mortality, volume, outcomes research

Introduction

The relationship between procedural volume and patient outcomes is an important consideration in the provision of PCI. Studies that have suggested the existence of a relationship have informed international guidelines[1-3] on the minimum procedural limits recommended for annual center volume to ensure safe and effective patient care. This is also reflected in recent UK guidance on the provision of percutaneous coronary interventions (PCI)[4]. For acute myocardial infarction, the establishment of high throughput, high-volume Heart Attack Centers (HACs) within networks of acute cardiac care has been promoted as a factor contributing to the decline in cardiovascular mortality in developed healthcare systems[5-9]. Such centers often also have high volumes of elective PCI and in much of the published literature compare favorably with lower volume centers where higher rates of adverse outcomes, longer lengths of hospital stay and increased costs have been observed[10-11]. These findings have been reflected in the reconfiguration of UK PCI services over the past decade; specifically the expectation that lower volume units undertake at least 400 procedures per annum.

It is timely and of international importance to review the evidence for and against a relationship between PCI center volume and clinical outcomes in the UK healthcare system. Such a national review contributes to the assessment of the UK's quality improvement initiative in PCI and has implications for provision of service in other countries. A meta-analysis of 10 studies (8 American, 2 Japanese, all prior to 2005) on PCI comprising 1,322,342 patients in 1746 hospitals finds in favor of an inverse relationship between center volume and risk-adjusted in-hospital mortality after PCI (odds ratio 0.865 (95% CI 0.827 to 0.905) for high vs. low volume center)[12]. However, evidence from studies published since the period covered by this meta-analysis have produced a more variable picture, with some studies supporting the presence of a relationship between center PCI volume and risk-

adjusted outcomes[10,11,13,14], and others not[15-18]. A more recent summary of the evidence by a joint task force from the American College of Cardiology Foundation, American Heart Association and American College of Physicians acknowledged that the large-scale studies in this area have produced heterogeneous findings[19]. Specifically in relation to primary PCI cohorts, a review by the National Clinical Guidance Centre[20] likewise noted that the evidence base is currently insufficient to establish a definitive understanding of the volume-outcome relationship.

In the United Kingdom (UK), continuous whole country data are collected through the British Cardiovascular Intervention Society (BCIS) registry of all PCI cases, are linked to the registry of deaths for all inhabitants in the UK collected independently by the Office for National Statistics and held by the National Institute for Cardiovascular Outcomes Research at University College London. This provides unique opportunities to understand outcomes after percutaneous interventions. We consequently used these mortality linked data to investigate the association between annual center volume of PCI cases and 30-day all-cause mortality over a seven year period up to 2013.

Methods

Setting and Design

This observational prognostic cohort study was based on data from the BCIS national registry of adult interventional procedures, participation in which is mandated for all PCI operators and all National Health Service (NHS) Trusts in England and Wales. Data for every PCI procedure performed were collected at the time of procedure at each hospital. These data were then encrypted and transferred on-line to a central database at the National Institute for Cardiovascular Outcomes Research (NICOR), hosted at University College

London, UK. The data for each PCI procedure comprise 113 core fields which describe the patient demographics and clinical presentation, indications for PCI, procedural details and outcomes during the hospital stay[21]. NICOR, which includes BCIS (Ref: NIGB: ECC 1-06 (d)/2011), has support under section 251 of the NHS Act 2006 to use anonymized patient information for medical research without consent. The study involved de-identified data and formal ethical approval was not required.

Patients

The sampling frame comprised all patients in England and Wales recorded in the BCIS database. Patients were eligible for analysis if they had received PCI to at least one lesion or vessel over a seven year period between 01 January 2007 and 31 December 2013, and were aged between 18 and 100 years. We excluded a total of 68,912 (11.7%) cases from 9 private hospitals as they did not represent NHS care, and from 14 hospitals in Scotland and Northern Ireland as mortality tracking is only consistently available for patients with a NHS number in England and Wales. The exclusion of private hospitals was also to account for potential differences in clinical practice; typically they reflect independent operators rather than teams, and treat almost exclusively elective cases. An additional 11,871 (2.0%) cases from within English or Welsh NHS hospitals were also excluded because of missing 30-day mortality. Ventilated patients (who mainly present with out of hospital cardiac arrest) were also excluded as the risk adjustment model was inapplicable to such patients. For patients with multiple admissions, the earliest record was used with subsequent admissions being excluded. The final analytical cohort comprised 427,467 patients (Figure 1). Two subgroups were selected for analysis: (i) all PCI cases and (ii) only primary PCI cases.

Patient characteristics were examined as part of an initial descriptive analysis, including indication for intervention, urgency of procedure (elective, urgent, emergency or salvage) and cardiogenic shock (based on clinical assessment including systolic blood pressure <100 mmHg, pulse >100 bpm, in a patient who was cool, clammy or requiring inotropes, intra-

cardiac balloon pump or cardiopulmonary support).

Outcome

Data for all-cause mortality were extracted through linkage to the Office for National Statistics using each patient's unique NHS number. Patients were followed-up for their vital status 30-days after the date of their PCI procedure.

Centre Volume

We took average center volume as the measure of the procedural volume exposure. Average center volume was determined for each center from its total number of PCIs registered in BCIS for the years 2007-13, divided by the number of years where PCI activity was non-zero. Records concerning pre-operatively ventilated patients, follow-up procedures and records with missing mortality outcome data were retained in the calculation of overall annual volume as these were deemed to contribute to the procedural volume. For the purpose of stratified analysis, bands of center average volume were established on the basis of existing standards and clinical experience. These bands were set at: 0-199, 200-399, 400-749, 750-1499, 1500-1999 and $\geqslant$2000 cases.

Case Mix Adjustment

Model based case mix standardization for 30-day mortality outcome was performed to adjust for patient characteristics. The model[22] was developed by an independent research group using data from the BCIS registry that comprised all eligible PCI records undertaken in England and Wales from 2007 through 2011. Clinical validation of the model subsequently undertaken by its developers showed that the model performed well in estimating risk for more recent cases. The model has 9 risk factors: age at time of procedure, sex, diabetes history, previous myocardial infarction, renal disease history, cerebrovascular event history, cardiogenic shock, indication for intervention and procedural urgency. These covariates

were selected for their clinical relevance, predictive utility, and low levels of missingness. The model includes interactions for age-diabetes, age-shock and indication-shock. We independently performed calibration and discrimination analyses to evaluate the model's suitability for our study (see supplementary materials).

Statistical Analyses

A statistical analysis plan was prepared and registered on www.clinicaltrials.gov prior to data analysis. Statistical analyses were performed using R version 3.1.2 (www.r-project.org) and Markov chain Monte Carlo software written in C++. Differences in baseline characteristics for average center volume bands were examined using analysis of variance for continuous variables and the chi-square test for categorical variables. All tests were two-tailed, and to correct for multiple comparisons, p-values were adjusted using the false discovery rate method[23].

Hierarchical logistic models for patient's 30-day mortality outcome nested in centers were applied to overall, and primary, PCI groups with adjustment for risk of adverse outcome. We included fixed effects for year of procedure to account for year by year change in risk-adjusted outcomes, resulting in estimates of center level effects with 95% confidence intervals (CI). We computed the ratio of the probability of the estimated center level effects under the hypothesis of no relationship with volume to the probability of the effects under the hypothesis of a relationship. In the relationship hypothesis we took a uniform non-informative prior for the gradient with respect to log-volume. Details are provided in the Supplementary Materials. Each probability captures how well the effects estimates match each hypothesis, and the ratio makes a comparison. This ratio is akin to the likelihood ratio, and is called a 'Bayes factor'[24]. The smaller than 1 the Bayes factor is, the greater our effects estimates support the hypothesis of a relationship. We repeated these calculations for a band-specific relationship analysis, using the pre-specified volume bands as defined above. We also

estimated the gradient of center level effect to log-volume under the hypothesis of a relationship.

Missing Data

Records with missing mortality status (2.0%) were excluded as part of the sampling criteria (Figure 1). Hospital name and year of procedure were 100% complete. Missing data in covariates used to assign 30-day mortality risk were handled using the same method employed in the model's derivation: missing categorical covariates were set to their lowest risk value; missing age was set to sex-specific median values. This imputation technique ensured the model was implemented in line with its intended use in clinical practice. Additional detail on missing data is provided in the Supplementary Materials.

Sensitivity Analyses

To validate our results, we first examined whether the use of alternative estimation methods in the hierarchical modeling work impacted upon the coefficient estimates and confidence intervals. Second, to explore the categorization method used in the primary analyses, we performed an alternative analysis of the center volume-outcome relationship using equally sized quintiles of the mean annual number of cases of PCI per year. Third, we excluded the 10% of patients who were in the top 30-day mortality risk decile (to correct for some over-prediction of mortality identified in our calibration testing of the risk model). Fourth, we excluded the 5% of patients who had missing data for cardiogenic shock (to remove additional uncertainty about missing data as this field had the highest potential influence over mortality risk estimates derived from the risk model). Fifth, we repeated the model with elective only patients. Finally, for the primary PCI cohort we re-investigated the volume outcome relationship using each center's primary PCI mean annual volume rather than the volume of all PCIs undertaken at that center.

Results

Baseline Characteristics

Our analysis included 427,467 PCI procedures in 93 NHS hospitals in England and Wales, of which 94,022 (22.0%) were primary PCI. The mean (SD) age was 64.9 (11.9) and 26.5% were female (Table 1). Overall, 17.6% had diabetes, 1.4% had a creatinine greater than 200 µmol/L, and of the primary PCI cohort (Table 2), 5.1% in total had cardiogenic shock. For the overall PCI cohort, 65.1% had a drug-eluting stent (DES) deployed, whilst 3.1% of the PCI procedures involved the use of intravascular ultrasound (IVUS) guidance. Among primary PCI patients, a smaller proportion of procedures involved IVUS use (1.5%), while 59.5% involved DES deployment.

Tables 1 and 2 also show that the frequency of many patient and procedural characteristics differed between bands of center average volume. All characteristics were statistically significantly different between bands at $p<0.001$ for the overall cohort following false discovery rate adjustment for multiple comparison. Most were significant at the same threshold for the primary PCI cohort. Compared to the higher volume centers ($\geqslant$2000), the lowest (0-199) volume centers had a smaller frequency of STEMI cases (2.8% in lowest vs. 24.7% in highest), as well as PCI for NSTEMI (18.9 vs. 34.4%), but greater frequency of elective (53.3 vs. 38.5%), stable (47.9 vs. 37.1%) and rescue (22.3 vs. 1.4%) cases. The second lowest volume band (200-399) captures a much larger number of cases than the lowest band. Compared to the highest volume units, this second lowest volume band had a greater level of NSTEMI patients (52% in second lowest vs. 34.4% in highest) and of urgent cases (49.6% vs. 32.6%).

Although higher volume units handled a greater proportion of STEMI cases and had higher absolute levels of patients with cardiogenic shock, results for the primary PCI cohort (Table 2) show that the second lowest volume units in that cohort had a higher relative proportion of patients with cardiogenic shock (8.4 vs. 3.7%) and of creatinine levels above 200 μmol/L (3.7 vs. 0.5%). Higher volume centers, on the other hand, had a greater proportion of primary PCI cases where the patient was a smoker (30.8 vs. 39%).

For the total cohort, the crude unadjusted rate for mortality at 30-days was 1.9%. From 2007 to 2013, these rates increased from 1.4% to 2.2%. By contrast, for primary PCI, the unadjusted 30-day mortality rate was 4.8% and remained unchanged in 2013 compared to 2007. Across this same interval, predicted mortality rates increased from 1.3% to 2.3% in the overall PCI cohort, and from 4.8% to 5.2% for primary PCI cases.

The median number of PCI cases treated annually per hospital was 659.5, and the mean was 878.5. The observed center average volumes ranged from 61 (almost always new centers starting up a PCI program) to 2794. Few centers (5.4%) undertook less than 200 PCI procedures per year, with most (87.1%) performing on average between 200 and 2000 procedures. Centre annual volumes increased over the study period from a mean of 889 in 2007 to 917 in 2013. A smaller increase occurred for the primary PCI sample, from 934 to 945 procedures per year.

Volume and Mortality

In both PCI and primary PCI groups, for 2007-13 in the UK, observed and predicted 30-day mortality rates depend on center average annual volume in a largely identical fashion (Figures 2 and 3).

Risk-adjusted estimates of 30-day mortality for each center were derived through our hierarchical modeling. The dose-response relationship between volume and outcome was

estimated to be 1.04 (95% CI 1.01 to 1.07, p-value = 0.01) per 2-fold increase in center average annual volume. The Bayes factor was 0.14 meaning that, taking into account the center level effects, the ratio of the chance that there is no volume-outcome relationship compared to the chance that there is such a relationship is increased by a factor of 0.14. Our summary of existing literature yielded a prior chance of a relationship of 0.5 (denoting equal chances of the relationship being absent or present). The current study's center-level effect estimates revise this down to 0.12. That is to say, the prior probability is adjusted in light of the evidence from our data. Thus there remains support, with probability greater than 0.05, for the hypothesis that there is no volume outcome relationship in or overall PCI cohort.

We also examined each of the pre-specified volume bands in our overall PCI cohort. Bayes factors for the hypothesis that a band-specific effect is absent relative to the hypothesis that it is present are reported in Table 3. Bands 0-199, 200-399 and 1500-1999 have Bayes factors less than 1, signifying that the hypothesis of no band-specific effect is less plausible[25] in the light of the center level effects for these bands. However, repeating the argument of the previous paragraph, under the assumption of a 0.50 prior chance of no band-specific effect, the chance of the band with the smallest Bayes factor, 1500-1999, having no effect is revised down to 0.12, i.e. there remains support, greater than 0.05, for the hypothesis that there is no band-specific effect for this, or any other, band.

In the primary PCI subset of cases, the dose-response relationship of volume outcome was estimated to be 1.01 (95% CI 0.99 to 1.04, p-value = 0.36) per 2-fold increase in center average annual volume. The Bayes factor was 1.4 meaning that the ratio of the chance of a volume-outcome relationship for primary PCI compared to the chance of no volume outcome relationship is increased by a factor of 1.4. Taking the before study chances of no relationship to be 0.50, our center level effects revise the chance up to 0.74, providing support, with probability greater than 0.05, for the hypothesis that there is no volume outcome relationship in the primary PCI cohort. For each pre-specified volume band in this

cohort, Table 3 also reports a Bayes factor for the hypothesis that there is a band-specific volume outcome effect relative to a hypothesis that there is not. Band 1500-1999 has a Bayes factor less than 1 signifying that the hypothesis of no band-specific effect is less plausible in light of the center level effects within that band. Under the assumption of a 0.50 prior chance of no 1500-1999 band-specific effect, the chance is revised down to 0.41, i.e. there again remains significant support for the hypothesis that there is no band-specific effect for this, or any other, band.

Sensitivity Analyses

We found very good agreement in center level effects between the MCMC and R estimations. Modest differences in uncertainties for center level effects between MCMC and R were identified but these were insufficient to alter our conclusions. The stratified analyses were replicated using quintiles of center average volume and the results showed clear similarity to our existing findings for both total PCI cases and primary PCI cases. Full details are provided in the supplemental materials. Notably, there was less variation in the lowest volume quintiles for both the overall and primary PCI volumes compared to their equivalent clinically based counterparts (Figures 2 and 3), which is likely indicative of the more evenly distributed volume sizes. When only centers' volumes of primary PCI cases (rather than their overall PCI volumes) were considered, we found no significant association between volume of primary PCI cases and risk of 30-day mortality. The exclusion of the 10% of patients who were in the top 30-day mortality risk decile, and separately the exclusion of the 5% of patients who had missing data for cardiogenic shock, did not change the overall finding regarding center volume-outcome relationship. A similar affirmation of the hierarchical findings was obtained for the elective-only cases and with the primary PCI cohort.

Discussion

This is the first whole–country, consecutive series patient-level analysis of the relationship between total center volume of PCI cases and risk-adjusted mortality at 30-days, undertaken using contemporary clinical data within a modern health care system. For the overall PCI cohort, the evidence for a trend between center average annual volume and risk-adjusted 30-day mortality was not sufficient to conclude the presence a relationship in the context of a priori evidence. For the primary PCI subset of cases, no evidence was found for a relationship between center average annual volume and risk-adjusted 30-day mortality.

The findings are consistent with earlier studies that have found no evidence of a relationship between PCI volume and risk-adjusted mortality outcomes[16-18,26,27]. Although many other existing studies have argued in favor of higher-volume centers, the importance of adjustment for case selection and hospital effects cannot be understated. One of the largest studies to date[15] found that whilst crude mortality estimates increased exponentially at lower volume institutions, there was no relationship between hospital volume and mortality after consideration of confounding factors.

The current study has additionally demonstrated the utility of Bayes factors, which can be computed as a guide to the weight of evidence in studies where alternative hypotheses are being evaluated, in contrast to p-values which only measure how extreme a test statistic derived from a study's data is under one hypothesis alone. In this study, their use enabled comparison of the evidence for the contrasting hypotheses that a relationship between volume and center effects is either absent or present. Bayes factors usefully enable the interpretation of study data in combination with a priori evidence[24]. Following the principles of Bayesian inference, we combined our study's Bayes factors with existing findings from comparable observational studies, with final results showing that, under the current UK PCI regimen, the evidence does not challenge a prior assumption which places reasonable

probability on no volume-outcome relationship. This Bayesian approach is a general one, with applicability beyond both the clinical context and observational design used in the present study.

We have identified important differences in the baseline cardiovascular risk and presenting phenotype between lower and higher volume centers. For example, we found that smaller centers had fewer patients with STEMI indications. However, STEMI cases handled at low volume centers were proportionally more likely to present with cardiogenic shock – a particularly influential factor in patient survival, as is empirically reflected by its high weighting in the risk adjustment model used in this work[22]. Since the risk adjustment accounted for these characteristics, it may be argued that there is evidence for a volume-dependent case selection bias which attenuates the relationship between center volume and mortality. A similar phenomenon has been observed in CABG research[28] but we can only speculate as to why this may be occurring. It may reflect that such cases are undertaken emergently at the presenting hospital if the risk of transfer to a specialist Heart Attack Centre (HAC) is deemed too high, or that Emergency Medical Services bring the sickest patients to the closest hospital. It may also reflect a different clinical approach to the definition of cardiogenic shock in lower volume centers. An alternative interpretation may be that higher volume centers are more selective in their choice of primary PCI cases. These possibilities warrant further inquiry, particularly given that recent work has shown that center volume of patients with cardiogenic shock is associated with improved patient outcomes[29].

It is important to consider wider contextual issues regarding clinical practice and policy in understanding the results we have established in this study. The UK has accommodated current international guidance with national recommendations that discourage low volume centers with consistently <400 PCI cases per annum and encourage regular practice with a minimum annual operator activity of >75 cases per year[4]. This may, in part, account for the absence of evidence for a center-volume outcome relationship. In many parts of the UK,

operators in lower volume centers also have PCI sessions in the regional higher volume centers, thus increasing their individual annual experience and allowing greater opportunity to select more complex cases to be performed at a higher volume regional center.

The development of new dedicated HACs as well as changes in individual practice have been associated with considerable expansion in the provision of PCI within the UK over the past decade –the current study's findings reflect these developments. It has meant that our study captures a section of the volume spectrum beyond that typically captured in prior research. The term "low volume" is context specific and varies between research settings. Many studies have used coarse volume categorizations that arguably lack measurement precision and make comparisons between research findings and clinical settings difficult[17,18]. In this study we explored volume using diverse strategies such as existing recommended volume thresholds, data-driven quantiles, and cohort-specific volume definitions (i.e. primary PCI case volume alone). This provides a detailed insight into the volume-outcome relationship, but does not overcome the fact that the range of volumes captured in this work may differ from previous studies. Consequently, while the current study has provided evidence that the relationship between hospital volumes and patient mortality is mitigated when adjustment is made for case mix, inferences should not be made regarding particularly low volumes not captured by this study. We cannot exclude the existence of a lower volume limit below which institutional competence cannot be assured. Rather, the findings suggest that the efforts made within the UK NHS to improve access to PCI and provide guidance for institutional standards of service provision have resulted in a uniformly high standard of care. We do not argue against the promotion of volume thresholds, given that its adoption has been a key aspect of the expansion of PCI provision in the UK. The policy whereby the acute management of STEMI is restricted to a limited number of dedicated HACs is driven largely by logistical necessity, and is not challenged by this study's findings.

Strengths and Limitations

The strengths of this study include the national data source of consecutive PCI cases, the depth of detail of clinical data and the robust mortality tracking and linkage. The findings of this work are also based on strong methodological foundations. More commonly employed fixed-effect regression methods would not have reflected the hierarchical nature of the data under investigation[30], namely the nesting of procedural results within centers. Hierarchical models were employed in this study to estimate center-level effects independently of center average volume, which were analyzed using Bayes factors to assess evidence for, and against, a relationship between volume and risk-adjusted outcome. Nonetheless, there are limitations to our study. These include the categorization of the center volumes using clinical consensus and existing guidelines. To address this limitation we also modeled volume as a continuous variable and undertook sensitivity analyses using quintiles of volumes; each method supported our main study findings and provided verification that our results were not the consequence of the a priori clinical categorization. Whilst BCIS data collection is mandated for all operators and all cases in England and Wales, it is possible that some cases will not have been recorded, though such omissions are likely to be minimal, as case ascertainment has been shown to be 100% for the majority of NHS hospitals in England and Wales[31]. Further, some of the cases had missing data which we treated in an identical manner to the way in which the risk model was derived. Multiple imputation may have allowed more cases to be modeled and with different precision[32]. However, sensitivity analyses showed that excluding records missing data in the highest weighted risk factor made no difference to our conclusions. Operator identifying data were not collected reliably by the BCIS registry until 2012, and so consultant volumes were not addressed in this study. While our research has not supported the presence of a relationship between center volume and outcomes, existing research[33] suggests that valuable additional insights will be obtained once sufficient data is available to replicate the current study at the consultant-level. Finally, due to the observational nature of data, the models produced in this work disclosed many important associations, but cannot provide evidence for causation. It would not have been

possible however to obtain such coverage of real-world practice as achieved in this work if an experimental design had been employed[34,35].

Conclusions

Data covering all cases of emergent and elective PCI in England and Wales has shown that most centers undertake between 200 and 2000 PCI procedures per year on average. Lower volume centers undertake proportionally less STEMI cases overall but proportionally more high risk primary PCI than higher volumes centers. Whilst observed and predicted mortality rates depend on annual center volume, we have found that once adjustment is made for patient case mix the volume-outcome relationship for PCI is not credible. Our analysis suggests that health system wide (re)organization of services in these countries leads to uniformly high quality of care.

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Disclosures

None

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Table 1. Patient and procedural characteristics for all PCI cases categorised by mean annual overall PCI volumes.

	MEAN ANNUAL OVERALL PCI VOLUME CATEGORIES						
	0-199	**200-399**	**400-749**	**750-1499**	**1500-1999**	**⩾2000**	**Total**
Hospital (count)*	5	26	24	23	8	7	93
Annual overall PCI volume (range of hospital means)*	61-155	203-391	403-747	759-1457	1526-1728	2016-2794	61-2794
Overall PCI procedures (count)*	2588	37133	67510	148751	76370	95115	427467
PATIENT CHARACTERISTICS							
Age in years (Mean±SD)*	64.9 +/-11.4	65.4 +/-11.7	65.6 +/-11.8	65.0 +/-11.9	63.9 +/-11.7	64.8 +/-12.0	64.9 +/-11.9
Female*	675 (26.1)	10076 (27.1)	17799 (26.4)	38618 (26)	20243 (26.5)	25861 (27.2)	113272 (26.5)
Diabetes*	251 (9.7)	5890 (15.9)	12589 (18.6)	27218 (18.3)	12606 (16.5)	16779 (17.6)	75333 (17.6)
Hypertension*	1505 (58.2)	17682 (47.6)	31655 (46.9)	80553 (54.2)	37411 (49)	45395 (47.7)	214201 (50.1)
Hypercholesterolemia*	1559 (60.2)	16535 (44.5)	32790 (48.6)	88195 (59.3)	40920 (53.6)	44434 (46.7)	224433 (52.5)
Family history of coronary artery disease*	1037 (40.1)	15351 (41.3)	24273 (36.0)	56444 (37.9)	29401 (38.5)	37260 (39.2)	163766 (38.3)
Current smoking*	415 (16.0)	7889 (21.2)	13271 (19.7)	34834 (23.4)	18864 (24.7)	21979 (23.1)	97252 (22.8)

Previous MI*	505 (19.5)	8147 (21.9)	13298 (19.7)	29954 (20.1)	14034 (18.4)	21241 (22.3)	87179 (20.4)
Previous CVA*	38 (1.5)	1232 (3.3)	2300 (3.4)	5614 (3.8)	2916 (3.8)	3782 (4.0)	15882 (3.7)
Previous PCI*	484 (18.7)	5214 (14.0)	8526 (12.6)	17926 (12.1)	7988 (10.5)	10120 (10.6)	50258 (11.8)
Renal Disease:							
*Creatinine>200 µmol**	19 (0.7)	641 (1.7)	971 (1.4)	2418 (1.6)	964 (1.3)	1037 (1.1)	6050 (1.4)
Acute or chronic*	9 (0.3)	137 (0.4)	666 (1.0)	1108 (0.7)	823 (1.1)	485 (0.5)	3228 (0.8)
PRESENTATION							
Indication:							
Stable*	1240 (47.9)	14238 (38.3)	24816 (36.8)	51230 (34.4)	25310 (33.1)	35310 (37.1)	152144 (35.6)
NSTEMI*	489 (18.9)	19314 (52.0)	28223 (41.8)	56866 (38.2)	30007 (39.3)	32688 (34.4)	167587 (39.2)
STEMI*	73 (2.8)	3110 (8.4)	12057 (17.9)	37169 (25)	18464 (24.2)	23514 (24.7)	94387 (22.1)
Rescue*	578 (22.3)	336 (0.9)	852 (1.3)	2896 (1.9)	2101 (2.8)	1342 (1.4)	8105 (1.9)
Shock*	21 (0.8)	519 (1.4)	1113 (1.6)	2867 (1.9)	1204 (1.6)	1182 (1.2)	6906 (1.6)
Urgency							
Elective*	1380 (53.3)	14240 (38.3)	25419 (37.7)	51401 (34.6)	25527 (33.4)	36665 (38.5)	154632 (36.2)
Urgent*	524 (20.2)	18424 (49.6)	27294 (40.4)	52782 (35.5)	28018 (36.7)	30984 (32.6)	158026 (37)

Emergency*	683 (26.4)	4291 (11.6)	14593 (21.6)	44174 (29.7)	22450 (29.4)	27391 (28.8)	113582 (26.6)
Salvage*	0 (0.0)	33 (0.1)	108 (0.2)	357 (0.2)	217 (0.3)	39 (0.04)	754 (0.2)
PROCEDURAL CHARACTERISTICS							
Multiple vessels attempted*	559 (21.6)	6518 (17.6)	12246 (18.1)	26902 (18.1)	14151 (18.5)	20461 (21.5)	80837 (18.9)
Stent deployed*	2491 (96.3)	34679 (93.4)	63098 (93.5)	137430 (92.4)	70510 (92.3)	85196 (89.6)	393404 (92)
DES deployed*	1835 (70.9)	25939 (69.9)	45183 (66.9)	98385 (66.1)	50995 (66.8)	60777 (63.9)	283114 (66.2)
IVUS use*	31 (1.2)	779 (2.1)	1605 (2.4)	5123 (3.4)	2499 (3.3)	3080 (3.2)	13117 (3.1)
UPLMS(where LMS attempted)*	19 (79.2)	457 (70.4)	1007 (69.5)	3179 (70.1)	1501 (62.7)	2527 (79.5)	8690 (71.1)

*=Significant between-volume category difference at p<0.001

SD=standard deviation; MI=myocardial infarction; CVA=cerebral vascular accident; PCI=percutaneous coronary intervention; NSTEMI=non-ST segment elevation myocardial infarction; STEMI=ST-segment elevation myocardial infarction; DES=drug-eluting stent; IVUS=intravascular ultrasound; (UP)LMS=(unprotected) left main stem

Table 2. Patient and procedural characteristics for primary PCI cases categorised by mean annual overall PCI volumes.

	MEAN ANNUAL OVERALL PCI VOLUME CATEGORIES						
	0-199	**200-399**	**400-749**	**750-1499**	**1500-1999**	**⩾2000**	**Total**
Hospitals (count)*	4	26	23	23	8	7	91
Annual overall PCI volume (range of hospital means)*	142-155	203-391	403-747	759-1457	1526-1728	2016-27941	142-2794
Primary PCI procedures (count)*	69	3075	11993	37058	18386	23441	94022
PATIENT CHARACTERISTICS							
Age in years(Mean± SD)*	65.8 +/-12.7	65.9 +/-13.3	64.1 +/-13.1	63.7+/-13.1	63.0 +/-12.9	63.2 +/-13.1	63.8 +/-13.1
Female*	20 (29.0)	847 (27.5)	3048 (25.4)	9385 (25.3)	4840 (26.3)	6307 (26.9)	24447 (26.0)
Diabetes*	4 (5.8)	365 (11.9)	1547 (12.9)	5019 (13.5)	2218 (12.1)	2939 (12.5)	12092 (12.9)
Hypertension*	27 (39.1)	1047 (34)	4093 (34.1)	15681 (42.3)	6986 (38.0)	8600 (36.7)	36434 (38.8)
Hypercholesterolemia*	21 (30.4)	793 (25.8)	3538 (29.5)	16070 (43.4)	7230 (39.3)	7932 (33.8)	35584 (37.8)
Family history of coronary artery disease*	13 (18.8)	964 (31.3)	3441 (28.7)	11540 (31.1)	5623 (30.6)	7842 (33.5)	29423 (31.3)

Current smoking*	20 (29.0)	946 (30.8)	3870 (32.3)	13570 (36.6)	6597 (35.9)	9146 (39)	34149 (36.3)
Previous MI*	8 (11.6)	356 (11.6)	1113 (9.3)	3644 (9.8)	1854 (10.1)	2428 (10.4)	9403 (10.0)
Previous CVA†	2 (2.9)	82 (2.7)	371 (3.1)	1360 (3.7)	693 (3.8)	789 (3.4)	3297 (3.5)
Previous PCI*	4 (5.8)	222 (7.2)	711 (5.9)	2380 (6.4)	1025 (5.6)	1168 (5.0)	551 (5.9)
Renal Disease*							
*Creatinine>200 µmol**	1 (1.4)	114 (3.7)	121 (1.0)	327 (0.9)	141 (0.8)	127 (0.5)	831 (0.9)
Acute or chronic*	0 (0.0)	11 (0.4)	74 (0.6)	147 (0.4)	73 (0.4)	68 (0.3)	373 (0.4)
PRESENTATION							
Indication STEMI	69 (100)	3075 (100)	11993 (100)	37058 (100)	18386 (100)	23441 (100)	94022 (100)
Shock*	6 (8.7)	258 (8.4)	789 (6.6)	2043 (5.5)	786 (4.3)	870 (3.7)	4752 (5.1)
Urgency:							
Emergency*	69 (100)	3064 (99.6)	11938 (99.5)	36967 (99.8)	18342 (99.8)	23427 (99.9)	93807 (99.8)
Salvage*	0 (0.0)	11 (0.4)	55 (0.5)	91 (0.2)	44 (0.2)	14 (0.1)	215 (0.2)
PROCEDURAL CHARACTERISTICS							

Multiple vessels attempted*	10 (14.5)	359 (11.7)	1122 (9.4)	3052 (8.2)	1825 (9.9)	2340 (10.0)	8708 (9.3)
Stent deployed*	64 (92.8)	2892 (94.0)	11371 (94.8)	34585 (93.3)	17084 (92.9)	21985 (93.8)	87981 (93.6)
DES deployed*	38 (55.1)	1908 (62.0)	7278 (60.7)	22270 (60.1)	11797 (64.2)	13955 (59.5)	57246 (60.9)
IVUS use	0 (0.0)	40 (1.3)	149 (1.2)	552 (1.5)	307 (1.7)	353 (1.5)	1401 (1.5)
UPLMS(where LMS attempted)*	0 (100)	50 (98.0)	162 (88.0)	482 (66.7)	228 (70.2)	361 (81.1)	1283 (74.2)

*=Significant between-volume category difference at $p<0.001$,

†=Significant between-volume category difference at $p<0.05$

Table 3. Bayes' factors for stratified analysis for all PCI cases and primary PCI cases categorised by mean annual overall PCI volumes

	MEAN ANNUAL OVERALL PCI VOLUME CATEGORIES					
	0-199	**200-399**	**400-749**	**750-1499**	**1500-1999**	**⩾2000**
All PCI	0.92	0.58	2.40	4.30	0.18	2.28
Primary PCI	1.78	4.68	5.40	5.44	0.70	3.49

Figure Titles/Legends

Figure 1. Data flow from sampling frame to analytical cohort.

Figure 2. Observed and predicted mortality and relative risk of mortality by mean annual center volume: All PCI cases

Legend:

Scatterpoints: Hospital-level estimates (with 95% CI bars for relative risk)

Colored panes: Linear estimates of mortality risk for each volume band, with 95% CI

Figure 3. Observed and predicted mortality and relative risk of mortality by mean annual center volume: Primary PCI cases

Legend:

Scatterpoints: Hospital-level estimates (with 95% CI bars for relative risk)

Colored panes: Linear estimates of mortality risk for each volume band, with 95% CI