# INTERVENTIONAL CARDIOLOGY AND SURGERY

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Hospital volume of throughput and periprocedural and medium-term adverse events after percutaneous coronary intervention: retrospective cohort study of all 17 417 procedures undertaken in Scotland, 1997–2003

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**Objective:** To determine whether percutaneous coronary intervention (PCI) hospital volume of throughput is associated with periprocedural and medium-term events, and whether any associations are independent of differences in case mix.

**Design:** Retrospective cohort study of all PCIs undertaken in Scottish National Health Service hospitals over a six-year period. **Methods:** All PCIs in Scotland during 1997–2003 were examined. Linkage to administrative databases

identified events over two years' follow up. The risk of events by hospital volume at 30 days and two years

Results: Of the 17 417 PCls, 4900 (28%) were in low-volume hospitals and 3242 (19%) in high-volume

hospitals. After adjustment for case mix, there were no significant differences in risk of death or myocardial infarction. Patients treated in high-volume hospitals were less likely to require emergency

surgery (adjusted odds ratio 0.18, 95% confidence interval (CI) 0.07 to 0.54, p = 0.002). Over two

years, patients in high-volume hospitals were less likely to undergo surgery (adjusted hazard ratio 0.52, 95% Cl 0.35 to 0.75, p = 0.001), but this was offset by an increased likelihood of further PCI. There was

was compared by using logistic regression and Cox proportional hazards models.

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Accepted 11 May 2006 Published Online First 18 May 2006 no net difference in coronary revascularisation or in overall events. **Conclusion:** Death and myocardial infarction were infrequent complications of PCI and did not differ significantly by volume. Emergency surgery was less common in high-volume hospitals. Over two years, patients treated in high-volume centres were as likely to undergo some form of revascularisation but less likely to undergo surgery.

hen first introduced more than 20 years ago, percutaneous coronary intervention (PCI) was undertaken in only a few hospitals, with on-site cardiac surgical cover in case patients had coronary occlusion or dissection as a complication of PCI. With the development of coronary stents, the need for emergency referral for surgery fell dramatically, and PCI is now undertaken in an increasing number of sites.

As with all interventions there is a balance to be struck. In low-volume centres, operators may find it more difficult to maintain their level of expertise and keep abreast of new advances. However, the likelihood has been well established that patients undergoing any procedure, including revascularisation, in part depends on their geographical distance from the intervention centre.<sup>1</sup> Restricting interventions to fewer high-volume centres therefore inevitably leads to geographical inequalities in access to health care.

It has been suggested that PCIs should be undertaken only in hospitals performing a minimum of 400 PCIs per annum.<sup>2</sup> PCI volume of throughput has even been proposed as a generic marker of quality of care within hospitals.<sup>3</sup> However, published studies have produced conflicting results on whether periprocedural complications are less likely to occur in higher-volume institutions.<sup>4–11</sup> Furthermore, we are unaware of any studies published to date examining whether hospital volumes of throughput are associated with mediumterm outcomes after PCI. We undertook a retrospective cohort study of all PCIs performed in Scottish National Health Service hospitals over a six-year period to determine whether hospital volume of throughput was associated with periprocedural and medium-term events, and whether any associations were independent of differences in case mix.

## **METHODS**

#### Data sources and study population

The Scottish Coronary Revascularisation Register collects detailed data prospectively on all patients undergoing PCI in all Scottish NHS hospitals. The Register does not cover private hospitals. However, in Scotland, the vast majority of PCIs are performed in NHS hospitals. The information collected includes demographic data, medical history, severity of cardiac disease, co-morbidities and procedural details. The Scottish Coronary Revascularisation Register was used to identify all PCIs performed between April 1997 and March 2003 inclusive.

The Scottish Morbidity Record (SMR) collects administrative data routinely on all admissions to all Scottish hospitals, both NHS and private. The information collected includes diagnoses and operative procedures undertaken.

Abbreviations: CABG, coronary artery bypass grafting; HR, hazard ratio; OR, odds ratio; PCI, percutaneous coronary intervention; SMR, Scottish Morbidity Record

These are classified according to the *International classification of diseases*, 10th revision and Office for Population Censuses and Surveys, 4th revision codes, respectively. The SMR database undergoes regular quality assurance checks and has been shown to be more than 95% accurate in recording the main procedure undertaken.<sup>12</sup> The General Registrar's Office collates information from death certificates on all deaths in Scotland, irrespective of whether the person has died in the community or in hospital. The Scottish Coronary Revascularisation Register was linked to the SMR and General Registrar's Office databases, thereby providing information on deaths, myocardial infarctions and procedures over a minimum of two years' follow up.

#### **Statistical analyses**

Within each financial year (April–March), hospitals were categorised into low (< 400), medium (400–750) and high (> 750) volume according to the number of PCIs performed that year. These cut offs are consistent with practice recommendations and the definitions applied in other studies.<sup>2 6 13-15</sup> All case-mix variables were treated as categorical. Age was classified into four age groups, and socio-economic deprivation scores were grouped into quintiles. The patient characteristics in the three hospital-volume categories were then compared by  $\chi^2$  tests for binary and non-ordinal categorical data and by  $\chi^2$  tests for trend for ordinal data.

The individual outcomes studied were all-cause death, fatal or non-fatal myocardial infarction, repeat PCI, coronary artery bypass grafting (CABG) and any coronary revascularisation (PCI or CABG). We also studied the standard periprocedural composite end point of major adverse cardiovascular events, defined as death, myocardial infarction or surgery. We studied the periprocedural (30-day) and medium-term (two-year) risk of each of these outcomes separately.

Univariate and multivariate binary logistic regression models were used to determine whether volume of throughput was associated with risk of adverse events at 30 days and whether associations were independent of differences in case mix. Kaplan–Meier product-limit estimators were used to determine the crude cumulative risk of each outcome over two years, and log rank tests were used to determine whether the risk varied by volume of throughput. We used multivariate Cox proportional hazards models to determine whether the associations between volume and medium-term outcomes were independent of differences in case mix. Time from procedure in days was used as the time variable. We forced into the multivariate models all of the patient characteristics that varied significantly by hospital volume of throughput.

Volume of throughput increased in all sites over the period studied. Outcomes may plausibly also have changed over time due to technical or therapeutic developments unrelated to changes in case mix. For example, the need for repeat intervention may have fallen due to increased use of coronary stents. To overcome potential confounding due to time trends, follow up was truncated at two years for all procedures and year of procedure was included as a covariate in the multivariate analyses.

The p values were two sided for all hypothesis tests, and we set significance at p < 0.05. We report p values without adjustment for multiple testing. Goodness of fit was assessed by the likelihood ratio  $\chi^2$  test. All statistical analyses were performed with the SPSS software package V.13.0 (SPSS Inc, Chicago, Illinois, USA).

#### Definitions

Emergency procedures were defined as those undertaken, by necessity, within 24 h of referral and included primary and

rescue PCI. Urgent procedures were defined as those undertaken on hospitalised patients who were clinically unfit to be discharged home between referral and PCI. Normal left ventricular function was defined as an ejection fraction of at least 50% and severe left ventricular impairment as an ejection fraction of less than 30%. A former smoker was defined as someone who had quit smoking at least one month before the procedure. Obesity was defined as a body mass index (kg/m<sup>2</sup>) of 30 or greater. Hypertension was defined as a systolic blood pressure of at least 140 mm Hg, a diastolic blood pressure of at least 90 mm Hg or treatment with a hypertension drug. Hyperlipidaemia was defined as total cholesterol of at least 5.2 mmol/l or treatment with a lipid-lowering drug. Postcode of residence was used to derive socioeconomic deprivation scores. These were based on 2001 census data on car ownership, unemployment, overcrowding and occupational social class within postcode sectors.<sup>16</sup> Use of troponin assays after PCI has increased over time and varies between hospitals. Therefore, to ensure consistency and avoid bias, post-PCI myocardial infarction was defined on the basis of symptoms and ECG findings, rather than on cardiospecific markers.

## RESULTS

Between April 1997 and March 2003, 17 417 PCIs were undertaken in six Scottish hospitals. Of the 36 hospital years, 13 were classified as low volume, 19 as medium volume, and four as high volume. There was a general increase in hospital volumes of throughput over the period studied ( $\chi^2$  trend, p< 0.001). Overall, 4900 (28%) procedures were undertaken in low-volume hospitals and 3242 (19%) in high-volume hospitals.

#### **Patient characteristics**

Overall, patients had a median age of 61 years (interquartile range 53–68 years), and 12 078 (69%) were men. Only 786 (5%) PCIs were primary or rescue procedures. The most frequent indication was chronic stable angina, which accounted for 46% of procedures. A total of 7331 (45%) patients had multivessel disease or left main stem stenosis, and 6617 (42%) had evidence of impaired left ventricular function. Overall, 4025 (26%) had previously undergone coronary revascularisation. In total, 4423 (28%) patients were current smokers and 5054 (34%) were former smokers. Overall, 3270 (27%) were obese, 1906 (12%) had diabetes mellitus, 10 501 (70%) had hyperlipidaemia and 5786 (38%) had hypertension.

Patient characteristics differed significantly according to hospital volume of throughput. In comparison with patients treated in low-volume hospitals, patients treated in high-volume hospitals were more likely to be older than 75 years (9% v 5%,  $\chi^2$  trend, p < 0.001), more likely to be in the lowest socioeconomic quintile (24% v 17%,  $\chi^2$  trend, p < 0.001), more likely to be obese (29% v 23%,  $\chi^2$  trend, p < 0.001) and more likely to be obese (29% v 23%,  $\chi^2$  trend, p < 0.01) and more likely to have left ventricular impairment (53% v 34%,  $\chi^2$  trend, p < 0.001), diabetes mellitus (14% v 10%,  $\chi^2$  trend, p < 0.001) and hyperlipidaemia (74% v 67%,  $\chi^2$  trend, p < 0.001) (table 1). In contrast, some of their risk characteristics were lower. Patients treated in high-volume hospitals were less likely to undergo emergency PCI (9% v 15%,  $\chi^2$  trend, p = 0.006) and were less likely to have multivessel disease (41% v 50%,  $\chi^2$  trend, p < 0.001).

#### Periprocedural outcomes

In comparison with patients in high-volume hospitals, more of the patients who underwent PCI in low-volume hospitals had a myocardial infarction (3.2%  $\nu$  1.7%,  $\chi^2$  trend, p < 0.001) or required cardiac surgery within 30 days

Age group (years) <56 56-65 66-75 >75 Missing Sex Male Female Missing Urgency Emergency Urgent Elective Missing Indication Primary Rescue Unstable angina Stable angina Other Missing Number of arteries with

0 2 3

None Mild/moderate Severe Missing Previous coronary reva

No Yes Missing Diabetes mellitus No Yes Missing Smoking status Non-smoker Current smoker Former smoker Missing Obesity No Yes Missing Hypertension No Yes Missing Hyperlipidaemia

No

Yes

3

Missing

Missing

Deprivation quintile (most affluent)

5 (most deprived)

Left main stem Missing Left ventricular impairm

| ristics of patients undergoing percutaneous coronary intervention<br>al volume of throughput, Scotland, 1997–2003 |  |   |  |          |  |
|---|--|---|--|----------|--|
|   | Low volume (<400<br>PCls pa) n=3756                                | Medium volume (400–750<br>PCIs pa) n = 10 419                         | High volume (>750<br>PCIs pa) n=3242                               | p Value* |  |
|   | 1259 (34%)<br>1376 (37%)<br>942 (25%)<br>179 (5%)<br>0             | 3426 (33%)<br>3594 (35%)<br>2730 (26%)<br>669 (6%)<br>0               | 925 (29%)<br>1125 (35%)<br>895 (28%)<br>297 (9%)<br>0              | <0.001   |  |
|   | 2554 (68%)<br>1202 (32%)<br>0                                      | 7202 (69%)<br>3212 (31%)<br>0   | 2322 (72%)<br>920 (28%)<br>0                                       | 0.004    |  |
|   | 567 (15%)<br>1285 (34%)<br>1904 (51%)<br>0                         | 1120 (11%)<br>3482 (33%)<br>5816 (56%)<br>1                           | 288 (9%)<br>1387 (43%)<br>1567 (48%)<br>0                          | 0.006    |  |
|   | 86 (2%)<br>223 (6%)<br>1412 (39%)<br>1536 (42%)<br>405 (11%)<br>94 | 111 (1%)<br>193 (2%)<br>3916 (38%)<br>4820 (47%)<br>1212 (12%)<br>167 | 48 (2%)<br>125 (4%)<br>1379 (43%)<br>1543 (48%)<br>147 (5%)<br>0   | <0.001   |  |
| 1 =   | 28 (1%)<br>1690 (49%)<br>1126 (33%)<br>509 (15%)<br>79 (2%)<br>324 | 431 (5%)<br>4751 (50%)<br>2650 (28%)<br>1399 (15%)<br>261 (3%)<br>927 | 307 (10%)<br>1603 (50%)<br>879 (27%)<br>338 (11%)<br>90 (3%)<br>25 | <0.001   |  |
| en  | f<br>2143 (66%)<br>1004 (31%)<br>89 (3%)<br>520                    | 5384 (58%)<br>3680 (40%)<br>183 (2%)<br>1172                          | 1525 (48%)<br>1610 (51%)<br>51 (2%)<br>56                          | <0.001   |  |
| scı   | Jarisation<br>2707 (80%)<br>697 (21%)<br>352                       | 6774 (73%)<br>2592 (27%)<br>1153                                      | 2263 (76%)<br>736 (25%)<br>243                                     | <0.001   |  |
|   | 3116 (90%)<br>337 (10%)<br>303                                     | 8095 (88%)<br>1154 (13%)<br>1170                                      | 2549 (86%)<br>415 (14%)<br>278                                     | <0.001   |  |
|   | 1089 (33%)<br>997 (30%)<br>1238 (37%)<br>432                       | 3323 (38%)<br>2473 (28%)<br>3037 (34%)<br>1586                        | 1164 (40%)<br>953 (33%)<br>779 (27%)<br>346                        | <0.001   |  |
|   | 2003 (77%)<br>609 (23%)<br>1144                                    | 5331 (73%)<br>1983 (27%)<br>3105                                      | 1644 (71%)<br>678 (29%)<br>920                                     | <0.001   |  |
|   | 2272 (66%)<br>1161 (34%)<br>323                                    | 5571 (63%)<br>3318 (37%)<br>1530                                      | 1610 (55%)<br>1307 (45%)<br>325                                    | <0.001   |  |

Table 1 Characte according to hospi

 $\chi^2$  test for trend for ordinal variables (age group, urgency, left ventricular impairment and deprivation quintile),  $\chi^2$  test for all other variables.

2701 (31%)

6129 (69%)

1626 (16%)

1798 (17%)

2094 (20%)

2181 (21%)

2657 (26%)

63

1589

pa, per annum; PCI, percutaneous coronary intervention.

1114 (33%)

2283 (67%)

821 (23%)

706 (20%)

759 (21%)

681 (19%)

610 (17%)

179

359

(1.8%  $\nu$  0.4%,  $\chi^2$  trend, p < 0.001) (table 2). The trend in case fatality did not reach significance. The overall risk of a major adverse cardiovascular event was 5.3% in a low-volume hospital compared with 2.5% in a high-volume hospital  $(\chi^2 \text{ trend, } p < 0.001).$ 

Adjustment for case mix and year attenuated the association between volume of throughput and risk of periprocedural myocardial infarction, which was no longer significant (adjusted odds ratio (OR) 0.73, 95% confidence interval (CI) 0.36 to 1.46, p = 0.372) (table 3). However, the association

< 0.001

< 0.001

723 (26%)

2089 (74%)

594 (19%)

518 (16%)

608 (19%)

719 (22%)

774 (24%)

29

430

Table 2Frequency of major adverse cardiovascular events within 30 days ofpercutaneous coronary intervention according to hospital volume of throughput, Scotland,1997–2003

|                       | Low volume<br>(<400 PCIs pa)<br>n = 3756 | Medium volume<br>(400–750 PCIs pa)<br>n = 10419 | High volume<br>(>750 PCIs pa)<br>n=3242 | p Value* |
|-----------------------|--|---|---|----------|
| All-cause death       | 72 (1.9)                                 | 144 (1.4)                                       | 46 (1.4)                                | 0.073    |
| Myocardial infarction | 122 (3.2)                                | 225 (2.2)                                       | 54 (1.7)                                | < 0.001  |
| CÁBG                  | 67 (1.8)                                 | 89 (0.9)  | 12 (0.4)                                | < 0.001  |
| Any MACE              | 199 (5.3)                                | 343 (3.3)                                       | 80 (2.5)                                | < 0.001  |

PCI, percutaneous coronary intervention.

with emergency surgery remained significant (adjusted OR 0.18, 95% CI 0.07 to 0.54, p = 0.002). Also, the risk of any major adverse cardiovascular event was lower in high-volume hospitals (adjusted OR 0.46, 95% CI 0.27 to 0.80, p = 0.006).

#### Medium-term outcomes

On Kaplan–Meier analysis, there was no obvious trend by volume of throughput in the cumulative risk of death or myocardial infarction over two years' follow up (table 4). However, patients who underwent PCI in high-volume hospitals were less likely to have proceeded to CABG (3.8% v 8.8%, linear log rank, p < 0.001). After adjustment for case mix and year in the multivariate Cox model, the lower risk of surgery persisted (adjusted hazard ratio (HR) 0.52, 95% CI 0.35 to 0.75, p = 0.001) (table 5).

On univariate analysis there was no significant difference in the likelihood of undergoing further PCI. However, adjustment for case mix and year showed that those attending high-volume centres were more likely to undergo a second PCI (adjusted HR 0.52, 95% CI 0.35 to 0.75, p = 0.001). As a result, the net risk of coronary revascularisation and any event over two years was comparable in low and high-volume hospitals.

#### DISCUSSION

The overall number of PCIs performed has increased steadily since the procedure was first introduced in the late 1970s. This increase has contributed to the rising cost of treating coronary heart disease, which stands at £3500 million per annum in the UK.<sup>17 18</sup> The expansion in PCI is due, partly, to a reduced threshold for intervention, resulting in PCI being performed on patients with less severe coronary disease who would not previously have undergone coronary revascularisation. In addition, PCI is now being used to treat patients with more severe disease who previously would have been referred for surgery.

In addition to an increase in the overall number of PCIs performed, the number of hospitals in which PCI is undertaken has increased.<sup>19</sup> When first introduced, PCI was undertaken in only a few hospitals with on-site cardiac surgical cover in case patients had acute occlusion or dissection as a complication of the procedure. After the development of coronary stents, the need for emergency referral for surgery fell dramatically, and PCI is now undertaken in an increasing number of sites.

Restricting PCI to fewer sites ensures sufficient numbers are undertaken to maintain expertise, keep abreast of new developments, and provide appropriate support and infrastructure. It has been suggested that centralisation of PCI services may also reduce procedural costs.<sup>20</sup> However, these benefits of centralisation must be balanced against a potential adverse effect on access. The likelihood of patients undergoing coronary revascularisation has been shown in part to depend on their geographical distance from the intervention centre.<sup>1</sup> Therefore, restricting PCI to fewer highvolume centres is likely to lead to geographical inequalities in access.

**Table 3** Binary logistic regression analysis of the risk of major adverse cardiovascularevents within 30 days of percutaneous coronary intervention, Scotland, 1997–2003

|                          | Crude               | Crude   |                     | Adjusted for case mix* and year |  |
|--------------------------|---------------------|---------|---------------------|---------------------------------|--|
|                          | OR (95% CI)         | p Value | OR (95% CI)         | p Value                         |  |
| All-cause death          |                     |         |                     |                                 |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |
| Medium volume            | 0.72 (0.54 to 0.95) | 0.022   | 1.25 (0.75 to 2.06) | 0.390                           |  |
| High volume              | 0.74 (0.51 to 1.07) | 0.108   | 0.88 (0.34 to 2.25) | 0.783                           |  |
| Acute myocardial infarct | ion                 |         |                     |                                 |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |
| Medium volume            | 0.66 (0.53 to 0.82) | < 0.001 | 0.90 (0.64 to 1.27) | 0.561                           |  |
| High volume              | 0.51 (0.37 to 0.70) | < 0.001 | 0.73 (0.36 to 1.46) | 0.372                           |  |
| Coronary artery bypass   | grafting            |         |                     |                                 |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |
| Medium volume            | 0.47 (0.35 to 0.65) | < 0.001 | 0.46 (0.29 to 0.73) | 0.001                           |  |
| High volume              | 0.21 (0.11 to 0.38) | < 0.001 | 0.18 (0.07 to 0.54) | 0.002                           |  |
| Any MACE                 |                     |         |                     |                                 |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |
| Medium volume            | 0.61 (0.51 to 0.73) | < 0.001 | 0.71 (0.54 to 0.93) | 0.013                           |  |
| High volume              | 0.45 (0.35 to 0.59) | < 0.001 | 0.46 (0.27 to 0.80) | 0.006                           |  |

\*Model adjusted for age, sex, urgency, indication, number of stenosed arteries, left ventricular impairment, previous coronary revascularisation, diabetes, smoking status, obesity, hypertension, hyperlipidaemia and deprivation quintile.

MACE, major adverse cardiovascular event; OR, odds ratio.

| Table 4                | Cumulative tr      | requency of majo  | or cardiovascu  | lar events two  | years atter          |
|------------------------|--------------------|-------------------|-----------------|-----------------|----------------------|
| percutaneo<br>1997–200 | ous coronary<br>)3 | intervention acco | ording to hospi | tal volume of t | hroughput, Scotland, |

|   | Low volume<br>(<400 PCIs pa)<br>n=3756 | Medium volume<br>(400–750 PCIs pa)<br>n = 10419 | High volume<br>(>750 PCIs pa)<br>n=3242 | p Value* |
|---|--|---|---|----------|
| All-cause death   | 5.3 (0.4)                              | 5.2 (0.2)                                       | 6.1 (0.5)                               | 0.322    |
| Acute myocardial infarction   | 6.3 (0.4)                              | 5.5 (0.2)                                       | 5.9 (0.5)                               | 0.113    |
| CABG  | 8.8 (0.5)                              | 5.6 (0.2)                                       | 3.8 (0.4)                               | < 0.001  |
| PCI   | 12.9 (0.6)                             | 15.3 (0.4)                                      | 13.5 (0.8)                              | < 0.001  |
| Coronary revascularisation  | 20.4 (0.7)                             | 16.7 (0.8)                                      | 16.7 (0.8)                              | < 0.001  |
| Any event   | 26.1 (0.7)                             | 25.3 (0.4)                                      | 23.2 (0.9)                              | 0.001    |
| Data are percentage (SE).<br>*Log rank test.<br>CABG, coronary artery bypas | s grafting; pa, per ar                 | nnum; PCI percutaneous c                        | oronary intervention.                   |          |

The risk of dying as a complication of PCI is low and we did not find any significant differences by hospital volume of throughput. Univariate analysis found an increased risk of periprocedural myocardial infarction in low-volume hospitals but after adjustment for case mix the association was attenuated and no longer significant. Low-volume hospitals are less likely to have on-site surgical facilities. However, patients undergoing PCI in low-volume hospitals had a significantly higher risk of having emergency surgery. This may reflect less technical expertise or may simply reflect poorer access to and use of devices and adjunctive treatments shown to reduce the risk of acute occlusions or dissections. Over the period studied, the percentage of PCIs involving use of coronary stents was 86% in high-volume centres compared with 65% in low-volume centres ( $\chi^2$  trend, p < 0.001). However, some of this difference reflected a general increase in stent use over time. When we included use of coronary stents as a covariate in the model, in addition to year, the results were unchanged. Patients undergoing PCI in low-volume hospitals were still at increased risk of surgery both at 30 days (adjusted OR 0.19, 95% CI 0.06 to 0.54, p = 0.002) and over two years (adjusted HR, 0.51, 95% CI 0.34 to 0.75, p = 0.001). Over the period studied, only 19 (0.1%) patients received drug-eluting stents.

Over two years' follow up, the overall likelihood of undergoing coronary revascularisation was similar in highand low-volume hospitals. However, the type of revascularisation procedure differed significantly. Patients who were initially treated in low-volume centres were significantly more likely to undergo surgery and significantly less likely to undergo another percutaneous intervention. These differences may simply reflect differences in access to percutaneous interventions. As the overall rates of coronary revascularisation were comparable, the differences are unlikely to reflect differences in the completeness of revascularisation achieved during the index procedure.

One limitation of our study was that we did not have complete follow-up information on patients who emigrated

|                          | Crude               | Crude   |                     | Adjusted for case mix* and year |  |  |
|--------------------------|---------------------|---------|---------------------|---------------------------------|--|--|
|                          | HR (95% CI)         | p Value | HR (95% CI)         | p Value                         |  |  |
| All-cause death          |                     |         |                     |                                 |  |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |  |
| Medium volume            | 0.97 (0.82 to 1.15) | 0.723   | 1.05 (0.83 to 1.33) | 0.681                           |  |  |
| High volume              | 1.11 (0.90 to 1.37) | 0.319   | 0.85 (0.57 to 1.26) | 0.414                           |  |  |
| Acute myocardial infarct | ion                 |         |                     |                                 |  |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |  |
| Medium volume            | 0.85 (0.73 to 0.99) | 0.041   | 1.02 (0.82 to 1.27) | 0.872                           |  |  |
| High volume              | 0.86 (0.70 to 1.06) | 0.150   | 0.85 (0.58 to 1.27) | 0.431                           |  |  |
| Coronary artery bypass   | grafting            |         |                     |                                 |  |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |  |
| Medium volume            | 0.63 (0.55 to 0.72) | < 0.001 | 0.62 (0.51 to 0.76) | < 0.001                         |  |  |
| High volume              | 0.45 (0.37 to 0.56) | < 0.001 | 0.52 (0.35 to 0.75) | 0.001                           |  |  |
| Percutaneous coronary in | ntervention         |         |                     |                                 |  |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |  |
| Medium volume            | 1.22 (1.10 to 1.35) | < 0.001 | 1.49 (1.29 to 1.73) | < 0.001                         |  |  |
| High volume              | 1.00 (0.87 to 1.15) | 0.996   | 1.55 (1.20 to 1.99) | 0.001                           |  |  |
| Coronary revascularisati | on                  |         |                     |                                 |  |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |  |
| Medium volume            | 0.98 (0.90 to 1.06) | 0.599   | 1.11 (0.98 to 1.25) | 0.104                           |  |  |
| High volume              | 0.79 (0.70 to 0.88) | < 0.001 | 1.04 (0.84 to 1.29) | 0.729                           |  |  |
| Any event                |                     |         |                     |                                 |  |  |
| Low volume               | 1.00                |         | 1.00                |                                 |  |  |
| Medium volume            | 0.96 (0.89 to 1.03) | 0.226   | 1.07 (0.96 to 1.19) | 0.219                           |  |  |
| High volume              | 0.84 (0.76 to 0.92) | < 0.001 | 1.01 (0.84 to 1.22) | 0.918                           |  |  |

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\*Model adjusted for age, sex, urgency, indication, number of stenosed arteries, left ventricular impairment, previous coronary revascularisation, diabetes, smoking status, obesity, hypertension, hyperlipidaemia and deprivation quintile. HR. hazard ratio. out of Scotland within two years of their index procedure. However, Scotland is a relatively stable population so we expect that the numbers would be small. Furthermore, a systematic bias is unlikely. We adjusted for differences in case mix between high- and low-volume centres and for potential confounding due to underlying temporal trends. Statistical adjustment can never be as robust as randomisation. However, it would be difficult, in practice, to conduct a randomised trial to determine the effect of hospital volume. We were unable to distinguish between target vessel revascularisation that was performed because of restenosis of the same vessel and revascularisation of a different vessel due to either incomplete revascularisation during the index procedure or underlying disease progression. Adjustment for the number of arteries with significant stenoses at baseline would, in part, address any differences in disease progression due to differences in case mix at baseline.

An important strength of our study is the ability to report both periprocedural and medium-term outcomes. In addition, we were able to examine differences in individual events, such as death, myocardial infarction and surgery, rather than merely examining the composite end point of major adverse cardiovascular events often reported. This enabled us to ascertain that the higher risk of periprocedural events in low-volume hospitals could be attributed to a higher risk of emergency surgery. It also enabled us to show that, although there was no overall difference in events over two years, the type of revascularisation used after the index procedure differed significantly, with patients initially treated in low-volume hospitals having a lower likelihood of undergoing a repeat PCI but a greater likelihood of undergoing surgery.

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