**Access site and outcomes for unprotected left main stem PCI: an analysis of the British Cardiovascular Intervention Society database**

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**Brief title:** Access site choice for left main PCI

**Conflicts of interest:** No conflicts of interest for any authors, no relevant relationship with industry

**Financial Support:** None

**Word count:** 4998

**Abstract**

**Background:** Data on arterial access site for left main stem percutaneous intervention (LMS-PCI) are poorly defined. **Objectives:** Using the British Cardiovascular Intervention Society PCI database, temporal trends, predictors and outcomes of radial (RA) vs. femoral access (FA) for unprotected LMS-PCI were studied. **Methods:** Data were analysed from 19,482 LMS-PCI procedures performed in England and Wales between 2007 and 2014. Multivariate logistic regression was used to identify predictors of access site choice and its association with outcomes. **Results:** The frequency of FA use fell from 77.7% in 2007 to 31.7% in 2014 (p<0.001 for trend). In the most contemporary study years (2012-14), the strongest associates of FA use for unprotected LMS-PCI were renal disease, PCI for restenosis, chronic total occlusion intervention and female sex. Use of intravascular imaging and chronic anticoagulation were associated with a higher likelihood of the RA use. Complexity of the PCI procedure in the RA cohort increased significantly during the study period. Length of stay was shorter (2.6±9.2 vs. 3.6±9.0, p<0.001) and same day discharge greater (43.0% vs. 26.6%, p<0.001) with RA use. After propensity matching, RA use was associated with significant reductions in in-hospital events including access site arterial complications, major bleeding, and major adverse cardiovascular events. Conversion to RA for LMS-PCI was associated with similar reductions in the whole patient cohort. RA use was not associated with lower 12-month mortality. **Conclusions:** In contemporary practice, the radial artery is the predominant access site for unprotected LMS-PCI, and its use is associated with shorter length of stay, less vascular complications, and less major bleeding than femoral access.

**Condensed abstract**

Using the British Cardiovascular Intervention Society database, temporal trends, predictors and outcomes of radial vs. femoral access for unprotected LMS-PCI were studied. In 19,482 LMS-PCI procedures performed in England and Wales between 2007 and 2014, femoral artery use fell from 77.7% in 2007 to 31.7%. In the most contemporary study years (2012-14), the strongest associates of FA use for unprotected LMS-PCI were renal disease, PCI for restenosis, chronic total occlusion intervention and female sex. After propensity score adjustment, FA use was associated with an excess of access site arterial complications, in-hospital major bleeding, and in-hospital major adverse cardiovascular events,.

**Keywords** Access site choice, left main artery, percutaneous coronary intervention, national database, access site complications, bleeding

**List of abbreviation**

BCIS - British Cardiovascular Intervention Society

CABG – coronary artery bypass surgery

FA - femoral access

LAD – left anterior descending

LMS - left main stem percutaneous intervention

MACCE - major adverse cardiac or cerebrovascular events

MI – myocardial infarction

NYHA – New York Heart Association

PCI - percutaneous coronary intervention

RA – radial access

**Introduction**

Radial arterial access has become the dominant access site in many countries for percutaneous coronary intervention (PCI).(1-2) Data demonstrating less access site complications, an improvement in patient experience, a reduction in length of stay, and a reduction in mortality in certain sub-groups compared to femoral access has, in part, driven this major change is practice.(3-4) There remains a significant variation in radial rates by country, centre and operator, but many centers and operators now perform over 90% of procedures using radial access.(5-7) However, certain complex case sub-groups may still be undertaken using femoral arterial access particularly where larger lumen catheters or dual arterial access is required. For example, data derived from the British Cardiovascular Intervention Society (BCIS) National PCI Audit demonstrates that the femoral artery remains the predominant access site in patients undergoing PCI with a previous history of CABG or where the target vessel has a chronic total occlusion.(8-9)

Although the predictors and outcomes of radial versus femoral access are well defined for unselected PCI procedures and certain sub-groups, there are few data for patients undergoing left main stem percutaneous coronary intervention (LMS-PCI) despite recent upgrades in the guidelines as to its appropriateness.(10) Indeed, of all the randomised trials in this area, only the Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease (EXCEL) trial reported any data on access site, with 26.9% of procedures being performed using radial access.(11) Even in the larger LMS-PCI registries, limited data have been published on access site, with no comparative analyses of radial versus femoral access yet performed. Furthermore, there have been no prior analyses focusing on access site practice in LMS PCI from a national perspective. There are several unanswered questions regarding PCI of the LMS using radial access including the feasibility of this access route, procedural success rates, and patient outcomes compared with femoral access. The aim of the present study was to address these questions by using the BCIS National PCI Audit data.

**Methods**

*Study design and participants*

We analysed data from all patients undergoing LMS-PCI in England and Wales between January 2007 and December 2014. The study focusses on patients undergoing unprotected LMS-PCI although data is presented in supplementary files on protected LMS-PCI. Participants with missing information on access site or target vessel were excluded. Additionally, due to its influence on access site choice, patients presenting with cardiogenic shock were also excluded.

*Study setting and sources of data*

Data on PCI practice from the BCIS dataset which records 113 clinical, procedural and outcomes variables with approximately 100,000 new records currently added each year. Entry of all PCI procedures by UK interventional operators is mandated as part of their professional revalidation. The accuracy of and quality of the BCIS dataset has previously been ascertained.(12) The participants of the database are tracked by linkage with life status information held by the Office of National Statistics using each patient’s unique NHS number.

*Study definitions*

Using the BCIS dataset, patients were categorised into either radial or femoral access during LMS-PCI. Study definitions were used as in the BCIS database. Pre- or post-PCI disease severity was defined as a stenosis ≥70% in the case of the LAD, circumflex or right coronary arteries, or ≥50% in the case of the left main artery. Intravascular imaging was a combination of intravascular ultrasound and optical coherence tomography. An access site complication is defined as either a false aneurysm, haemorrhage (without haematoma), haemorrhage with delayed discharge, retroperitoneal haematoma, arterial dissection, or any access site complication requiring surgical repair. In-hospital major bleeding was defined as either gastrointestinal bleed, intra-cerebral bleed, retroperitoneal haematoma, blood or platelet transfusion, access site haemorrhage, or an arterial access site complication requiring surgery. In-hospital major adverse cardiac or cerebrovascular events (MACCE) were defined as a combination death, stroke, or myocardial infarction (or re-infarction, depending on indication) after PCI.

*Data analyses*

All study years (2007-2014) are presented to study temporal changes in femoral access site, and protected vs. unprotected LMS during LMS-PCI. We also investigated if there was a trend over time of radial access adoption in different sub-groups. This was done using a linear regression model and testing for the slope of the regression line. The trend over time for different patient sub-groups was analysed by fitting a linear regression model with time, access type and an interaction term between time and access type. An annualised analysis was also performed focusing on the radial cohort to examine temporal changes in case complexity. Included in this analysis was vessels treated, number of stents used, and use of imaging, rotational atherectomy, micro-catheters or penetration catheters.

For the purposes of examining the predictors of access site for LMS-PCI, analysis was restricted to the final three years of data (2012-2014), firstly to encompass more contemporary interventional practice including minimal changes in access choice , and, secondly, because for these years operator level data were available using tracked GMC numbers. We plotted individual operator and centre volumes and analysed the relationship using linear regression. We then examined the baseline characteristics of participants by access site. We tested for associations between each categorical variable and access site using a Chi-squared test, and for continuous variables we used one-way analysis of variance. We then performed an analysis of the predictors of access site in 2012-2014 using multivariate logistic regression to investigate the influence of baseline and procedural characteristics variables that have the potential for being included in the linear component of a proportional hazard model. Covariates included in the model were age, gender, NYHA class, previous MI, previous CABG, previous PCI, diabetes, BMI, LV function, presentation type, history of hypertension or renal failure, peripheral vascular disease, Q wave on ECG, chronic anticoagulation, chronic total occlusion (CTO) attempted, restenosis indication, rotational atherectomy use, mechanical LV support, left main protection status, tertiles of centre volume, and tertiles of operator volume. To correct for missing values, we first imputed missing data on baseline covariates using multiple imputations with chained equations to adjust for missing data. We then ran a stepwise forward selection with a proportional hazard model with p<0.02 as entry criteria.

For clinical outcomes we initially calculated the crude rates by access site. To assess the impact of an access site switch over time for LMS-PCI on the whole population of patients undergoing LMS-PCI, we also calculated total clinical events by year for both cohorts combined. Individual logistic regressions were done on the imputed data set for each of the MACE events according to the access site to quantify the independent association between access site and outcomes. To adjust for baseline characteristics that might influence outcomes and thus to attempt to quantify the independent effects of access site on outcomes, we performed a propensity score analysis. We used multiple imputation to generate 10 complete datasets, 10 distinct propensity scores from a logistic regression for all patients and considered a patient’s propensity score the average over all 10 values.(13) When then ran a 1:1 propensity matching within a calipher defined as 1/4 the propensity-score standard deviation.(14) Out of the 2611 femoral patients, 2478 pairs of subject were created. Finally, we performed a further analysis of the multi-variate predictors of 12-month mortality using multiple imputation to generate 10 complete datasets, and running a Cox-proportional hazard model on each of them. To find candidates for inclusions in the model, we compared all the data points available in the BCIS dataset for those alive or dead at 12-months and included any differences with a p-value of <0.1. Therefore entered into the model were age, clinical syndrome, NYHA class, previous MI, previous PCI, diabetes, ejection fraction, history of hypertension, history of peripheral vascular disease, history of valve disease, history of renal disease, Q wave on ECG, number of baseline diseased vessels, use of imaging, use of rotational atherectomy, acute kidney injury, tamponade, in-hospital major bleeding, prasugrel use, ticagrelor use, access site, coronary perforation, major side-branch loss and operator LMS-PCI volume.

**Results**

*Temporal changes in left main PCI and access site choice between 2007 and 2014*

The study flow is illustrated in Supplementary Figure 1 with 19,482 patients who underwent PCI to the left main stem between 2007 and 2014 included in the trends analysis. Crude numbers of LMS-PCI increased significantly during the study period, as did the percentage of LMS-PCI out of the total PCI (increasing from 2.6% to 4.5%, p<0.001 for trend, Figure 1). However, the percentage of the total LMS-PCI represented by unprotected vs. protected LMS disease did not change significantly during the study period (p-value=0.696, r2=0.027 for trend comparison, Figure 2). The use of femoral artery access for unprotected LMS-PCI fell significantly year on year with 77.7% of procedures performed femorally in 2007 compared with 31.7% in 2014 (Figure 3 left panel, p<0.001 for trend). There were significantly higher rates of right than left radial artery use for every study year, but use of the left radial artery also increased significantly during the study period (Figure 3, right panel). Although trends in radial access use in most patient sub-groups increased in a similar pattern to the whole patient cohort, adoption of radial access was slower in female patients, those with renal failure or valve disease, and in patients undergoing PCI for restenosis (Supplementary Figure 2).

*Baseline demographics, volumes and procedural details by access site for LMS-PCI between 2012 and 2014*

In the most contemporary study years (2012-14), a total of 3,171 patients with a protected LMS and 6,903 patients with an unprotected LMS underwent PCI. Patients undergoing unprotected LMS-PCI who were treated via femoral access were older, more likely to be women, and have a greater degree of comorbidity including diabetes, hypertension, previous MI, LV dysfunction, be treated with chronic anticoagulation and have chronic renal disease (Table 1) than those patients treated using radial access. Patients treated using femoral access were also more likely to have had previous revascularisation with PCI and had a greater baseline disease severity (2.09±1.11 vs. 1.84±1.07 vessels, p<0.001) and less likely to be treated with more potent P2Y12 antagonists. The baseline demographics of patients undergoing PCI with a protected LMS are presented in Supplementary Table 1 and demonstrate a younger population with less comorbidity than the unprotected cohort. However, the differences between the femoral and radial sub-groups were similar to the unprotected cohort.

Femoral access for unprotected LMS-PCI was also associated with certain characteristics representing PCI complexity including CTO intervention, treatment of restenosis, use of rotational atherectomy and the requirement for circulatory support although glycoprotein inhibitor was used less frequently that the radial cohort. However, radial access was associated with intervention involving the left main stem plus the proximal LAD, the left main stem plus any other vessel and with use of intravascular imaging. Radial access was also associated with a larger maximal stent diameter and a longer maximal stent length. In comparison, the procedural characteristics of patients undergoing PCI with a protected LMS are presented in Supplementary Table 2 and illustrate that the majority of cases involved the LMS only. The contrasts between the radial and femoral cohort were much less marked than in the unprotected LMS-PCI cohort with only CTO and restenosis indications, glycoprotein inhibitor use and ad-hoc PCI rates significantly different. In a serial analysis of the radial cohort only, PCI to vessels in addition to the LMS (including LMS bifurcation), the number of stents used, and use of rotational atherectomy, microcatheter or penetration catheters all increased significantly over time indicating increasingly complex LMS procedures despite using radial access (p<0.001 for all trends, Figure 4).

*Operator and centre volume and access site choice for LMS-PCI from 2012 to 2014*

Access site plotted by operator and centre volume for LMS-PCI is illustrated in Supplementary Figure 3. There was a negatively skewed distribution of operator volume of LMS-PCI cases with a significant number of low volume operators, and a median total operator volume of 9 cases over the three years examined. There was also negatively skewed distribution of centre volume of LMS-PCI cases with a significant number of low volume centres, and a median total centre volume of 51 cases over the three years examined. There was a correlation between individual operator volume and femoral access (p=0.005, Figure 4), and a trend for a correlation between individual centre volume and femoral access (p=0.076). However, there was a very wide variation in access site choice for a particular LMS-PCI operator volume.

*Independent associates of femoral access for unprotected LMS-PCI from 2012 to 2014*

Using multivariate analyses, the predictors of femoral artery use for unprotected LMS-PCI are presented in Table 3 with the strongest associates including history of renal disease (OR 2.29, 95% CI [1.76-3.00], p<0.001), PCI for restenosis (OR 1.69, 95% CI [1.27-2.26], p<0.001), CTO intervention (OR 1.66, 95% [1.25-2.12], p<0.001) and female sex (OR 1.56, 95% CI [1.35-1.79], p<0.001). Use of intravascular imaging (OR 0.57, 95% CI [0.50-0.65], p<0.001) and chronic anticoagulation (OR 0.42, 95% CI [0.24-0.75], p<0.001) were associated with a higher likelihood of the radial artery use for LMS-PCI. Operator and centre volumes did not predict access site choice.

*Clinical outcomes by access site for unprotected LMS-PCI between 2012 and 2014*

The number of successful lesions was similar between radial and femoral access (1.97±0.83 vs. 2.00±1.04, p=0.281) (Table 4). However, as a result of greater baseline disease, the residual disease burden in the femoral cohort was greater (0.51±0.83 vs. 0.45±0.75 vessels, p=0.004). Femoral access was strongly associated with increases in any access site complication (1.7% vs. 0.5%, p<0.001), access site haemorrhage (0.8% vs. 0.05%, p<0.001), and access site surgical repair (0.5% vs. 0.02%, p<0.001). Radial access for unprotected LMS-PCI was associated with decreased length of stay compared to femoral access (2.6±9.2 vs. 3.6±9.0, p<0.001) (Table 4). In the stable angina sub-group, same-day discharge was significantly more likely in the radial cohort (43.0% vs. 26.6%, p<0.001). Crude unadjusted clinical end-points including transfusion (0.9% vs. 0.3%, p=0.009), in-hospital major bleeding (1.6% vs. 0.7%, p<0.001), in-hospital death (4.2% vs. 2.5%, p<0.001), and in-hospital MACE (6.3% vs. 3.7%, p<0.001) were all more frequent in the femoral cohort. Following discharge, 30-day mortality (5.9% vs. 4.4%, p=0.021) and 12-month mortality were also higher with femoral access (17.3% vs. 11.7%, p<0.001).

The baseline characteristics of the matched femoral and radial cohorts after propensity score analysis are presented in presented in Supplementary Table 3. After matching, an excess of transfusion (OR 2.71 [1.14-6.46], p=0.024), arterial access complications (OR 2.37 [1.32-4.28], p=0.004), in-hospital major bleeding (OR 1.79 [1.02-3.15], p=0.033), in hospital MACE (OR 1.48 [1.14-1.92], p=0.003) and in-hospital mortality (OR 1.37 [1.01-1.86], p=0.047) in the femoral cohort persisted (Table 5). However, 30-day mortality was not significantly difference between the radial and femoral cohorts. Amongst the predictors of 12-month mortality, use of femoral access demonstrated only a trend for adverse survival (OR 1.17 [0.97-2.49], p=0.096] with patient age, use of imaging, acute kidney injury, chronic renal disease, and operator volume were most strongly associated with 12-month survival (Table 6).

Conversion to a predominantly radial access strategy was associated with significant temporal reductions in total access site complications, in-hospital major bleeding, transfusion and mortality for the whole patient cohort undergoing LMS-PCI (p<0.001 for all trends, Figure 5). However, despite the changes in access site between 2007 and 2014, there were no significant changes in mean or median length of stay for the LMS-PCI cohort during the study period.

**Discussion**

The United Kingdom has steadily adopted radial artery access for PCI. However, despite the major change in overall access site practice, data derived from the BCIS registry reveals the femoral artery to be the dominant access site in several sub-groups including PCI for chronic occlusive disease and PCI in patients with a history of CABG.(8-9) The current study demonstrates that the radial artery is now the predominant access site for unprotected LMS-PCI in contemporary practice with only 31% of cases still utilising femoral access in the latest year included in the study. This figure is similar the overall United Kingdom radial access usage of 26% of all PCI procedures for the same year, suggesting that the left main as a target vessel is no longer a significant influencing factor in access site decision-making.(15) Indeed, the temporal changes evident in case complexity in the current data is consistent with operators selecting more straightforward LMS-PCI cases early in their transition to radial access, but over time being comfortable taking on increasingly complex procedures.

It is noteworthy that the uptake of radial access for LMS-PCI was slower in certain sub-groups including female patients, the elderly, in those with renal failure or valve disease, and in patients undergoing PCI for restenosis presumably reflecting challenging anatomy, the need for larger bore guide catheters and/or difficult radial access. In contemporary practice as a result of this differential in the rate of change, it was these factors that were predictive of femoral artery access for LMS-PCI. These data also confirm the “radial paradox” i.e. that patients such as the elderly and female who have most to benefit from radial access in terms of bleeding reduction are more likely to have their procedure performed femorally.(16-18) The lower rates of vascular access complications and bleeding observed in the whole population in this study are likely to be amplified in these high-risk groups, and these data should encourage operator to further expand radial access use in sub-groups with most to gain.

The BCIS registry does not record sheath size and therefore it is not possible adjust for this factor. Nevertheless, many bifurcation techniques such as mini-crush, T-stenting and culotte can be completed using 6F catheters, particularly with the latest generation lower profile stents and delivery systems. Given the caliber of the left main and the proximal left coronary vessels, however, it may not be possible to simultaneously deliver the required devices through a 6F guide, even when the most contemporary platforms are used. Although using the radial artery restricts larger sheath sizes due to its smaller diameter (especially in women), several emerging technologies and techniques have facilitated more predictable use of larger guide catheters and therefore partly ameliorated the influence of sheath size required on access site choice. These include using 7F hydrophilic thin-walled sheaths and/or dedicated sheathless guide-catheters with high success rates reported for a 7.5F system.(19-20) Other emerging techniques such as balloon tracking to facilitate standard guide catheter use but without the use of sheath might also support increased use of radial access for complex PCI such as rotational atherectomy.(21-22)

In the NOBLE, SYNTAX LEFT MAIN, PRECOMBAT and LE MANS CRT randomised trials, whilst detailed anatomical and procedural data were reported, no data were presented on access site.(23-26) The EXCEL trial reported that 26.9% of cases were undertaken using radial access, although the outcomes by different access sites within the PCI sub-group have not been reported.(11) Although a previous series derived from the BCIS national PCI Audit reported increased bleeding and vascular complications with radial versus femoral access for LMS-PCI, these data were from PCIs performed between 2005-2010 with radial access use only 30% and did not focus specifically on predictors and outcomes by access site as in the current study.(27) The DELTA-2, LEMAX and a Chinese registry have reported access site data, with radial artery utilisation ranging from 32.0% to 61.1%, but without any comparative data between access sites.(28-30) The only study exploring the relationship between access site and outcomes comes from modest sized studies in unselected patients, and a single small study in octogenarians.(31-34) These broadly demonstrate similar procedural success and clinical outcomes when comparing radial against femoral access for LMS-PCI. The current study is the first to present temporal trends in access site change, predictors of access site choice and to focus on outcomes by access site for LMS-PCI on a national basis.

The results of the current analysis suggest that there are several potential major advantages to radial artery access over femoral artery access for unprotected LMS-PCI. As has been observed in many previous comparisons between femoral and radial access for PCI, there were significantly more access site complications in the femoral cohort. This was associated with higher rates of transfusion, major bleeding and in-hospital mortality. Although previous data has suggested that as operators increasingly utilise radial access, vascular complications increase in frequency in the remaining patients treated using femoral access – the so-called Campeau paradox – in contemporary United Kingdom practice, evolution to a routine radial strategy resulted in a significant reduction in total access site complications, transfusion and bleeding in the whole population undergoing LMS-PCI.(5,18,35) This data further supports the overall benefits of transitioning to radial access for even complex PCI.

Previous data from our group and others have confirmed the association of vascular complications, bleeding and transfusion with higher patient morbidity and mortality (15, 23-29, 36-37) These adverse outcomes may in part contribute to the longer length of stay seen in the femoral cohort. However, the more rapid ambulation after a radial procedure compared to a femoral procedure is also likely to underpin these observations.(38) The importance of the reduction in length of stay should not be underestimated in part because it enhances patient experience but also because of potential cost savings. The financial implications of even modest changes in access site have been estimated to lead to potential annual savings in the United States of $300 million.(39)

The current analysis suggests that whilst radial access improved in-hospital outcomes - likely related to reduced access site complications and bleeding - its use was not associated with improved longer term outcomes. Amongst the predictors of 12-month mortality there was only a trend for improved survival with radial access. Other factors such as age, comorbidity, baseline disease burden and operator volume were independently associated with improved survival. Additionally, improved survival was observed with use of intravascular imaging. A recent meta-analysis of ten studies representing 6,480 patients undergoing LMS-PCI showed that IVUS-guided PCI was associated with a 40% reduction in all-cause mortality at follow-up.(40) In the current analysis, intravascular imaging was strongly associated with improved 12-months survival and is likely reflective of better stent sizing and optimisation, total lesion coverage, and early identification of complications.

In considering the limitations of the present study, as with any database, the robustness of the conclusions are directly related to the quality of data entered. Additionally, the BCIS database does not capture details of anatomical data such as the location of disease with the LMS, complexity of lesions such as calcification or the presence or type of distal LMS bifurcation disease. Therefore, we cannot provide data on the relationship to the exact pattern of disease and access site. In an attempt to partly address this limitation, we categorised patients as a surrogate into LMS only and several sub-categories of LMS with other vessels treated. Similarly, whilst there are robust data regarding the type and number of stents used, there are no data provided on the interventional approach used to treat distal bifurcation LMS disease. Finally, because of the observational nature of this study, any conclusions may be influenced by unmeasured confounders such as comorbidity and frailty. These factors in particular might influence any associations between access site and reported outcomes such as 30-day and 12-month mortality.

**Conclusions**

In England and Wales in contemporary practice, the radial artery is now the predominant access site for unprotected LMS-PCI. Use of radial access compared to femoral access is associated with shorter length of stay, lower rates of vascular complication, and less major bleeding and transfusion. However, access site choice was not independently predictive of 12-month mortality.

**Clinical Perspective**

**What is known?:** Left main stem PCI is increasingly accepted as a viable alternative to CABG. However, data on access site choice for left stem PCI are limited and the effect of radial artery access on patient outcomes is uncertain.

**What is new?:** In a very large cohort observational study, radial artery access for left main stem PCI compared to femoral access was associated improved patients outcomes with significant reductions in in-hospital events including access site arterial complications, major bleeding, and major adverse cardiovascular events, and shorter length of stay.

**What's next?** As left main stem PCI continues to become more inclusive with increasingly complex patients and procedures in an aging population, whether these outcomes can be maintained in future years remains uncertain and will be the subject of future and on-going studies.

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**Figure Legends**

**Figure 1:** Left panel: Crude numbers of LMS (dark grey bars) and non-LMS PCI (light grey bars) performed in England and Wales 2007-2014; Right panel: Percentage of total PCI performed in England and Wales 2007-2014 represented by LMS-PCI (p<0.001 for trend).

**Figure 2** Left panel: Patients undergoing LMS-PCI with an unprotected left main stem as a percentage of total LMS-PCI volume in England and Wales per year (p-value=0.696, r2=0.027 for trend comparison); Right panel: Crude numbers of protected LMS-PCI (light grey bars) vs. unprotected LMS-PCI (dark grey bars) performed in England and Wales 2007-2014.

**Figure 3:** Left panel - Temporal change in femoral access use for unprotected LMS-PCI in England and Wales 2007-2014 (p<0.001 for trend); Right panel - Changes in left and right radial access for unprotected LMS-PCI in England and Wales 2007-2014 (p<0.001 for both trends, p<0.001 for comparison between trends).

**Figure 4:** Temporal changes in case complexity in the radial cohort of patients undergoing unprotected LMS-PCI in England and Wales 2007-2014 (p<0.001 for all trends).

**Figure 5:** Temporal changes in event rates per year for the combined radial and femoral cohorts of patients undergoing unprotected LMS-PCI in England and Wales 2007-2014 (p<0.001 for all trends.