Graphical Abstract summarises the CHiP analysis’s key findings according to the type of surgical cover.

Abbreviations: CHiP, complex high-risk but indicated percutaneous coronary interventions; GP, glycoprotein; HTN, hypertension; IABP, intra-aortic balloon pump; LM, left main; LV, left ventricle; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease.
Complex High-risk Percutaneous Coronary Intervention Types, Trends, and Outcomes in Non-surgical Centres

Running Title: CHiP Types and Outcomes in Non-surgical Centers

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Patient Consent Statement:
By submitting this manuscript to the Canadian Journal of Cardiology (CJC), the authors confirm that all patient data presented herein has received Section 251 approval under the NHS Act 2006. This approval permits the utilization of patient data for audit and research purposes without the formal requirement for individual patient consent. The authors recognize
and adhere to the ethical guidelines and regulatory approvals governing the use of patient information, ensuring confidentiality and compliance with applicable laws.

Word count 2888

Abstract

Background: Limited data are available on complex, high-risk percutaneous coronary intervention (CHiP) trends and outcomes in non-surgical centres (NSC), particularly in healthcare systems where most centers are NSCs.

Methods: Using data from a national registry, we studied the characteristics and outcomes of CHiP procedures performed for stable angina between 2006 and 2017 according to the presence or absence of on-site surgical cover. Multivariate regression analyses and propensity score matching were used to determine risks for in-hospital death, major bleeding, and major cardiovascular or cerebral events (MACCE).

Results: Out of 134,730 CHiP procedures, 42,433 (31.5%) were performed in NSCs, increasing from 12.5% in 2006 to 42% in 2017. Compared with surgical centres (SCs), patients who had a CHiP procedure undertaken in NSCs were, on average, 2.4 years older and had a
greater prevalence of cardiovascular risks. Common CHiP procedures performed in NSCs included poor LV function (41.6%), chronic renal failure (38.8%), and CTO PCI (31.1%). NSC-based CHiP is associated with lower mortality (aOR: 0.7 (0.5-0.8)) and major bleeding odds (aOR: 0.7 (0.6-0.8)). In both groups, MACCE odds were similar (aOR: 1.0 (0.9-1.1)).

**Conclusion:** CHiP numbers have steadily increased in NSCs. NSCs patients were older and had a higher prevalence of cardiovascular risks than the SCs patients. Mortality and major bleeding odds were significantly lower in those cases undertaken in NSCs, although MACCE odds were not different between the groups.

**Keywords (Non-surgical Centers, complex PCI, high-risk PCI, stable angina)**

**Abbreviation list**

- **CHiP**, complex high-risk but indicated percutaneous coronary interventions
- **CAD**, coronary artery disease
- **CABG**, coronary artery bypass graft surgery
- **PCI**, percutaneous coronary intervention
- **LM**, left main stem
- **BCIS**, British Cardiovascular Intervention Society
- **NICOR**, National Institute of Cardiovascular Outcomes and Research
- **MACCE**, major adverse cardiovascular and cerebral events
- **aOR**, adjusted odds ratio
- **CTO**, chronic total occlusion
Introduction

Complications following percutaneous coronary intervention (PCI) that necessitate emergency coronary bypass surgery (CABG) are rare in contemporary practice, occurring in <0.5% of cases, compared to a rate of 6-10% in the 1980s (1-4). PCI complications that would have previously required emergent CABG are effectively managed in the catheterization laboratory in contemporary practice. As a result, over the past decade, many centres in the world have started successful PCI programs in non-surgical centres (NSC)(5,6).

While evidence from both observational studies (7,8) and randomized control trials (RCT) (9,10) support PCI in NSCs in patients with stable coronary artery disease (CAD), less is known about the outcomes of complex, high-risk percutaneous coronary intervention (CHiP) procedures in these centres. Specifically, high-risk procedures were excluded from many of the original studies or only represented a small number of procedures, so outcome data from this group of patients is limited (9,11).

This analysis sought to examine the characteristics and outcomes of CHiP undertaken in patients with stable angina over 12 years according to the type of centre (surgical versus non-surgical) using data from a national PCI registry.

Methods

Data source

The data were obtained from the British Cardiovascular Intervention Society (BCIS), which is managed by the National Institute of Cardiovascular Outcomes and Research (NICOR). Over 95% of PCI procedures undertaken in England and Wales are recorded annually in the BCIS database by healthcare professionals, and data input is mandatory for professional revalidation(12). Data recorded include important demographics, cardiovascular comorbidities, pharmacological treatments, procedural characteristics, and in-hospital outcomes. The BCIS
dataset has been used for research and national audit purposes, and its quality and accuracy have been previously ascertained\(^{(13)}\). All data have section 251 approval of NHS Act 2006, allowing for audit and research matters without the formal need for individual patient consent. \(^{(14)}\)

**Study design and definitions**

This is a retrospective analysis of prospectively collected data from patients who underwent a CHiP procedure for stable angina in England and Wales between January 1\(^{st}\), 2006, and December 31\(^{st}\), 2017. All non-elective cases and acute coronary syndrome cases were excluded. CHiP was defined based on our previous work \(^{(15-17)}\) as any patient who met at least one of the following characteristics: previous coronary artery bypass graft (CABG), chronic renal failure (CRF), Severely impaired left ventricle (LV) function, PCI to a left main (LM) or a chronic total occlusion vessel (CTO), treatment for severe vascular calcification, or use of LV support devices. The collected data were then categorized into Surgical Center (SC) and Non-Surgical Center (NSC) groups.

We defined: CRF as creatinine>200 umol/L or dialysis-dependent patients, as it is predefined in the BCIS dataset; LV support use as any elective case required the elective / ad hoc and or bail out use of Impella or intra-aortic balloon pump (IABP); Severely impaired function as LV with an ejection fraction of \(\leq 30\%\); extensive vascular calcification as any case involving the use of cutting balloons or rotational or laser atherectomy.

**Study endpoints**

The primary outcome of interest was inpatient mortality. Secondary outcomes included a) major bleeding events or b) major cardiovascular and cerebral events (MACCE).
Major bleeding events were defined as any case that has met the Bleeding Academic Research Consortium’s definition for Bleeding Type 2 and above\(^{(18)}\); this includes a) access site bleeding requiring intervention or surgery; b) access site bleeding complications such as retroperitoneal hematoma or bleeding, arterial dissection, or false aneurysm; b) clinically evident bleeding into the gastrointestinal tract; c) radiological evidence of bleeding into the brain or retroperitoneal space; d) any periprocedural overt bleeding that required blood transfusion.

MACCE was defined as the cumulative incidence of in-hospital death, peri-procedural cerebrovascular accidents (CVA) or myocardial infarction (MI). We defined peri-procedural MI as a composite of Q-wave MI or non-Q-wave MI, reinfarction, and reintervention (emergency PCI or CABG), all predefined within, albeit not adjudicated in, the BCIS registry.

**Statistical analysis**

Following the initial selection process detailed earlier, we divided the study population into Non-surgical (NSC) and Surgical Centers (SC) groups. All missing observations in the age, sex, and outcomes variables were excluded. We then summarized the patient baseline demographics and characteristics as a) median (interquartile range) for continuous data and compared it using the Kruskal Wallis test; b) frequencies (percentages) for categorical data and compared it using Pearson's Chi-squared test. Details about the missing data are shown in Supplemental Table S1. We used multiple imputations with chained equations to impute missing data to create 10 datasets, assuming that data were missing at random\(^{(19)}\). The following variables were included in our model: surgical site, age, sex, and outcomes variables (all registered as complete variables); whereas the following variables required imputation: ethnicity, dyslipidaemia, previous MI, previous CABG, previous PCI, previous stroke, hypertension, diabetes mellitus, smoking, CRF, peripheral vascular disease (PVD), clopidogrel, family history of coronary artery disease (CAD), LV function, vascular access,
coronary imaging, left main PCI, intra-aortic balloon support (IABP), severe vascular
calcifications, number of treated lesions, number of stents used, stent size and length, and body
mass index (BMI). Variables with significant missing observations (such as ethnicity and LV
function) were also included in the multiple imputation models; studies have confirmed the
robustness of the multiple imputation frameworks even at an extremely high level of
missingness, although they can offer some protection when data are missing not at random (20-
22). Subsequent analyses were performed on the imputed dataset, and results were pooled using
Rubin’s rule (23). Multivariate logistic regression analyses were used to generate adjusted odds
ratios (aOR), 95% confidence intervals (CI) and corresponding p-values of outcomes between
the SC and NSC groups. We used forward stepwise variables selection on the data with an
inclusion criterion of p<0.1 to help select predictors into the final multivariate model. We ran
additional analyses using propensity scores matching PSM (mi estimate:teffects psmatch) to
evaluate the robustness of our results and to control for differences and imbalances in the
baseline characteristics between the 2 groups. The following variables were matched: age, sex,
etnicity, dyslipidaemia, previous MI, previous CABG, previous PCI, previous stroke,
hypertension, diabetes mellitus, smoking, CRF, PVD, LV function, clopidogrel, family history
of CAD, vascular access, intracoronary imaging, IABP, severe vascular calcifications, LM PCI
, number of treated lesions, number of stents used, stent size and length, and BMI. We then
performed logistic regression to estimate the propensity score and matching to the nearest
algorithm (Supplemental Figure S1). We then converted the coefficients to odd ratios to help
with a better interpretation of the results. Finally, we performed sensitivity analyses
(Supplemental Table S2) on the non-imputed dataset to better assess the consistency of the
results obtained. Stata version 14.1 was used to conduct the analyses (StataCorp, College
Station, Texas). Statistical significance was evaluated at a type I error at a rate of 0.05.
Results

We included 119 centres, of which 75 (63%) were non-surgical. 134,730 (31.8%) out of 424,290 procedure records of patients with stable angina treated with PCI between 1st January 2006 and 31st December 2017 met the eligibility criteria. Figure 1 summarizes the selection process for this analysis. Figure 2 shows that around two-thirds of procedures for each CHiP factor (type) were performed in a SC (see also CHiP factors section in Table 1). However, there was a gradual increase in the number of CHiP performed across all CHiP types in NSCs (Overall CHiP trends in NSCs: 2006, 12.5 % to 2017, 42%) (Figure 3). Table 1 details the baseline clinical and procedural characteristics of the study cohorts as follows:

A) Demographic and Clinical characteristics

Overall, 92,297 (68.5%) of the cases were performed in an SC vs 42,433 (31.5%) in NSCs. On average, the NSC patients were 2.4 years older than the SC patients. The two groups had a similar sex case mix, although more black, Asian, and other ethnic minorities patients had their CHiP undertaken in NSCs. SC patients had a higher prevalence of current smokers and previous history of MI. In contrast, NSC patients, compared to SCs, had a higher prevalence of hypertension (66.9 vs 64.2 %), severely impaired LV function (11.9 vs 9.3 %), dyslipidaemia (65.1 vs 64.2 %), family history of CAD (49.9 vs 45.2%), previous PCI (40.1 vs 38.1 %), stroke (5.7 vs 4.1 %), and PVD (8.1 vs 6.3 %), respectively; p<0.001 for all.

B) Procedural characteristics

A greater proportion of CHiP cases were performed via the radial access in a NSC vs SC (58.2 vs 41.8%, respectively; p<0.001. Similarly, intracoronary imaging was used in 15.1% of CHiP undertaken in NSC vs 10.8% in the SC (p<0.001). Intra-aortic balloon pump (IABP) was used slightly less frequently in NSCs than SCs (0.4 vs 0.6 % respectively; p<0.001). More NSC patients had two or more lesions treated than SC patients (38.4% vs 35%, respectively;
p<0.001). PCI to a graft (11 vs 8.2 %) or LM artery (12.6 vs 11.5 %), respectively (p <0.001 for both), was performed more frequently in SCs than NSCs.

**Inpatient clinical outcomes**

Mortality and major bleeding crude rates were significantly lower in the NSCs than SCs group (Mortality: 0.2 vs 0.3 %; major bleeding: 0.4 vs 0.6 %, respectively; p<0.001). Following adjustment for baseline covariates, odds for both mortality (aOR 0.7, 95% CI (0.5-0.8)) and major bleeding (aOR 0.7, 95% CI (0.6-0.8)) were 30% lower in the NSCs than SCs. PSM confirmed lower odds for mortality (OR 0.6, 95% CI 0.3-0.8) and major bleeding (OR 0.5, 95% CI 0.2-0.7) in NSCs. However, the odds for MACCE did not differ between the groups (Tables 2 and 3, Supplemental Figure S1).

**Discussion**

This study represents the first nationwide analysis comparing CHiP characteristics and outcomes in surgical versus non-surgical centres. The findings of this analysis confirmed that all types of CHiP procedures were more commonly performed in SC centres; more interestingly, it noted a gradual increase in the number of cases performed in NSCs across all CHiP types (2006, 12.5 % to 2017, 42%). At NSC, CHiP procedures are more likely to be performed via the radial approach and with intracoronary imaging guidance. Although NSC patients have higher cardiovascular risk profiles than SC patients, we observed lower odds for mortality and major bleeding during CHiPs undertaken in NSCs, while MACCE risks did not differ. Our analysis suggests that selected CHiP procedures are performed safely in NSC. Of note, the overall mortality and major bleeding events in the CHiP cohort was below 1%.
The introduction of PCI in NSC was initially driven by a number of factors, including (a) the evidence-based drive to treat ST-elevation MI (STEMI) patients with primary PCI as quickly as possible, (b) unacceptable delay in accessing evidence-based early revascularisation in NSTEMI patients, and (c) patient preference to have access to this treatment as close to where they lived as possible. PCI services inevitably expanded to include increasingly complex elective cases as the evidence for safety became apparent (24). This expansion of complex PCI into NSCs has been supported by the evolution of multidisciplinary decision-making (Heart Team) meetings, which have become more accessible to NSC interventionalists and accommodate increasing patient and procedural complexity. Despite these advances in clinical practice, the most recent AHA/ACC/ESC guidelines on CHiP in the NSC settings are less supportive and more cautious about such activity (25–28). For example, the ESC guidelines on myocardial revascularisation from 2010 recommended that high-risk procedures such as distal LM or complex bifurcation stenosis that involves large side branches should be performed in SCs (29). The SCAI 2020 guidelines recommended transferring stable patients to SCs for unprotected LM PCIs or for complex cases where advanced approach such as atherectomy is indicated and was not available / cannot be carried safely (30). However, there is a body of evidence on the safety and success of PCI in NSCs from randomized control trials (RCTs) such as CPORT-E (The Cardiovascular Patient Outcomes Research Team) (9) and the MASS COMM (Massachusetts Hospitals with Cardiac Surgery On-Site and Community Hospitals without Cardiac Surgery On-Site) (10) that have led to guideline recommendations supporting PCI in stable patients in non-surgical centres (31). Still, less is known about the outcomes of CHiP per se in these centres.

There was a clear difference between the two groups' baseline characteristics in our study. Overall, prior history of MI and current smokers were prevalent among the SC group. In contrast, the NSCs patients had a higher prevalence of stroke and hypertension, which may
relate to the fact that patients treated in NSC were older. This case mix differs from other registries comparing PCI outcomes between NCS and SC. For example, a study from the National Cardiovascular Data Registry (NCDR) in 2009 reported a heavier burden of both risks for and established cardiovascular diseases and diabetes in SCs patients\(^{(32)}\). We also noted differences in the types of procedures undertaken between the two different centre types. PCI procedures for LM or CTO vessels were more frequently performed at the SCs, in line with the current guideline recommendations on LM PCI\(^{(27)}\).

Even when baseline differences between the two groups were adjusted for, in-patient mortality and major bleeding events were 30% lower in procedures undertaken in NSCs compared to SCs, although the odds for MACCE were similar. These findings must be interpreted with caution, taking into account our inability to exclude certain confounders such as frailty, anaemia, anatomical complexity of CAD and other unrecorded comorbidities that are associated with worse outcomes such as COPD and cancer\(^{(33)}\). Furthermore, the severity of coronary diseases is not captured in the BCIS dataset, with no measures of the severity of calcification or the severity of disease as defined by SYNTAX score\(^{(34)}\), or classification of CTOs by complexity\(^{(35)}\). The worse outcomes seen in SCs may be driven by a higher risk case selection. In contrast, it is possible that lower-risk CHiP cases are performed in NSCs. Interestingly, we observe more frequent use of radial access and intracoronary imaging in NSC.

It is unclear why this may be the case, although may potentially reflect newer faculty, whose trained routinely incorporated intracoronary imaging, practising in NSC.

There is a growing body of evidence from single centre experiences\(^{(36)}\), RCTs\(^{(9,10)}\), and observational registries\(^{(8)}\), all of which demonstrated similar outcomes of PCI in general in NSCs vs SCs. The current study extends this knowledge to those patients undergoing CHiP procedures. This is pertinent since the expansion of CHiP to NSCs is met with many advantages, such as a greater opportunity for patients to remain in their own community, as
well as supporting the primary PCI program in NSCs by increasing the volume of PCI performed at such centres. Whilst there have been no reports around CHiP in NSC, other studies looked specifically into LM outcomes in NSCs vs SCs. For example, an analysis from the Victorian Cardiac Outcome Registry data showed that SCs were neither a predictor for in-hospital mortality (aOR 0.68, 95% CI 0.32-1.43, p=0.350), 30 days mortality, nor long term survival at 60 months (Hazard ration 0.88, 95% CI 0.62-1.27, p=0.510) (37). Furthermore, studies around CTO PCI in NSCs are rare; one prospective analysis in 2009 on 152 patients from 10 NSCs in China showed higher odds for procedure failure (OR 13.023, 95% CI 6.67-13.69, p=0.002) (38).

Study strength and limitations

This is the first study, at a national level, that examined, in a real-world, unselected setting, CHiP outcomes according to the type of surgical cover. The study was powered to determine real differences between the groups. The cohort represents the UK national practice, given that 95% of the PCI cases in England and Wales are recorded in the BCIS dataset. The study’s limitations are mainly related to its observational nature, including errors during reporting and coding, which could result in potential bias such as the under-reporting of comorbidities, and self-reporting of complications without external validation. Furthermore, lesion complexity and severity of coronary artery disease are not captured by the BCIS registry, which may confound outcome data. Moreover, there were significant differences between the two groups in major bleeding events, this must be interpreted after considering the differences in baseline demographics as well as the possibility of other unmeasured confounders like anaemia, frailty, lesion complexity, and surgical turndown status that may contribute to the observed differences. Despite our efforts to adjust for numerous variables through propensity score matching, the possibility of residual confounding remains. Specifically, the channelling
of higher-risk cases to surgical centres could influence the outcomes, and lesion complexity may play a role. Also, while the incidence of periprocedural MI is clearly defined in the BCIS dataset, the dataset fails to specify whether this diagnosis was based on a particular definition (for example, the fourth or third universal MI definition etc.). Lastly, as the BCIS dataset only captures in-hospital outcomes, we cannot rule out significant differences in the longer term.

Conclusion

In conclusion, this extensive nationwide analysis underscores a significant uptick in the adoption of CHiP cases in NSCs, suggesting a trend towards managing complex cases in these centres. Our findings suggest that PCI in non-surgical centres may be safe, with no excess mortality demonstrated. Nevertheless, these findings must be interpreted with recognition that given the inherent limitations in observational studies, the possibility of unmeasured confounders influencing the observed trends cannot be excluded. This study emphasizes the need for further research to discern the factors driving these patterns and their implications for patient care.

References


Figures’ titles and legends

Figure 1
Flow diagram illustrating the process of patients' inclusion and exclusion for the CHiP analysis.

Figure 2 Title: Prevalence of CHiP factors (types) stratified by the type of surgical cover provided.

Legend: Figure 2 illustrates the distribution of procedures for each CHiP factor (type), indicating that approximately two-thirds of the interventions were performed under Surgical Cover (SC). Abbreviation: CHiP, complex high risk but indicated percutaneous coronary interventions; CABG, coronary artery bypass graft; CTO, chronic total occlusion; CRF, chronic renal failure; LV, left ventricle; LM, left main stem; PCI, percutaneous coronary intervention.

Figure 3 Title: Temporal changes in CHiP procedures' prevalence and percent changes over time in the entire CHiP cohort and in each CHiP factor, stratified by the type of surgical cover.

Legend: Figure 3 depicts the temporal evolution of Complex High-risk but Indicated Percutaneous Coronary Interventions (CHiP) across all CHiP types in Non-Surgical Cover
A gradual increase is observed, with overall CHiP trends in NSCs rising from 12.5% in 2006 to 42% in 2017. Abbreviation: CHiP, complex high risk percutaneous coronary interventions; CABG, coronary artery bypass graft; CRF, chronic renal failure; CTO, chronic total occlusion; LV, left ventricle; LMS, left main stem; PCI, percutaneous coronary intervention.

Table 1: Baseline clinical and procedural characteristics of CHiP undertaken in patients with stable angina, stratified by type of surgical cover.

<table>
<thead>
<tr>
<th></th>
<th>Total, n</th>
<th>On-site cover</th>
<th>Off-site cover</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of participants</strong></td>
<td>134,730</td>
<td>92,297 (68.5%)</td>
<td>42,433 (31.5%)</td>
<td></td>
</tr>
<tr>
<td><strong>Female sex, n (%)</strong></td>
<td>29,320 (22.7%)</td>
<td>29,320 (21.6%)</td>
<td>9,355 (22.1%)</td>
<td>0.080</td>
</tr>
<tr>
<td><strong>Age Median, (IQR)</strong></td>
<td>69.5 (61.1 - 77.6)</td>
<td>68.8 (60.5 - 76.9)</td>
<td>71.2 (62.7-79.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>BMI Median, (IQR)</strong></td>
<td>28.1 (25.4-31.6)</td>
<td>28.1 (25.4-31.4)</td>
<td>28.2 (25.4-31.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>• White</td>
<td>84,240 (84.3%)</td>
<td>60,549 (85.8%)</td>
<td>23,691 (87.7%)</td>
<td></td>
</tr>
<tr>
<td>• BAME</td>
<td>16,400 (16.3%)</td>
<td>9,991 (14.2%)</td>
<td>6,409 (21.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>CHiP risk factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) <strong>Patients' factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Prior CABG</td>
<td>46,232 (33.4%)</td>
<td>32,818 (71.0%)</td>
<td>13,414 (29.1%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>• Chronic Renal Failure</td>
<td>14,890 (11.6%)</td>
<td>9,106 (61.2%)</td>
<td>5,784 (38.8%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>• Poor LV function</td>
<td>7,835 (10.2%)</td>
<td>4,574 (58.4%)</td>
<td>3,261 (41.6%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>b) <strong>Procedural factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• LMS PCI</td>
<td>16,204 (12.3%)</td>
<td>11,396 (70.3%)</td>
<td>4,808 (29.7%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>• CTO PCI</td>
<td>44,129 (34.8%)</td>
<td>30,399 (68.9%)</td>
<td>13,730 (31.1%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>• Severe coronary calcifications</td>
<td>25,743 (23.6%)</td>
<td>19,352 (75.2%)</td>
<td>6,391 (24.8%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>• Use of LV support</td>
<td>767 (0.6%)</td>
<td>584 (76.1%)</td>
<td>183 (23.9%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Cardiovascular risk factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hypertension</td>
<td>82,254 (65.0%)</td>
<td>55,210 (64.2%)</td>
<td>27,044 (66.9%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>• Dyslipidaemia</td>
<td>81,557 (64.5%)</td>
<td>55,215 (64.2%)</td>
<td>26,342 (65.1%)</td>
<td>0.001</td>
</tr>
<tr>
<td>• Diabetes Mellitus</td>
<td>33,890 (26.4%)</td>
<td>23,060 (64.2%)</td>
<td>10,830 (26.4%)</td>
<td>0.962</td>
</tr>
<tr>
<td>• Smoking</td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Never</td>
<td>47,968 (41.1%)</td>
<td>33,431 (42.0%)</td>
<td>14,537 (39.1%)</td>
<td></td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>57,147 (48.9%)</td>
<td>37,876 (47.6%)</td>
<td>19,271 (51.8%)</td>
<td></td>
</tr>
<tr>
<td>Current smokers</td>
<td>11,654 (10.0%)</td>
<td>8,275 (10.4%)</td>
<td>3,379 (9.1%)</td>
<td></td>
</tr>
<tr>
<td>• Family history of CAD</td>
<td>54,613 (46.7%)</td>
<td>36,388 (45.2%)</td>
<td>18,225 (49.9%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pharmacology</td>
<td></td>
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<tr>
<td>Warfarin</td>
<td>2,562 (2.1 %)</td>
<td>1,747 (2.1 %)</td>
<td>815 (2.1 %)</td>
<td>= 0.831</td>
</tr>
<tr>
<td>GPIIb IIIa inhibitors</td>
<td>9,611 (7.7 %)</td>
<td>6,693 (7.9 %)</td>
<td>2,918 (7.3 %)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>98,527 (81.3 %)</td>
<td>64,767 (78.6 %)</td>
<td>33,760 (87.1 %)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>1,126 (0.9 %)</td>
<td>793 (1.0 %)</td>
<td>333 (0.9 %)</td>
<td>= 0.079</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>4,260 (3.5 %)</td>
<td>2,717 (3.3 %)</td>
<td>1,543 (4.0 %)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Vascular access</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radial artery</td>
<td>58,852 (45.0 %)</td>
<td>37,440 (41.8 %)</td>
<td>21,412 (58.2 %)</td>
<td></td>
</tr>
<tr>
<td>Femoral artery</td>
<td>71,826 (55.0 %)</td>
<td>52,117 (58.2 %)</td>
<td>19,709 (47.9 %)</td>
<td></td>
</tr>
<tr>
<td>Intracoronary imaging</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVUS or OCT</td>
<td>13,631 (12.2 %)</td>
<td>8,062 (10.8 %)</td>
<td>5,569 (15.1 %)</td>
<td></td>
</tr>
<tr>
<td>Circulatory support</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IABP</td>
<td>713 (0.6 %)</td>
<td>550 (0.6%)</td>
<td>163 (0.4 %)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Impella</td>
<td>57 (0.04%)</td>
<td>37 (0.04%)</td>
<td>20 (0.05%)</td>
<td>0.607</td>
</tr>
<tr>
<td>Number of treated lesions</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One</td>
<td>85,677 (64.3 %)</td>
<td>59,764 (65.6 %)</td>
<td>25,913 (61.6 %)</td>
<td></td>
</tr>
<tr>
<td>Two</td>
<td>33,293 (25.1 %)</td>
<td>22,020 (24.1 %)</td>
<td>11,273 (26.8 %)</td>
<td></td>
</tr>
<tr>
<td>Three or more</td>
<td>14,161 (10.6 %)</td>
<td>9,283 (10.9 %)</td>
<td>4,878 (11.6 %)</td>
<td></td>
</tr>
<tr>
<td>Stent size Median, (IQR)</td>
<td>3.5 (3.0-3.75)</td>
<td>3.5 (3.0-3.5)</td>
<td>3.5 (3.0-4.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stent length Median, (IQR)</td>
<td>24 (18-36)</td>
<td>24 (18-33)</td>
<td>24 (18-38)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Procedural devices</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>83,775 (76.6 %)</td>
<td>56,533 (74.7 %)</td>
<td>27,242 (81.3 %)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cutting Balloon</td>
<td>15,268 (14.0 %)</td>
<td>12,522 (16.5 %)</td>
<td>2,746 (8.2 %)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rotational atherectomy</td>
<td>10,542 (9.6 %)</td>
<td>7,007 (9.3 %)</td>
<td>3,535 (10.5 %)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Laser atherectomy</td>
<td>868 (0.8 %)</td>
<td>442 (0.6%)</td>
<td>426 (1.3 %)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Number of stents used</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One stent</td>
<td>53,483 (40.1 %)</td>
<td>37,221 (40.8 %)</td>
<td>16,262 (38.4 %)</td>
<td></td>
</tr>
<tr>
<td>Two stents</td>
<td>33,903 (25.4 %)</td>
<td>22,911 (25.1 %)</td>
<td>10,992 (26.0 %)</td>
<td></td>
</tr>
<tr>
<td>Three or more stents</td>
<td>26,845 (20.1 %)</td>
<td>18,229 (20.0 %)</td>
<td>8,616 (20.4 %)</td>
<td></td>
</tr>
</tbody>
</table>

• History of AMI
• Previous PCI
• Previous stroke
• History of PVD
• LV systolic function

Normal (EF>50)

Impaired (EF 30-50)

Severe (EF<30)
### Target Vessel PCI

- **Left main stem (LMS)**: 16,204 (12.3 %) | 11,396 (12.6 %) | 4,808 (11.5 %) | < 0.001
- **LAD**: 52,920 (40.2 %) | 35,035 (38.8 %) | 17,885 (42.8 %) | < 0.001
- **LCX**: 33,835 (25.6 %) | 22,753 (25.2 %) | 11,082 (26.5 %) | < 0.001
- **RCA**: 47,210 (35.7 %) | 32,118 (35.5 %) | 15,092 (36.1 %) | = 0.039
- **Graft**: 13,397 (10.1 %) | 9,958 (11.0 %) | 3,439 (8.2 %) | < 0.001

### Number of target vessel PCI

<table>
<thead>
<tr>
<th>Type</th>
<th>Count (Rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>One</td>
<td>97,392 (74.6 %)</td>
</tr>
<tr>
<td>Two</td>
<td>26,183 (20.1 %)</td>
</tr>
<tr>
<td>Three or more</td>
<td>6,994 (5.3 %)</td>
</tr>
</tbody>
</table>

Abbreviations: CHiP, complex high risk percutaneous coronary intervention; CABG, coronary artery bypass graft; CTO, chronic thrombus occlusion; CAD, coronary artery disease; GPIIbIIIa, glycoprotein IIaIIIb; LV, left ventricle; LMS, left main stem; LCX, left circumflex; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; RCA, right coronary artery.
Table 2

Crude and adjusted outcomes of patients with stable angina who had a CHiP procedure, stratified by type of surgical cover.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total, n (%)</th>
<th>On-site, n (%)</th>
<th>Off-site, n (%)</th>
<th>Adjusted Odd Ratio (95% CI), P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>396 (0.3%)</td>
<td>300 (0.3%)</td>
<td>96 (0.2%)</td>
<td>0.7 (0.5-0.8), &lt; 0.001</td>
</tr>
<tr>
<td>Major bleeding events</td>
<td>694 (0.5%)</td>
<td>517 (0.6%)</td>
<td>177 (0.4%)</td>
<td>0.7 (0.6-0.8), &lt; 0.001</td>
</tr>
<tr>
<td>MACCE</td>
<td>1,964 (1.5%)</td>
<td>1,332 (1.4%)</td>
<td>632 (1.5%)</td>
<td>1.0 (0.9-1.1), = 0.420</td>
</tr>
</tbody>
</table>

Abbreviation: CHiP, complex high risk percutaneous coronary intervention; MACCE, major cardiovascular and cerebral events.
Table 3
Average treatment effect (ATE) and adjusted odds (aOR) for adverse outcomes of patients with stable angina following a CHiP procedure using Propensity Score Matchings (PMS) (reference, on-site surgical cover).

<table>
<thead>
<tr>
<th>Variables</th>
<th>ATE (95% CI)</th>
<th>aOR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>-.0013523 (-.0021744 -.0005302)</td>
<td>0.6 (0.3-0.8)</td>
<td>= 0.001</td>
</tr>
<tr>
<td>Bleeding</td>
<td>-.0028264 (-.0039191 -.0017338)</td>
<td>0.5 (0.2-0.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MACCE</td>
<td>-.0009283 (-.0028826 .0010259)</td>
<td>0.9 (0.8-1.1)</td>
<td>= 0.351</td>
</tr>
</tbody>
</table>

Abbreviation: ATE, Average Treatment Effect; CAD, coronary artery disease; CHiP, complex high-risk but indicated percutaneous coronary intervention; CI, confidence interval; MACCE, major cardiovascular and cerebral events.
Figure 1
Flow diagram illustrating the process of patients' inclusion and exclusion for the CHP analysis.

Abbreviations: CHP, complex high-risk; BCIS, British Coronary Intervention Society; PCI, percutaneous coronary intervention.

*Coding errors are those variables with ambiguous terms for example, unidentified hospital code.

**Inclusion criteria: left main PCI, PCI to chronic total occlusion vessel, chronic total occlusion vessel, poor left ventricle function, severe vessel calcification, previous coronary artery bypass graft, and the use of LV support devices.
Figure 2

Prevalence of CHiP factors (types) stratified by the type of surgical cover provided.

Abbreviation: CHiP, complex high risk but indicated percutaneous coronary interventions; CABG, coronary artery bypass graft; CTO, chronic thrombus occlusion; CRF, chronic renal failure; LV, left ventricle; LM, left main stem; PCI, percutaneous coronary intervention.
Figure 3
Temporal changes in CHiP procedures’ prevalence and percent changes over time in the entire CHiP cohort and in each CHiP factor, stratified by the type of surgical cover.

Figure 3 A) Changes in the entire cohort over time.
Figure 3 B) Changes in individual CHiP factors

Abbreviation: CHiP, complex high risk percutaneous coronary interventions; CABG, coronary artery bypass graft; CRF, chronic renal failure; CTO, chronic thrombus occlusion; LV, left ventricle; LMS, left main stem; PCI, percutaneous coronary intervention.