NATIONAL CARDIAC AUDIT PROGRAMME

NATIONAL AUDIT OF PERCUTANEOUS CORONARY INTERVENTION (NAPCI)

2022 Summary Report

(2020/21 data)

NICOR

BCIS

The National Institute of Cardiovascular Outcomes Research (NICOR)

NICOR is a partnership of clinicians, IT experts, statisticians, academics and managers who, together, are responsible for six cardiovascular clinical audits (the National Cardiac Audit Programme – NCAP) and a number of new health technology registries, including the UK TAVI registry. Hosted by Barts Health NHS Trust, NICOR collects, analyses and interprets vital cardiovascular data into relevant and meaningful information to promote sustainable improvements in patient well-being, safety and outcomes. It is commissioned by the Healthcare Quality Improvement Partnership (HQIP) with funding from NHS England and GIG Cymru/NHS Wales.

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British Cardiovascular Intervention Society

The British Cardiovascular Intervention Society promotes education, training and research in cardiovascular intervention and develops and upholds clinical and professional standards.

www.bcis.org.uk

Barts Health NHS Trust

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The Healthcare Quality Improvement Partnership (HQIP)

HQIP is led by a consortium of the Academy of Medical Royal Colleges, the Royal College of Nursing and National Voices. Its aim is to promote quality improvement in patient outcomes, and in particular, to increase the impact that clinical audit, outcome review programmes and registries have on healthcare quality in England and Wales. HQIP holds the contract to commission, manage and develop the National Clinical Audit and Patient Outcomes Programme (NCAPOP), comprising around 40 projects covering care provided to people with a wide range of medical, surgical and mental health conditions. The programme is funded by NHS England, the Welsh Government and, with some individual projects, other devolved administrations and crown dependencies.

www.hqip.org.uk

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NAPCI AT A GLANCE

Data from the period April 2020 to March 2021

During the pandemic period, percutaneous coronary intervention (PCI) procedures were down 10% from just over 100,000 in 2019/20 to 90,708 in 2020/21.

In 2020/21 intravascular imaging was used in 67% of cases involving left main stem PCI to assist the optimal deployment of stents, which ensures fewer acute and longer-term complications and improves outcomes. This is up from 57% the previous year.

PCI activity

Significant fall in total PCI procedures

- Elective PCI activity down 70% in the first wave of the pandemic and 47% in the second
- PCI for non-ST-elevation myocardial infarction (NSTEMI) cases down 35% and 14% during these two waves
- PPCI for ST-elevation myocardial infarction (STEMI) cases down 14% in the first wave

However some areas remained the same or slightly improved

- Fall in total PCI procedures only 1.2% in Wales, compared to England (10.3%) and Northern Ireland (19.7%)
- Primary PCI (PPCI) was up 2% compared with 2019/20

Day case PCI

Greater adoption of same day discharge has the potential to improve patient satisfaction, increase bed availability, and reduce hospital costs without increasing adverse patient outcomes. It also reduces exposure to hospital-acquired infections, especially important during the pandemic.

- 69% of elective PCI procedures carried out as a day case, up from 64% in 2018/19 (though wide variation between hospitals)

Executive summary

This report summarises selected key findings from the National Audit of Percutaneous Coronary Intervention (NAPCI) which is a part of the National Cardiac Audit Programme (NCAP).

It covers the financial year 2020/21, during which the COVID-19 pandemic has challenged the capacity of healthcare systems around the world, including substantial disruptions to cardiovascular care across key areas of healthcare delivery. This has included reductions in percutaneous coronary intervention (PCI) activity, both in elective and acute settings.

The report focuses on a number of specific quality improvement (QI) metrics in relation to the delivery of PCI services derived from national and/or international standards and guidelines.

KEY MESSAGES

Where things worsened/causes for concern	
A significant fall in total PCI procedures	PCI procedures down 10% from just over 100,000 in 2019/20 to 90,708 in 2020/21. Elective PCI activity down 70% in the first wave of the pandemic and 47% in the second. PCI for non-ST-elevation myocardial infarction (NSTEMI) cases down 35% and 14% during these two waves. Primary PCI (PPCI) for ST-elevation myocardial infarction (STEMI) cases down 14% in the first wave.
Many hospitals need to increase use of ICI	Wide variation in use of intracoronary imaging (ICI) in PCI when undertaking PCI to treat the unprotected left main stem (LMS).
Where levels of care were maintained or remained stable	
Good use of Drug Eluting Stents	Almost all hospitals perform well, with a high proportion of Drug Eluting Stent use across all clinical syndromes.
PCI procedures largely maintained in Wales	The fall in total PCI procedures was only 1.2% in Wales.
Use of Primary PCI slightly up over the whole year	PPCI activity up 2% in 2020/21 compared with the previous year.
Where things improved/practices changed	
Increase in the proportion of day cases	69% of elective PCI procedures performed as a day case, up from 64% in 2018/19 (though wide variation in practice, determined by local logistic issues and not patient characteristics).
More use of intravascular imaging to support PCI	Intravascular imaging used in 67% of cases involving left main stem PCI, rising from 57% the previous year (though wide variability between hospitals).

Summary of recommendations

1. **It is recommended that operators undertaking Left Main Stem PCI use intravascular imaging to guide interventional strategy and optimise stent expansion and apposition, in line with international consensus statements around best practice.**
2. **Hospitals should seek to modify their pathways and ward structures to reduce unnecessary overnight stays for patients undergoing elective PCI.**

   The explanation for the wide variation seen between hospitals will include differences in the management of wards and day units, pressure on beds from emergency admissions and differences in patient pathways.
3. **Hospitals not meeting the standards for the use of drug-eluting stents during primary PCI should review their cases to see where improvements can be made.**

1 Introduction

This report summarises selected key findings from the National Audit of Percutaneous Coronary Intervention (NAPCI) which is a part of the National Cardiac Audit Programme (NCAP).

It covers the financial year 2020/21, during which the coronavirus disease (COVID-19) pandemic has challenged the capacity of healthcare systems around the world, including substantial disruptions to cardiovascular care across key areas of healthcare delivery. This has included reductions in percutaneous coronary intervention (PCI) activity, both in elective and acute settings.

The report focuses on a number of specific quality improvement (QI) metrics in relation to the delivery of PCI services derived from national and/or international standards and guidelines. It records the activity and performance of hospitals as they responded rapidly to the enormous uncertainty and upheaval that resulted from the pandemic.

The data generated by NAPCI is also used as the basis for two other publications:

- A slide deck of comprehensive analyses published as the British Cardiovascular Intervention Society BCIS Audit. This is the full audit report of all adult interventional procedures performed in the UK from 1st April 2020 to 31st March 2020. The report can be found on the BCIS website.
- The annual Clinical Outcomes Publication (COP) which provides 3-year rolling data on individual PCI operators and centres and includes an assessment of risk-adjusted 30-day survival for England and Wales. The COP analysis was due to be published in 2022, but has been delayed. Current publication date is uncertain..

For the first time this year, data from NAPCI is also being combined with data in the Myocardial Ischaemia National Audit Project (MINAP) to create a report that focuses on the care given to individuals admitted to hospital with a heart attack. For many patients suffering a heart attack, optimal care includes a PCI procedure. Consequently, the time delays to treatment for patients presenting with ST-segment elevation myocardial infarction or non-ST-segment elevation (STEMI and NSTEMI) appear within that report.

The rest of this report is structured as follows:

- **Section 2** highlights the principal impacts of the COVID-19 pandemic
- **Section 3** focuses on a small number of Quality Improvement (QI) metrics which should continue to be a priority, either for teams within hospitals or for those leading service commissioning and development at Integrated Care System (ICS) level
- **Section 4** provides some pointers towards the future direction of the audit

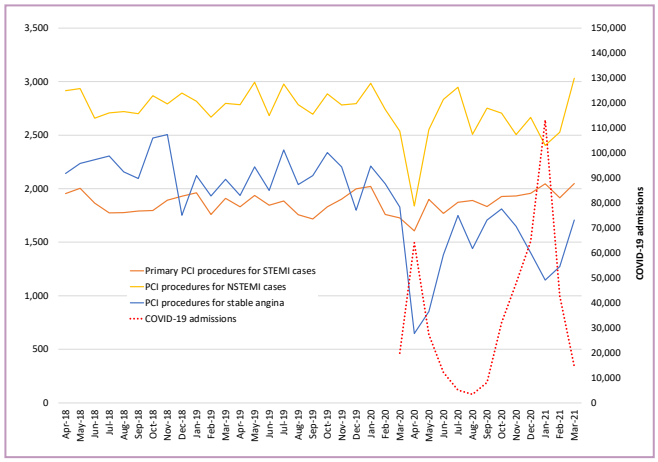
2 Principal impacts of the COVID-19 pandemic

Overall there has been a marked reduction in number of PCI procedures performed in the UK during this audit period, which coincides with the first year of the COVID-19 pandemic. Total PCI procedures fell by almost 10,000 to 90,708 in 2020/21 from just over 100,000 in 2019/20. Given a slight increase in population estimates, this represents a fall from 1,499 to 1,352 pmp (a 9.8% decrease).

In comparing the different countries of the UK, the largest fall was in Northern Ireland (19.7%), next England (10.3%), with the least reduction being found in Wales (1.2%).

The greatest reduction in PCI activity was for patients treated for stable coronary artery disease or 'stable angina' [Figure 2.1]. During the first wave elective PCI procedures fell to 70% of usual levels. They then recovered to reach 24% below previous levels before then falling again in the second wave to 47% of usual activity.

Figure 2.1: Total PCI and Primary PCI procedures for STEMI, NSTEMI and stable angina in England and Wales, against number of UK COVID-19 admissions, 2018/19 – 2020/21 [NAPCI data]



For primary PCI, there was only a slight reduction during the first peak, but no obvious change relative to the second COVID admission peak.

In addition, we saw increased delays in the emergency treatment for myocardial infarction. Call-To-Balloon (CTB) times (that include both emergency service delays and hospital delays) deteriorated, with a smaller percentage of patients being treated within 150 mins of a call for help. Door-To-Balloon (DTB) times, a measure of the PCI hospital's response, were also increased, but to a lesser extent. The reduction was most apparent during the first wave, less marked in the second.

For patients being treated for NSTEMI, there was evidence of improved access to care, with a reduction in the usual delays to treatment for this cohort of patients. The percentage of patients treated within 72 hours of first hospital admission was higher during both waves of COVID-19 hospitalisations. During the first spike, the percentage of those receiving PCI within 72 hours of admission increased from around 55% to over 80% before falling back to about 60%. It rose to more than 65% in the second wave but dropped under 60% again in March 2021.

Full details of these changes and figures are presented in the separate 'Heart Attack' report that combines data from the NAPCI and MINAP report audits.

3 | Selected quality improvement metrics

3.1 Use of intravascular imaging for left main stem (LMS) PCI

3.1.1 Overview of QI Metric: The use of intravascular imaging to guide PCI of left main stem lesions

QI Metric Description/Name	The use of intravascular imaging to guide PCI of left main stem lesions
Why is this important?	The use of intravascular imaging assists the optimal deployment of stents during LMS PCI, which ensures fewer acute and longer-term complications and improves outcomes. See additional detail below.
QI theme	Safety and Outcomes.
What is the standard to be met?	Intracoronary imaging should be used in more than 75% of PCI procedures of the unprotected LMS.
Key references to support the metric	See reference list.[1, 2, 3] 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularisation.[4] Class 2a, level of evidence B-R. In patients undergoing coronary stent implantation, implantation, intravascular ultrasound (IVUS) can be useful for procedural guidance, particularly in cases of left main or complex coronary artery stenting, to reduce ischemic events. Class 2a, Level of evidence B-R. In patients undergoing coronary stent implantation, implantation, optical coherence tomography (OCT) is a reasonable alternative to IVUS for procedural guidance, except in ostial left main disease.
Numerator	All PCI procedures to treat LMS stenosis in patient without prior bypass grafts, on which either intravascular ultrasound or optical coherence tomography has been used. This is defined as: A PCI (3.11 lesions attempted >0), AND LMS – defined as '3.09 vessel attempted =2.Lmain' AND protected LMS defined as '5.25 Left Main protected = 1.' AND either IVUS (3.19 option 1) OR OCT (3.19 option of 6) is selected.
Denominator	All PCI procedures to treat LMS stenosis in patient without prior bypass grafts. Defined as: A PCI (3.11 lesions attempted >0), AND LMS – defined as '3.09 vessel attempted =2.Lmain' AND protected LMS defined as '5.25 Left Main protected = 1.'
Trend	There has been a slow improvement in the use of intracoronary imaging from 56.6% in 2018/19 to 66.6% in 2020/21 [Figure 3.1].
Variance	Wide differences in practice between hospitals are documented [Figure 3.2 and Figure 3.3].

Three main coronary artery branches provide the blood supply to the myocardium (1. Left anterior descending, 2. Circumflex and 3. Right coronary artery). The first two of these both branch from a single vessel – the left main stem (LMS). Patency of the left main stem is therefore critical as it provides the blood supply to most of the heart. Abrupt occlusion of this vessel is almost always fatal.

It is therefore of paramount importance that when treating the LMS by PCI, the risk of complications such as acute or longer-term vessel occlusion (by stent thrombosis) and longer-term re-narrowing (restenosis) are minimised by ensuring that the stent is well expanded and well opposed to the vessel wall, as well as ensuring that there are no tears in the artery outside of the area of stenting that can lead to complications.

While many PCI procedures can be safely performed using angiography alone, angiography only provides some information to help guide PCI. Angiography shows only x-ray shadows of the coronary vessel lumen, and cannot be used to determine the characteristics of the vessel wall or the precise anatomy of the vessel relative to an intra-coronary stent.

Intracoronary imaging with ultrasound (intravascular ultrasound – IVUS) or laser (optical coherence tomography – OCT) provides a large amount of addition information. Both these tools provide detailed images from within the coronary artery, including assessment of the vessel wall, its size and tissue characteristics including characteristics of any atheroma. In addition, they provide detailed images of stents and the relationship of stent struts to the vessel wall, so that a number of features of suboptimal stent deployment can be identified that are invisible on angiography alone.

These features include poor apposition of the stent struts to the vessel wall, incorrect stent sizing, incorrect stent position relative to vessel atheroma, and vessel tears (dissections) at the edge of the stents. All these features can increase the risk of potentially fatal vessel occlusion, and increase the risk of longer-term narrowing necessitating further procedures and can only be clearly identified with intracoronary imaging.

A number of trials and meta-analyses have shown reduced clinical events such as mortality, stent thrombosis and repeat revascularisation when intracoronary imaging is used to guide PCI particularly in the LMS, when there is no protection from previous bypass grafts (a so called 'unprotected' left main stem). A recent publication derived from UK national data has shown that intravascular imaging is associated with a 30% decrease in mortality at 1 year following LMS PCI.[1] More recently the European Association of Percutaneous Coronary Intervention, a group of the European Society of Cardiology, has published a consensus statement recommending the use of intracoronary imaging in complex PCI cases, including LMS PCI, as best practice.[2, 3] This recommendation is also now part of the latest guidelines for coronary artery revascularisation from the American College of Cardiology and American Heart Association.[4]

3.1.2 Audit results

Figure 3.1: Use of intravascular imaging (%) by IVUS or OCT during LMS PCI procedures, 2018/19 to 2020/21 [NAPCI data]

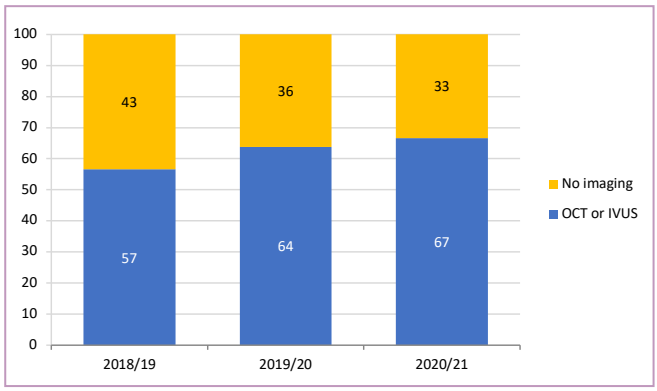
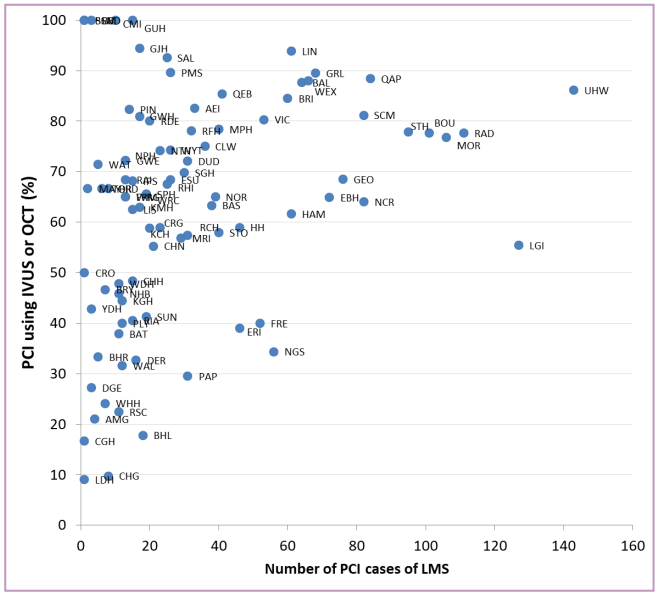
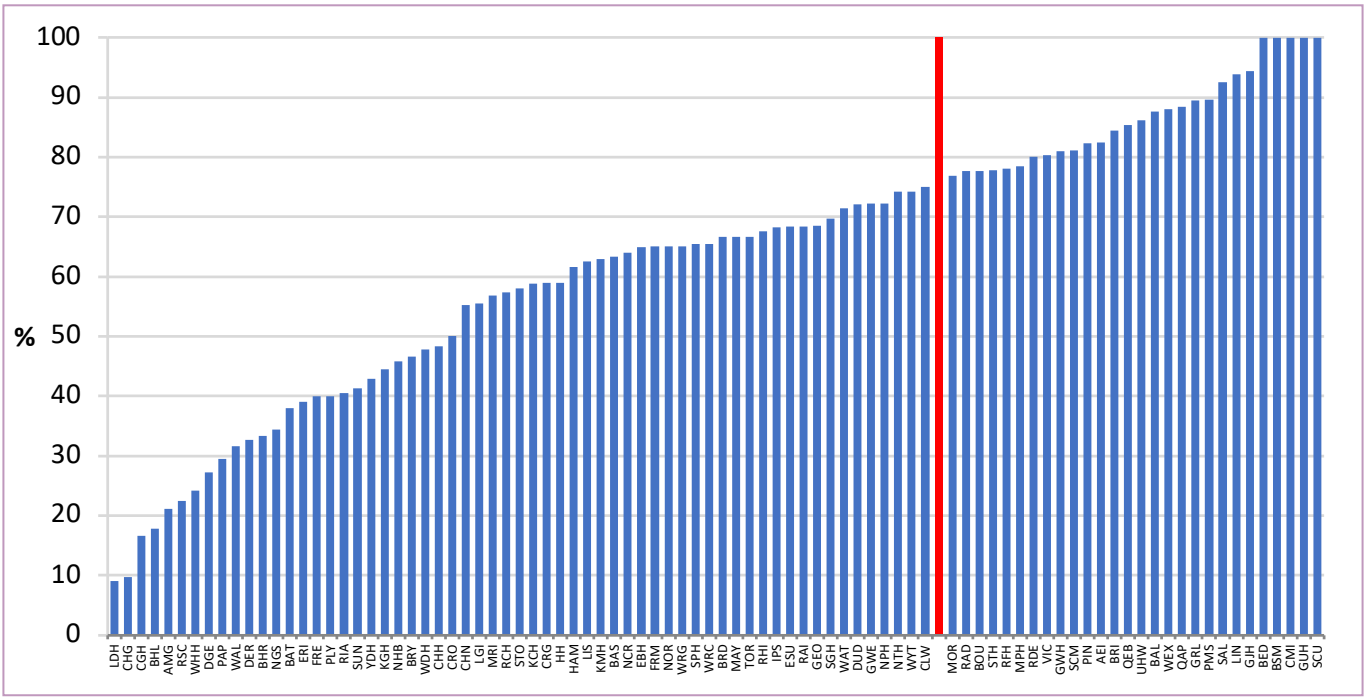


Figure 3.2: Funnel plot to show inter-hospital variance in use (%) of intravascular imaging by IVUS or OCT for LMS PCI procedures, 2020/21 [NAPCI data]



See here for site codes.

Figure 3.3: Use of intravascular imaging (%) by IVUS or OCT for LMS PCI, by hospital in rank order, 2020/21 [NAPCI data]



*Hospitals to the left of the red line do **not** perform intravascular imaging in >75% of LMS PCI procedures.*

3.1.3 Recommendations for those not achieving the standard

It is recommended that operators undertaking Left Main Stem PCI use intravascular imaging (either IVUS or OCT) to guide interventional strategy and optimise stent expansion and apposition, in line with international consensus statements around best practice.[2, 3, 4]

3.2 Much more could be done to offer day case PCI

3.2.1 Overview of QI metric

QI Metric Description/Name	Proportion of patients treated by PCI for stable symptoms who are treated as a day case
Why is this important?	Patient experience – see additional detail below.
QI theme	Effectiveness.
What is the standard to be met?	>75% as day cases. The BCIS Domain Expert Working Group recommended that >75% of PCI procedures performed electively for stable symptoms should be discharged on the same day as the procedure.
Key references to support the metric	References in text below are in reference list at end of report. [5, 6, 7, 8, 9]
Numerator	Day case procedure for PCI for stable elective patients defined as: 2.03 Procedure Urgency = 1. Elective & 3.11 Number of lesions attempted >0 AND 3.01 Date and time of operation = same DATE as 4.04 Discharge Date.
Denominator	PCI for stable elective patients defined as: 2.03 Procedure Urgency = 1. Elective & 3.11 Number of lesions attempted >0.
Trends	Only a slight increase in day case elective work over the last 3 years [Figure 3.4].
Variance	This audit has demonstrated that there is extremely wide variation in day case rates, with some centres performing day case PCI in almost all elective cases, and some where almost all patients are kept in overnight following their procedure [Figure 3.5, Figure 3.6 and Figure 3.7].

When PCI was first introduced, in the first few hours after the procedure serious complications would occur in about 5% of cases, requiring emergency intervention including surgery. As a result all patients were kept in hospital overnight and monitored carefully. However, the PCI has evolved and has become a much safer treatment. This is because of a number of developments including the use of stents, special anti-platelet (blood-thinning) drugs, and radial artery access (see above).

While patients who need PCI for a heart attack usually still need to stay in hospital overnight, patients who are being treated electively for symptoms of stable angina usually do not.

The safety of same day discharge following uncomplicated PCI for stable symptoms has been demonstrated in several trials,[5] and analyses of the BCIS dataset across a broad range of cases.[6, 7, 8, 9] Greater adoption of same day discharge has the potential to improve patient satisfaction, increase bed availability, and reduce hospital costs without increasing adverse patient outcomes. This is particularly relevant in the COVID era, where same day discharge would minimise any potential exposure to hospital acquired infections, particularly in periods when COVID-19 admissions increase.

3.2.2 Audit results

Figure 3.4: Mean percentage of elective PCI patients treated as Day Cases, 2018/19 – 2020/21 [NAPCI data]

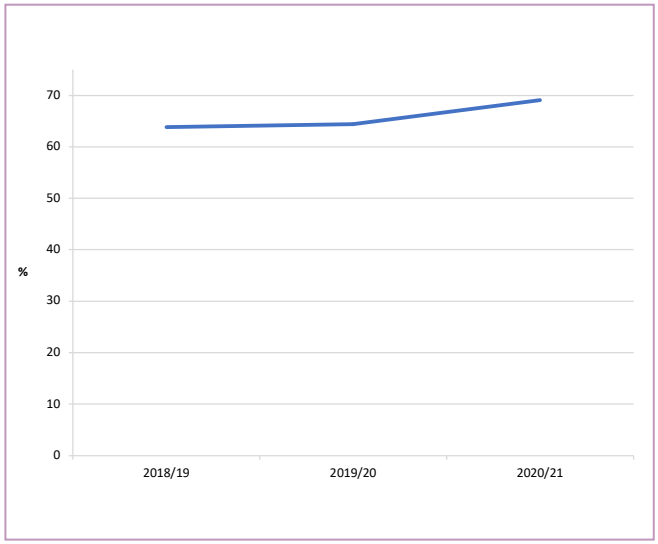
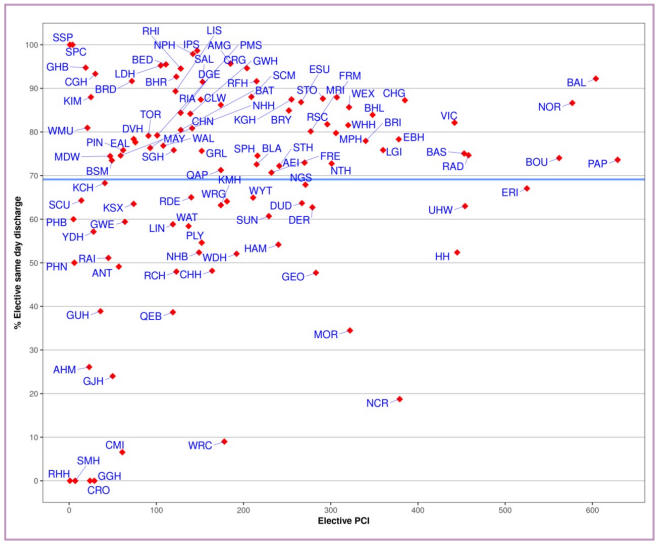
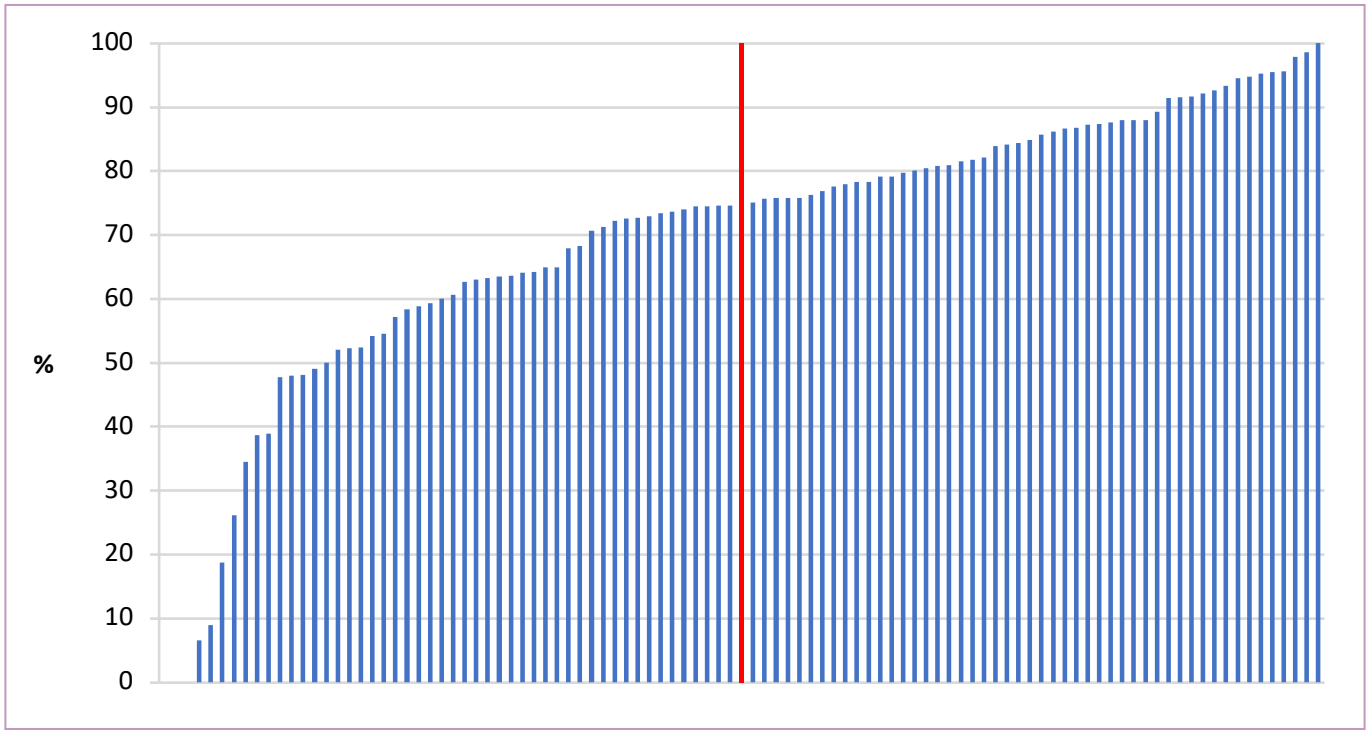


Figure 3.5: Proportion (%) of elective PCI performed as a day case by hospital, according to overall hospital PCI activity, 2020/21 [NAPCI data]



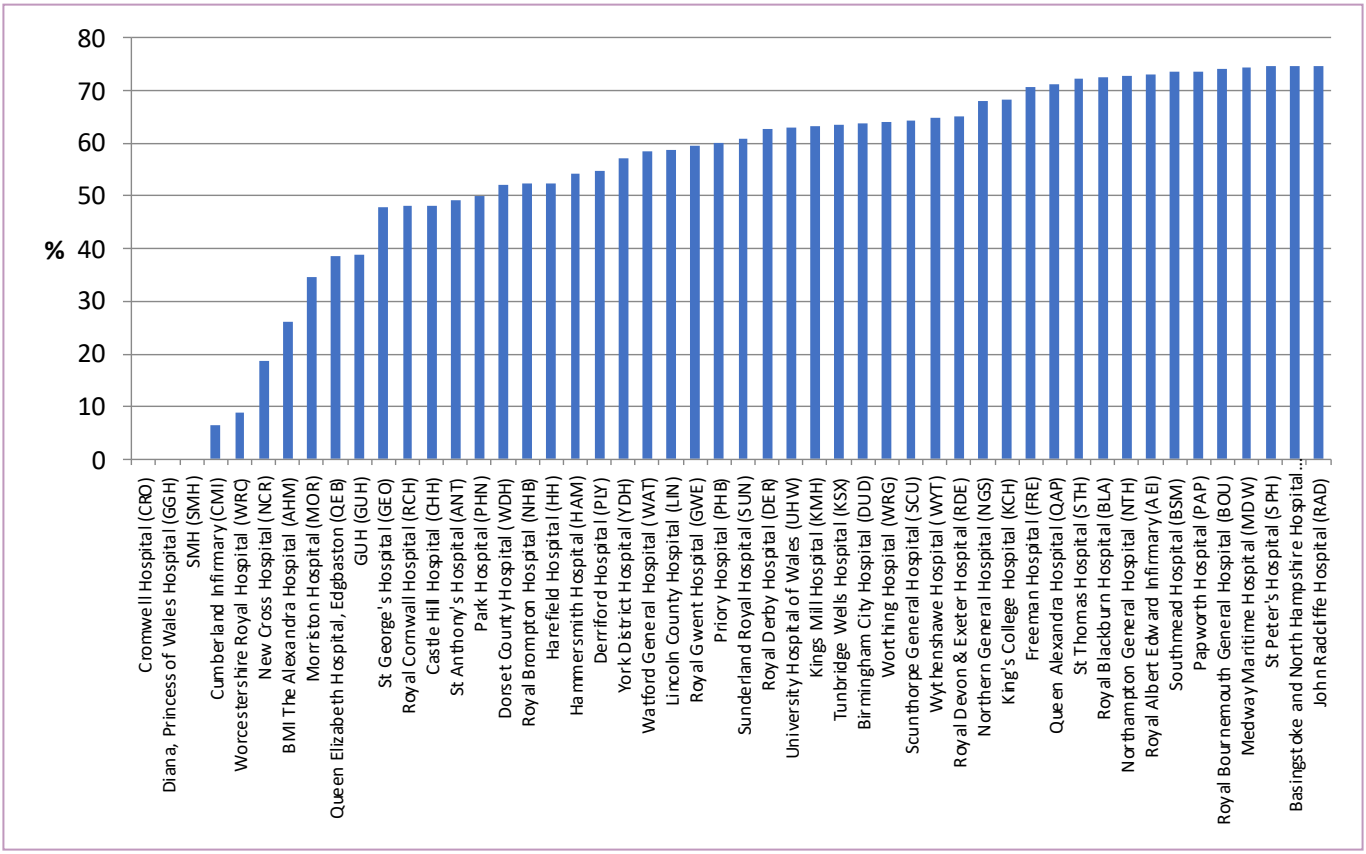
See here for site codes.

Figure 3.6: Percentage of elective PCI cases performed as a day case by hospital, 2020/21 [NAPCI data]



*Hospitals to the left of the red line do **not** perform PCI as a day case in >75% of elective PCI procedures.*

Figure 3.7: Hospitals with less than 75% of elective procedures performed as a day case, 2020-21 [NAPCI data]



See here for site codes.

3.2.3 Recommendations for those not achieving the standard

Hospitals should seek to modify their pathways and ward structures to reduce unnecessary overnight stays for patients.

The explanation for this wide variation will include differences in the management of wards and day units, pressure on beds from emergency admissions and differences in patient pathways.

3.3 High adherence to expected standard for the use of Drug Eluting Stents (DES) during primary PCI (PPCI)

3.3.1 Overview of QI metric

QI Metric Description/Name	DES as proportion of stented cases in PPCI
Why is this important?	Evidence of benefit over bare metal stents. When drug eluting stents were first developed to reduce the rate of restenosis observed with bare metal stents, there were concerns about the potential for these new stents to be at increased risk of later thrombotic occlusion (stent thrombosis). These concerns have now been assuaged by recent trials of the latest (third generation) drug eluting stents. These trials show that new generation drug eluting stents maintain the benefits of reduced restenosis, without increasing the risk of stent thrombosis. In fact, the most recent trials show DES are associated with less stent thrombosis than bare metal stents and better longer-term outcomes, particularly around restenosis and the further need for future interventions.
QI theme	Effectiveness, outcomes.
What is the standard to be met?	>90% use of DES where a stent is deployed to treat STEMI.
Key references to support the metric	2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularisation.[4] Class 1, Level of evidence A. In patients undergoing PCI, DES should be used in preference to BMS to prevent restenosis, MI, or acute stent thrombosis.
Numerator	Primary PCI where the stent used is a DES, defined as: 3.11 Number of lesions attempted >0 AND 2.02 Indication for Intervention = 4. ACS – Primary PCI for STEMI (no lysis) AND 3.15 Number Stents used >0 AND DES = 3.16 Number of Drug-eluting stents used >0.
Denominator	Primary PCI where a stent is used, defined as: 3.11 Number of lesions attempted >0 AND 2.02 Indication for Intervention = 4. ACS - Primary PCI for STEMI (no lysis) AND 3.15 Number Stents used >0.
Trends	There has been a small drop overall in the proportion of patients receiving a stent during PCI over the last few years, possibly because of an emerging evidence around the use of drug-eluting balloons. This technology was only added to the dataset in 2019, so it is too soon to use the dataset to address this issue although analyses are planned in the future (provisional data are presented in the full slide deck on the BCIS website). Where a stent is used, there remains a very high use of DES. Assessing stent type use by presenting syndrome shows consistently high use in all [Figure 3.8]. Use of drug eluting stent for primary PCI by centre shows almost all centres with >90% usage.
Variance	This audit has assessed the use of DES during PPCI for all centres, and shown very high levels of compliance with these recommendations in almost all centres [Figure 3.9 and Figure 3.10].

3.3.2 Audit results

Figure 3.8: Use of DES (%) during PCI procedures in specific syndromes, 2017/18 – 2020/21 [NAPCI data]

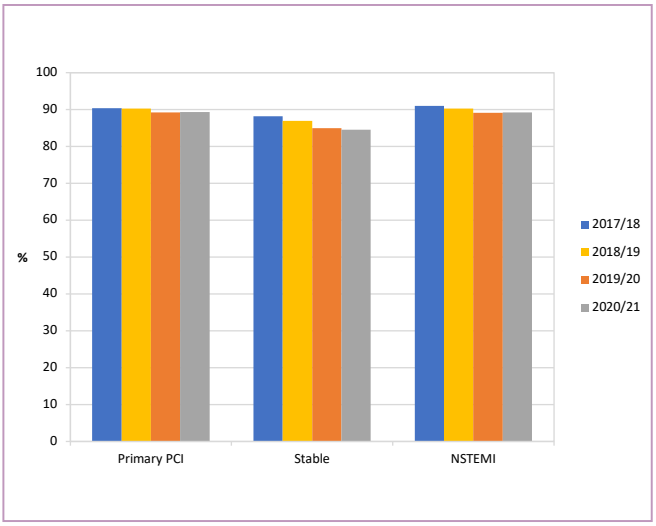


Figure 3.9: Use of DES in PPCI by hospital, 2020/21 [NAPCI data]

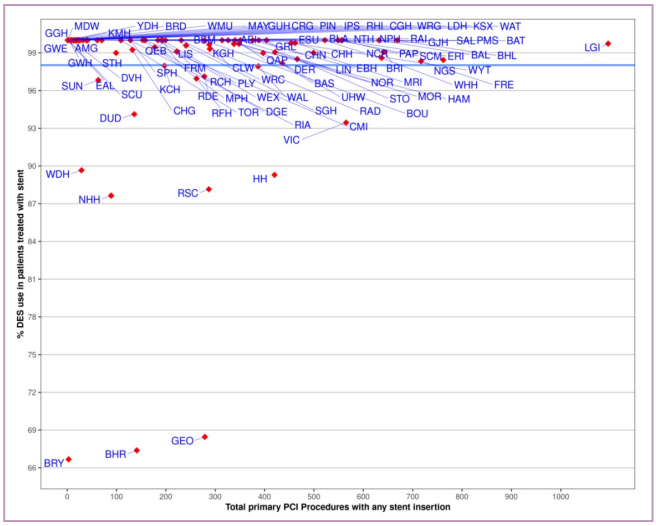


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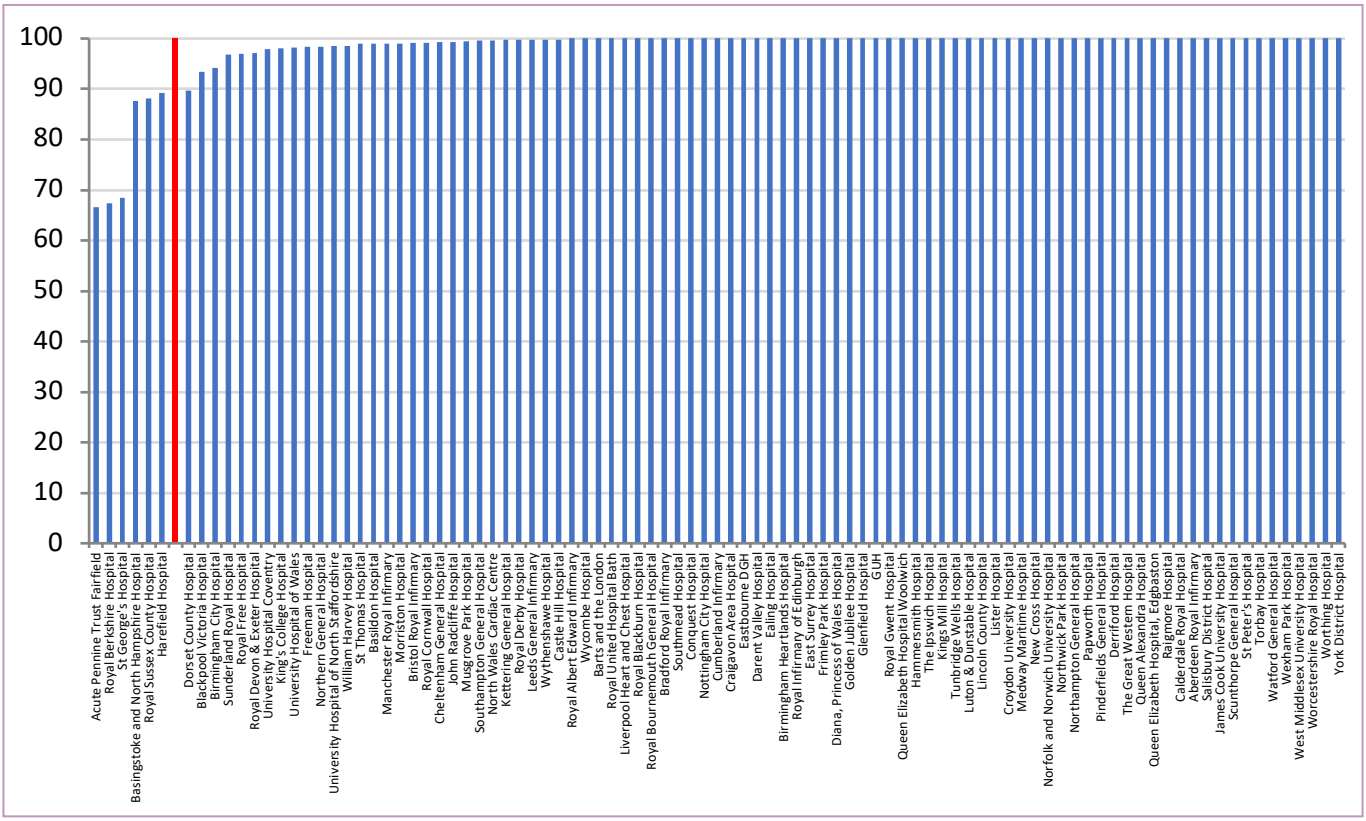
Figure 3.10: Use of DES (% of total cases) in PPCI in individual hospitals, 2020/21 [NAPCI data]



*Hospitals below the red line do **not** use DES in ≥90% of PPCI procedures requiring a stent. See here for site codes.*

3.3.3 Recommendations for those not achieving the standard

Hospitals not meeting the standards for the use of drug-eluting stents during primary PCI should review their cases to see where improvements can be made.

3.4 Data Completeness

3.4.1 Overview of QI metric

An assessment of data completeness forms part of the Clinical Outcomes Publication that will be available later in the year. For completeness the rationale and description is provided below.

QI Metric Description/Name	1. Data completeness of key fields required for risk adjusted outcome analysis. 2. Data completeness for time delays to STEMI treatment. 3. Data completeness for time delays to NSTEMI treatment.
Why is this important?	1. To allow accurate assessment of outcomes. 2. To allow accurate assessment of delays to PCI in ACS.
QI theme	Safety and effectiveness and surrogate for outcomes.
What is the standard to be met?	>95% completeness of each of the key fields.
Key references to support the metric	BCIS data monitoring group recommendation.

4 Future direction

Currently the audit benchmarks the practice of individual operators and hospitals through analysis of 30-day mortality outcomes. This uses risk models that adjust for differences in patient and procedural characteristics and links to mortality data derived from the Office for National Statistics.

Development of stent platforms, the introduction of newer drugs and refinements of procedural practices has meant that mortality rates associated with PCI have declined over time. Nevertheless, this has meant that now that mortality is a rare event following PCI, its sensitivity as a quality metric is uncertain. Furthermore, recent literature has suggested that only 60% of 30-day deaths following PCI are thought to be related to a cardiac cause in the UK.[10] This has meant that other outcome measures are increasingly explored to use as quality metrics.

Currently in the UK the national audit does not capture unplanned readmissions. These are considered to be a quality metric in many healthcare systems and 30-day unplanned readmissions are nationally reported at an individual centre level in North America. Unplanned readmissions may occur following PCI because of a post discharge complication such as a major bleed, a stroke or a heart attack, a new cardiovascular event or as a consequence of another medical condition that a patient may have. A recent analysis of over 800,000 PCI procedures has suggested that 9% of PCIs undertaken in the US have an unplanned readmission within 30 days.[11]

In the UK, the frequency, causes and outcomes of such readmissions are unknown and there are no data around whether they vary by operator or centre. It is hoped that linkage of the NICOR datasets to hospital episode statistics (HES) will provide a means of capturing these data, and providing further information around the safety and efficacy of PCI, particularly in relation to the capture of post discharge complications that necessitate hospital admission and whether there are differences at the hospital or individual operator level.

Invasive treatment of coronary artery disease can be through PCI or cardiac surgery. Whilst there are patient characteristics and coronary artery disease distribution that are undoubtedly better treated by PCI or cardiac surgery, there are also cases that can be treated by either modality, for example three vessel disease or left main coronary artery disease. There are few data in the UK about whether the treatment of such cases differs by region / unit and whether these differences in treatments impact on clinical outcomes. Future work will aim to report the proportion and type of these cases that are treated through either PCI or surgical means at an individual unit level. We aim to study whether differences in practice at the unit level impact on longer-term clinical outcomes.

Finally, the aim is to subject future analyses from the national audit to external peer review and publication in the scientific literature. External peer review and scientific publications are important both from a quality perspective, but also importantly provide the evidence basis for future guidelines and practice statements in a rapidly advancing field. This approach is widely adopted and considered an accepted norm both in Sweden in the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART) registry and the United States in the National Cardiovascular Data Registry (NCDR), where the analyses that form the audit reports are published as peer reviewed articles in the scientific literature.

5 | References

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