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ORIGINAL RESEARCH

Rates of Elective Percutaneous Coronary Intervention in England and Wales: Impact of COURAGE and ORBITA Trials

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BACKGROUND: There are limited data about how COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) and ORBITA (Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina) trials have impacted percutaneous coronary intervention (PCI) practices at regional or national level. We evaluated temporal trends in elective PCI rates for stable angina and, specifically, examined the impact of the COURAGE and ORBITA trials on PCI practices in England and Wales.

METHODS AND RESULTS: We used national PCI data comprising >1.2 million patients undergoing PCI between January 2006 and December 2019. Patient demographics, procedural details, and clinical outcomes were analyzed, and temporal trends in PCI rates for stable angina were compared before and after the publication of the COURAGE and ORBITA trials. Of 1 245 802 PCI procedures, 430 248 (34.5%) were performed for stable angina. Over the study period, the number of elective PCI procedures per year (30 823 in 2006 to 34 103 in 2019) and per 100 000 population estimates (50.7 in 2006 to 58.4 in 2019) remained stable. The proportion of patients undergoing elective PCI without angina symptoms almost doubled from 5.1% to 9.7%. The incidence rate of elective PCI volume after the COURAGE trial, published in 2007, was not different from before the trial was published (incidence rate ratio, 1.06 [95% CI, 0.69–1.62]). It also remained stable after the publication of the ORBITA trial in 2017 (incidence rate ratio, 0.96 [95% CI, 0.74–1.23]).

CONCLUSIONS: In this nationwide analysis, rates of elective PCI for stable angina remained stable over 14 years. Publication of the COURAGE and ORBITA trials had no impact on elective PCI activity.

Key Words: angina, stable ■ COURAGE ■ England ■ insulin receptor-related receptor ■ percutaneous coronary intervention ■ Wales

Percutaneous coronary intervention (PCI) is the most commonly performed revascularization modality for coronary artery disease.[1,2] PCI has been shown to reduce mortality and reinfarction in patients presenting with the acute coronary syndrome.[3–8] However, the role of PCI in the management of stable coronary artery disease has been controversial.[1,9,10] Randomized controlled trials (RCTs) and subsequent meta-analyses have failed to illustrate a statistically significant prognostic benefit of PCI in preventing myocardial infarction or cardiovascular death in patients with stable coronary artery disease.[11–14]

The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial, published in 2007, showed no prognostic benefit of PCI over optimal medical therapy in patients with stable coronary artery disease.[14] Similarly, the ORBITA (Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina) trial, published in 2017, demonstrated no significant difference in either symptom relief or change in exercise capacity.[15] RCTs are considered the gold standard for scientific quality in contributing to the

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CLINICAL PERSPECTIVE

What Is New?

- This study shows a stable trend in number and rates of percutaneous coronary intervention procedures for elective angina over a 14-year period.
- More important, there were no changes in percutaneous coronary intervention practices even within trial participating centers of ORBITA (Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina) trial.

What Are the Clinical Implications?

- Our study shows that publications of 2 landmark trials did not meaningfully change the rates of elective percutaneous coronary intervention and that there is a major discordance between the case mix of nationally representative cohort of patients with stable angina compared with 2 landmark trials in this field.
- Further studies are required to study the factors associated with these discrepancies and to facilitate translation of randomized controlled trials into clinical practice.

Nonstandard Abbreviations and Acronyms

BCIS	British Cardiovascular Intervention Society
COURAGE	Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation
ORBITA	Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina

evidence base for international guideline recommendations. However, the translation of RCT data into real-life practice is often less uniform.[16] The impact of the publication of landmark clinical trials, such as COURAGE or ORBITA trial, on subsequent rates of elective PCI and the clinical profile of patients treated with PCI has not yet been studied at a national level.

Using the BCIS (British Cardiovascular Intervention Society) registry from England and Wales, we studied the temporal trends in rates of elective PCI over 14 years. We also examined changes in the risk profile of the population and indications for procedures undertaken. Finally, we specifically assessed whether there were any changes in PCI volume or the risk profile of PCI procedures undertaken nationally following the presentation of the COURAGE and ORBITA trials and whether any changes in case mix or practice were seen within the trial participating centers of the ORBITA trial, given that the ORBITA trial was an exclusively UK trial.

METHODS

The data underlying this article were provided by a third party, including the National Institute of Cardiovascular Outcomes Research. Data could be accessed on request to the third party.

Study Setting

Data were acquired from the BCIS registry, details of which have been described previously.[17] In brief, the BCIS registry is a national PCI registry in England and Wales that collects data from almost every PCI procedure undertaken in the National Health System for audit, public reporting, and research purposes. Data about the indication for PCI, clinical and angiographic characteristics, pharmacology, interventional treatment, and in-hospital outcomes are collected prospectively by the participating centers before being transferred to the National Institute of Cardiovascular Outcomes. The National Institute of Cardiovascular Outcomes has a section 251 approval under the National Health System Act 2006, which allows the use of data set for medical research and audit purposes without seeking patient consent.[18,19] All data used in this study were anonymized; therefore, institutional review board approval was not required.

Study Cohort

The study cohort comprises all adults aged ≥18 years undergoing PCI between January 1, 2006, and December 31, 2019. Procedures with missing data about age, sex, indication, in-hospital outcomes, diagnostic procedure, or pressure wire only were excluded from the analysis. PCI procedures undertaken for acute coronary syndrome indication were excluded while making group comparisons only (Figure S1). Given that the ORBITA trial was a UK-based study, we further stratified individual centers according to whether they were recruited into ORBITA trial. All 5 centers that participated in the ORBITA trial were categorized into ORBITA center trials, and the remaining cohort was categorized into non-ORBITA center trial groups for the subgroup analysis.

Statistical Analysis

Categorical variables were compared using the Pearson χ^2 test, whereas continuous or ordinal variables were compared using the Wilcox rank-sum test. For the trend analysis, proportions of stable PCI

procedures were calculated for each month using the total number of PCI procedures as the denominator. Cochrane Armitage test was used to study statistically significant differences in trends. Population estimates from the Office of National Statistics were used to calculate rates of PCI per 100 000 for each year. The incidence rate of PCI volume for stable angina was examined between periods before and after the publication of COURAGE and ORBITA trials using the Poisson regression model adjusted for temporal trend.

We undertook 4 separate analyses: (1) temporal trends nationally on a triennial basis; (2) rates of elective PCI before and after the publication of the COURAGE trial; (3) rates of elective PCI before and after the publication of the ORBITA trial; and (4) rates of elective PCI before and after ORBITA trial in the 5 centers that recruited into the trial. The PCI volume rates were calculated per 100 000 population using publicly available population estimates from the Office of National Statistics.[20] To minimize the impact of historical bias, the COURAGE and ORBITA trial cohorts were limited to 12-month period before and after the publication of the full trial results. All statistical analyses were performed using Stata 16 MP (College Station, TX).

RESULTS

Temporal Trends

Between January 1, 2006, and December 31, 2019, 1 245 802 PCI procedures were undertaken in England and Wales, of which 430 248 (34.5%) were for stable angina (Figure S1). Overall, the elective PCI volume rates per 100 000 population increased from 50.7 in 2006 to 58.4 in 2019. The number of patients undergoing nonelective PCI increased from 45.9 in 2006 to 99.6 in 2019 per 100 000 population (Figure S2). The incidence rate of elective PCI volume after the COURAGE trial was published in 2007 was not different from before the trial was published (incidence rate ratio, 1.06 [95% CI, 0.69–1.62]). It also remained stable after the publication of the ORBITA trial in 2017, as shown in Figure 1 (incidence rate ratio, 0.96 [95% CI, 0.74–1.23]).

Clinical Characteristics

There were significant temporal trends in the clinical characteristics and procedural profile of patients undergoing elective PCI for stable angina during the study period. The mean age of patients undergoing elective PCI increased from 64.9±10.3 to 66.8±10.7 years. The proportion of men (74.8%–76.9%) and ethnic minorities (15.6%–19.1%) also increased during the study period. The proportion of patients who underwent PCI for Canadian Cardiovascular Society (CCS) angina classification class I almost doubled (5.1%–9.2%), whereas those who underwent PCI for CCS class IV angina remained stable (2.7%–3.1%). Equally, the proportion of patients who underwent PCI despite no limitation of physical activity (New York Heart Association class I) increased (36.9%–41.7%), with a much higher increase (45.9%–71.4%) in the rates of PCI in the absence of ischemia on stress test between 2006 and 2019. The frequency of relevant comorbidities, such as diabetes, hypercholesterolemia, hypertension, previous acute myocardial infarction, and previous PCI, also increased over time (P<0.001), as reported in Table 1. Finally, the use of adjuvant PCI interventions, such as intracoronary imaging, pressure wire, and rotational atherectomy, increased during the study period.

Table 2 shows the clinical and procedural characteristic changes 12 months before and after the COURAGE trial results were published in April 2007. Overall, there were no significant differences in the baseline demographics, comorbidities, and angiographic characteristics of patients before and after the publication of the trial results. The trends were generally similar to the historical trends, as shown in Table 1. However, the proportion of patients undergoing PCI for CCS class I angina declined from 5.1% to 4.8% after the publication of the COURAGE trial. Patients undergoing elective PCI without evidence of ischemia on stress test declined from 49.6% to 44.9% after the COURAGE trial was published in 2007. The clinical characteristics and procedural profile of patients undergoing elective PCI remained similar before and after the publication of the ORBITA trial, as reported in Table 3. The mean age, race, and sex were similar as well as the proportion of patients with CCS class I or CCS class IV. There were no significant changes in the risk profile, the indication of procedures, preprocedure stress testing, or CCS angina classification between the ORBITA trial participating centers and non-ORBITA trial participating centers.

Subgroup Analysis

Temporal analysis of centers that recruited patients into the ORBITA trial from ORBITA trial participating centers showed similar stable trends in the rates of elective PCI volume (4.0 in 2006 to 6.2 in 2019) per 100 000 population compared with all other PCI centers (47.5 in 2006 to 52.2 in 2019) in England and Wales during the study period (Figure 2). In the sensitivity analysis of each participating center in the ORBITA trial, the PCI volume remained relatively stable across each center during the 12 months before and after 12 months of the trial result publication (Figure 3).

DISCUSSION

This analysis of an all-comer, national PCI registry from England and Wales shows temporal trends of PCI

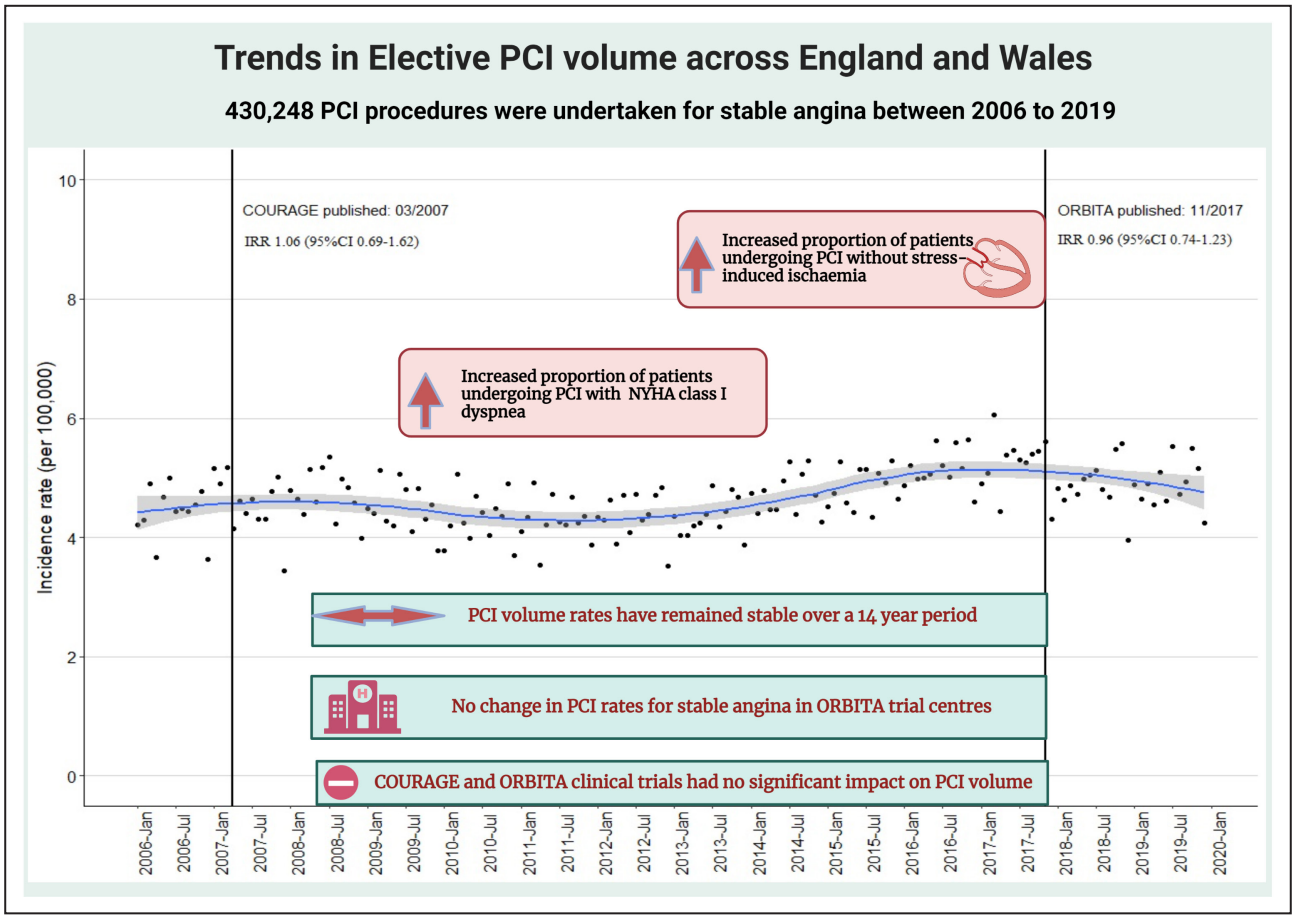

Figure 1. Temporal trends in rates of elective percutaneous coronary intervention (PCI) volume per 100 000 population for stable angina in England and Wales.
COURAGE indicates Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; IRR, incidence rate ratio; NYHA, New York Heart Association; and ORBITA, Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina.

practice for stable angina over 14 years. Publication of the COURAGE trial and, more recently, ORBITA trial has shown no significant effect on elective PCI practice in England and Wales, with little detectable change in the clinical or procedural characteristics of patients undergoing these procedures. There were no significant changes on elective PCI activity following the publication of ORBITA trial, even in the ORBITA trial participating centers, despite the ORBITA trial showing no benefit of PCI over placebo procedure on angina symptoms. We found that almost 1 in 10 patients undergoing PCI for stable angina had no angina symptoms, and two-thirds had no evidence of ischemia on stress testing, highlighting a significant discordance in current clinical practice, guideline recommendations, and adoption of major trial results.

A notable finding of our analysis was the lack of impact of COURAGE[14] and ORBITA[15] trials on PCI rates for stable angina. It is particularly interesting that the rate of elective PCI remained stable even in the 5 ORBITA trial recruiting centers before and after the trial was reported. There are several possible explanations for the apparent lack of impact of such landmark trials on clinical practice in elective PCI. First, it could be that PCI practice in England and Wales was already consistent with the results of the COURAGE and ORBITA trials. The United Kingdom has a universal National Health System, which is well integrated with primary care. Patients with stable coronary disease are likely to have benefited from intensive primary prevention and optimization of medical therapy.[21,22] Nevertheless, the fact that a significant proportion of patients undergoing PCI were without angina symptoms would be discordant with such a hypothesis. The COURAGE and ORBITA trials generated much debate about the invasive management of stable angina. In both cases, there was a school of thought questioning their relevance to routine all-comers practice,[1,9] with other studies, such as Fractional Flow Reserve versus Angiography for Multivessel Evaluation 2, suggesting that PCI in stable coronary artery disease may reduce longer-term acute myocardial infarction.[23] This may explain why the

Table 1. Temporal Trends in the Baseline Patient Demographics, Procedural Details, and Unadjusted Outcomes

Variable	Total	2006/2007/2008	2009/2010/2011	2012/2013/2014	2015/2016/2017	2018/2019	*P* trend value
No. of procedures	430 428	86 836	89 087	92 024	98 649	63 652	
Age, y	430 428	64.9±10.3	65.6±10.6	66.0±10.8	66.6±10.8	66.8±10.7	<0.001
BMI, kg/m^2	257 761	28.6±4.9	28.9±5.1	29.0±5.1	29.0±5.2	29.1±5.1	<0.001
Female sex	104 181	21 925 (25.2)	21 780 (24.4)	21 791 (23.7)	23 351 (23.7)	15 334 (24.1)	<0.001
Race							<0.001
White	266 704	50 334 (84.4)	59 518 (86.0)	56 952 (82.7)	60 377 (81.8)	39 523 (80.9)	
BAME	53 708	9337 (15.6)	9689 (14.0)	11 910 (17.3)	13 446 (18.2)	9326 (19.1)	
Left ventricular ejection fraction							<0.001
Good (≥50%)	381 156	78 115 (90.0)	77 577 (87.1)	81 714 (88.8)	87 672 (88.9)	56 078 (88.1)	
Fair (30%–49%)	39 919	6909 (8.0)	9633 (10.8)	8485 (9.2)	8732 (8.9)	6160 (9.7)	
Poor (≤29%)	9173	1812 (2.1)	1877 (2.1)	1825 (2.0)	2245 (2.3)	1414 (2.2)	
CCS angina grade							<0.001
No angina	24 772	3606 (5.1)	4084 (5.2)	4824 (5.7)	7136 (8.0)	5122 (9.2)	
No limitation of physical activity	38 478	8676 (12.2)	7684 (9.8)	7549 (8.9)	8644 (9.7)	5925 (10.7)	
Slight limitation of ordinary activity	164 864	33 172 (46.8)	34 188 (43.7)	36 006 (42.7)	37 501 (42.3)	23 997 (43.2)	
Marked limitation of ordinary activity	138 711	23 599 (33.3)	29 789 (38.1)	33 645 (39.9)	32 956 (37.2)	18 722 (33.7)	
Symptoms at rest or minimal activity	11 005	1901 (2.7)	2510 (3.2)	2389 (2.8)	2469 (2.8)	1736 (3.1)	
ECG ischemia							<0.001
No	193 624	25 455 (45.9)	31 905 (44.2)	43 097 (55.7)	54 758 (65.0)	38 409 (71.4)	
On resting ECG	45 922	8167 (14.7)	10 502 (14.6)	10 242 (13.2)	10 577 (12.6)	6434 (12.0)	
On stress ECG	76 206	18 710 (33.8)	23 535 (32.6)	17 244 (22.3)	11 703 (13.9)	5014 (9.3)	
On perfusion scan	27 145	3078 (5.6)	6167 (8.6)	6795 (8.8)	7168 (8.5)	3937 (7.3)	
NYHA dyspnea							<0.001
No limitation of physical activity	136 791	24 477 (36.9)	25 421 (33.6)	29 274 (35.7)	35 328 (41.7)	22 291 (41.7)	
Slight limitation of ordinary activity	154 967	30 673 (46.3)	34 463 (45.5)	35 595 (43.4)	33 518 (39.6)	20 718 (38.8)	
Marked limitation of ordinary physical activity	63 927	10 384 (15.7)	14 350 (19.0)	15 655 (19.1)	14 349 (16.9)	9189 (17.2)	
Symptoms at rest or minimal activity	6368	762 (1.1)	1478 (2.0)	1414 (1.7)	1494 (1.8)	1220 (2.3)	
Smoking status							<0.001
Nonsmoker	157 929	27 270 (39.5)	31 348 (39.5)	34 623 (41.9)	38 399 (43.5)	26 289 (45.9)	
Current smoker	46 834	8998 (13.0)	10 698 (13.5)	10 577 (12.8)	10 223 (11.6)	6338 (11.1)	
Ex-smoker	171 655	32 732 (47.4)	37 280 (47.0)	37 384 (45.3)	39 573 (44.9)	24 686 (43.1)	
Comorbidities							
Prior PCI	151 086	20 495 (25.9)	29 257 (33.7)	34 798 (39.0)	39 827 (41.1)	26 709 (42.7)	<0.001
Prior MI	138 424	23 544 (32.4)	28 469 (35.1)	30 688 (35.3)	33 703 (35.1)	22 020 (35.2)	<0.001
Diabetes	93 284	15 211 (19.2)	18 558 (21.6)	20 296 (23.2)	23 489 (24.5)	15 730 (25.3)	<0.001
Hypertension	251 234	42 418 (55.2)	52 792 (62.1)	55 123 (63.4)	61 220 (64.6)	39 681 (65.3)	<0.001
Hypercholesterolemia	265 371	49 194 (64.0)	59 066 (69.4)	57 962 (66.7)	61 639 (65.1)	37 510 (61.8)	<0.001
Family history of heart disease	180 105	34 325 (50.6)	39 813 (51.4)	38 616 (47.4)	40 893 (45.8)	26 458 (45.3)	<0.001
Renal disease	8985	1475 (2.0)	1834 (2.1)	2126 (2.4)	2107 (2.2)	1443 (2.3)	<0.001
Peripheral vascular disease	19 278	3465 (4.5)	4726 (5.6)	4583 (5.3)	4134 (4.4)	2370 (3.9)	<0.001
Prior cerebrovascular accident	14 804	2364 (3.1)	3306 (3.9)	3368 (3.9)	3516 (3.7)	2250 (3.7)	<0.001
Procedural details							
Femoral	160 199	62 539 (76.0)	46 392 (53.4)	29 015 (32.2)	16 167 (16.8)	6086 (9.9)	<0.001
Radial	235 032	18 662 (22.7)	37 826 (43.6)	56 074 (62.3)	72 560 (75.5)	49 910 (81.5)	

(*Continued*)

Table 1. Continued

Variable	Total	2006/2007/2008	2009/2010/2011	2012/2013/2014	2015/2016/2017	2018/2019	*P* trend value
Multiple	21 149	1063 (1.3)	2600 (3.0)	4921 (5.5)	7335 (7.6)	5230 (8.5)	
Glycoprotein IIb/IIIa inhibitor	27 450	13 733 (17.8)	6560 (8.0)	3924 (4.6)	2199 (2.4)	1034 (1.9)	<0.001
Ticagrelor	20 534	0 (0.0)	7 (<1)	3199 (3.8)	10 316 (11.9)	7012 (13.0)	<0.001
Prasugrel	4407	1 (<1)	541 (0.7)	1775 (2.1)	1440 (1.7)	650 (1.2)	<0.001
Warfarin	5550	829 (1.2)	1028 (1.3)	1581 (1.9)	1558 (1.8)	554 (1.0)	<0.001
IVUS	31 001	2257 (3.2)	4818 (6.5)	6667 (8.3)	9080 (10.3)	8179 (14.3)	<0.001
Pressure wire	59 730	3876 (5.6)	9100 (12.4)	13 682 (17.1)	17 831 (20.3)	15 241 (26.7)	<0.001
OCT	9325	975 (1.4)	1024 (1.4)	2161 (2.7)	2781 (3.2)	2384 (4.2)	<0.001
No. of drug-eluting stents							
0	73 975	27 209 (33.8)	21 872 (25.5)	13 264 (15.1)	10 701 (11.3)	929 (12.8)	<0.001
1	150 925	28 114 (34.9)	34 519 (40.3)	40 192 (45.8)	44 693 (47.1)	3407 (47.0)	
2	81 455	15 527 (19.3)	18 593 (21.7)	21 195 (24.2)	24 301 (25.6)	1839 (25.4)	
≥3	49 670	9603 (11.9)	10 756 (12.5)	13 041 (14.9)	15 194 (16.0)	1076 (14.8)	
No. of lesions treated							
1	241 803	53 232 (63.2)	59 571 (67.4)	60 833 (67.3)	63 286 (65.8)	4881 (65.9)	<0.001
2	91 023	21 596 (25.6)	21 381 (24.2)	21 851 (24.2)	24 379 (25.3)	1816 (24.5)	
≥3	33 839	9427 (11.2)	7471 (8.4)	7653 (8.5)	8578 (8.9)	710 (9.6)	
No. of stents used							
0	34 008	6183 (7.4)	8138 (9.3)	8339 (9.3)	10 390 (10.8)	958 (13.1)	<0.001
1	177 896	41 227 (49.1)	44 123 (50.3)	44 088 (49.3)	45 068 (46.9)	3390 (46.5)	
2	93 942	22 055 (26.3)	22 434 (25.5)	22 839 (25.5)	24 759 (25.8)	1855 (25.4)	
≥3	58 651	14 449 (17.2)	13 110 (14.9)	14 161 (15.8)	15 840 (16.5)	1091 (15.0)	
No. of vessels treated							<0.001
1	322 483	65 459 (76.2)	68 264 (77.7)	69 882 (77.1)	72 409 (75.0)	46 469 (74.9)	
2	83 128	17 365 (20.2)	16 480 (18.8)	17 118 (18.9)	19 665 (20.4)	12 500 (20.1)	
≥3	17 244	3028 (3.5)	3071 (3.5)	3607 (4.0)	4431 (4.6)	3107 (5.0)	
Target vessel for PCI							
Graft*	12 809	2920 (3.6)	3012 (3.4)	2722 (3.0)	2626 (2.7)	1529 (2.5)	<0.001
LMS*	19 859	2354 (2.9)	3036 (3.5)	4718 (5.2)	6049 (6.3)	3702 (6.1)	<0.001
LAD*	212 862	40 299 (49.3)	43 398 (49.5)	45 628 (50.5)	50 299 (52.3)	33 238 (54.6)	<0.001
LCX*	107 141	21 970 (26.9)	22 876 (26.1)	22 705 (25.1)	24 483 (25.5)	15 107 (24.8)	<0.001
RCA*	146 085	31 104 (38.0)	31 212 (35.6)	30 918 (34.2)	32 322 (33.6)	20 529 (33.7)	<0.001
Multiple vessels*	100 967	19 675 (24.1)	19 392 (22.1)	20 847 (23.1)	24 765 (25.8)	16 288 (26.8)	<0.001
Chronic total occlusion	44 696	9716 (13.0)	10 998 (13.6)	11 330 (13.5)	11 774 (12.8)	878 (12.0)	<0.001
Stent length	300 501	23.3±12.6	24.8±14.4	27.2±16.3	30.1±17.9	31.5±18.1	<0.001
Stent diameter	291 698	3.2±0.5	3.3±0.6	3.3±0.6	3.4±0.6	3.4±0.6	<0.001
Outcomes							
In-hospital MACCE	5448	1468 (1.7)	1240 (1.4)	1124 (1.2)	992 (1.0)	624 (1.0)	<0.001
In-hospital mortality	503	97 (0.1)	96 (0.1)	91 (0.1)	139 (0.1)	80 (0.1)	0.070
Bleeding complications	1399	359 (0.4)	306 (0.3)	287 (0.3)	300 (0.3)	147 (0.2)	<0.001

Data are given as mean±SD or number (percentage). BAME indicates Black, Asian and Minority Ethnic; BMI, body mass index; CCS, Canadian Cardiovascular Society; IVUS, intravascular ultrasound; LAD, left anterior descending; LCX, left circumflex artery; LMS, left main stem; MACCE, major adverse cardiac and cerebrovascular event; MI, myocardial infarction; NYHA, New York Heart Association; OCT, optical coherence tomography; and PCI, percutaneous coronary intervention; and RCA, right coronary artery.

*Not mutually exclusive, cumulative total percentage may be >100%.

publication of these trials has not significantly changed the practice, and some operators may not have concurred with these trial results. Finally, although there are no financial incentives for treating physicians in the National Health System driven by volume of procedures undertaken, some patients may have given preference to invasive management with PCI over optimal medical therapy.

Table 2. Changes in Clinical Characteristics and Procedural Profile 12 months Before and After the Publication of COURAGE Trial

Variable	Total	Pre-COURAGE trial (March 2006–March 2007)	Post-COURAGE trial (April 2007–April 2008)	*P* value
No. of procedures	61 999	30 461	31 538	
Age, y	61 999	64.7±10.2	64.9±10.3	0.007
BMI, kg/m^2	38 594	28.4±4.8	28.8±4.9	<0.001
Female sex	15 592	7697 (25.3)	7895 (25.0)	0.50
Race				0.004
White	36 597	18 151 (86.7)	18 446 (85.7)	
BAME	5870	2793 (13.3)	3077 (14.3)	
Left ventricular ejection fraction				<0.001
Good (≥50%)	56 126	27 891 (91.6)	28 235 (89.5)	
Fair (30%–49%)	4671	2069 (6.8)	2602 (8.3)	
Poor (≤29%)	1202	501 (1.6)	701 (2.2)	
CCS angina grade				<0.001
No angina	2474	1243 (5.1)	1231 (4.8)	
No limitation of physical activity	6253	3087 (12.7)	3166 (12.3)	
Slight limitation of ordinary activity	23 631	11 884 (48.8)	11 747 (45.8)	
Marked limitation of ordinary activity	16 254	7508 (30.8)	8746 (34.1)	
Symptoms at rest or minimal activity	1388	622 (2.6)	766 (3.0)	
ECG ischemia				<0.001
No	17 890	8770 (49.6)	9120 (44.9)	
On resting ECG	5388	2584 (14.6)	2804 (13.8)	
On stress ECG	12 768	5567 (31.5)	7201 (35.5)	
On perfusion scan	1941	772 (4.4)	1169 (5.8)	
NYHA dyspnea				0.99
No limitation of physical activity	17 237	8375 (36.9)	8862 (37.0)	
Slight limitation of ordinary activity	21 476	10 454 (46.1)	11 022 (46.0)	
Marked limitation of ordinary physical activity	7391	3581 (15.8)	3810 (15.9)	
Symptoms at rest or minimal activity	537	260 (1.1)	277 (1.2)	
Smoking status				*<0.001*
Nonsmoker	19 132	9159 (40.8)	9973 (38.8)	
Current smoker	6169	2908 (12.9)	3261 (12.7)	
Ex-smoker	22 854	10 406 (46.3)	12 448 (48.5)	
Comorbidities				
Prior PCI	14 003	6509 (24.4)	7494 (25.9)	<0.001
Prior MI	16 514	7755 (31.1)	8759 (33.0)	<0.001
Diabetes	10 565	4771 (18.1)	5794 (19.4)	<0.001
Hypertension	29 791	13 518 (53.1)	16 273 (57.1)	<0.001
Hypercholesterolemia	34 721	15 693 (61.7)	19 028 (66.8)	<0.001
Family history of heart disease	23 660	10 970 (49.5)	12 690 (49.9)	0.35
Renal disease	1007	461 (1.9)	546 (1.9)	0.63
Peripheral vascular disease	2351	1108 (4.4)	1243 (4.4)	0.96
Prior cerebrovascular accident	1555	659 (2.6)	896 (3.1)	<0.001
Procedural details				
Femoral	45 638	24 030 (82.2)	21 608 (73.7)	<0.001
Radial	12 222	4904 (16.8)	7318 (25.0)	<0.001
Glycoprotein IIb/IIIa inhibitor	10 256	5689 (21.2)	4567 (16.4)	<0.001
Warfarin	578	289 (1.2)	289 (1.2)	0.95

(*Continued*)

Table 2. (Continued)

Variable	Total	Pre-COURAGE trial (March 2006–March 2007)	Post-COURAGE trial (April 2007–April 2008)	*P* value
IVUS	1394	527 (2.1)	867 (3.5)	<0.001
Pressure wire	2495	992 (4.0)	1503 (6.1)	<0.001
OCT	775	379 (1.5)	396 (1.6)	0.39
No. of drug-eluting stents				<0.001
0	19825	8784 (31.7)	11041 (38.0)	
1	19656	10043 (36.2)	9613 (33.1)	
2	10662	5429 (19.6)	5233 (18.0)	
≥3	6630	3452 (12.5)	3178 (10.9)	
No. of lesions treated				<0.001
1	37633	17356 (60.7)	20277 (64.9)	
2	15418	7636 (26.7)	7782 (24.9)	
≥3	6827	3624 (12.7)	3203 (10.2)	
No. of stents used				<0.001
0	4233	1825 (6.2)	2408 (8.0)	
1	29278	14242 (48.6)	15036 (49.9)	
2	15577	7806 (26.6)	7771 (25.8)	
≥3	10346	5424 (18.5)	4922 (16.3)	
No. of vessels treated				<0.001
1	46690	22311 (74.3)	24379 (77.8)	
2	12529	6530 (21.7)	5999 (19.1)	
≥3	2159	1196 (4.0)	963 (3.1)	
Target vessel for PCI				
Graft*	2139	965 (3.5)	1174 (3.9)	0.002
LMS*	1631	781 (2.8)	850 (2.8)	0.72
LAD*	28507	13960 (50.0)	14547 (48.8)	0.002
LCX*	15659	7784 (27.9)	7875 (26.4)	<0.001
RCA*	22031	10864 (38.9)	11167 (37.4)	<0.001
Multiple vessels*	14263	7319 (26.2)	6944 (23.3)	<0.001
Chronic total occlusion	6916	3258 (13.4)	3658 (13.1)	0.42
Stent length, mm	43167	23.0±12.2	23.2±12.7	0.024
Stent diameter, mm	41779	3.2±0.5	3.2±0.5	<0.001
Outcomes				
In-hospital MACCE	1070	559 (1.8)	511 (1.6)	0.04
In-hospital mortality	71	36 (0.1)	35 (0.1)	0.79
Bleeding complications	263	140 (0.5)	123 (0.4)	0.18

Data are given as mean±SD or number (percentage). BAME indicates Black, Asian and Minority Ethnic; BMI, body mass index; CCS, Canadian Cardiovascular Society; COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; IVUS, intravascular ultrasound; LAD, left anterior descending; LCX, left circumflex artery; LMS, left main stem; MACCE, major adverse cardiac and cerebrovascular event; MI, myocardial infarction; NYHA, New York Heart Association; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; and RCA, right coronary artery.

*Not mutually exclusive, cumulative total percentage may be >100%.

The integration of the results of RCTs into clinical practice is important. Still, it remains suboptimal because of the highly selected nature of the trial population, strict inclusion/exclusion criteria, and use of surrogate or diverse composite end points that may not be relevant to clinical practice.[16,24] By contrast, observational registry data often provide important insights into real-world implications of randomized controlled trials, clinical practice changes, and physician behavior. There are a dynamic range of factors that can determine how the results of RCTs influence subsequent clinical practice. Previous studies evaluating how clinical practice responds to changes in guidelines and trial data have found significant variations, such as use of thrombus aspiration devices during primary PCI, intra-aortic balloon pump in patients with myocardial

Table 3. Changes in Practice 12months Before and After the Publication of ORBITA Trial by ORBITA Trial–Participating Centers Versus Nonparticipating Centers

Variable	Total ORBITA trial–participating centers	Pre-ORBITA trial (October 2016–October 2017)	Post-ORBITA trial (November 2017–November 2018)	*P* value	Total nonparticipating centers	Pre-ORBITA trial (October 2016–October 2017)	Post-ORBITA trial (November 2017–November 2018)	*P* value
No. of procedures	7.485	3756	3729		63914	32556	31358	
Age, y	7485	68.3±10.5	67.9±10.3	0.13	63914	66.6±10.8	66.7±10.7	0.33
BMI, kg/m^2	4751	28.8±5.2	28.9±5.1	0.56	37038	29.0±5.3	29.1±5.2	0.097
Female sex	1819	917 (24.4)	902 (24.2)	0.82	15352	7717 (23.7)	7635 (24.3)	0.057
Race				<0.001				0.34
White	3981	1832 (71.3)	2149 (76.1)		40107	20471 (82.0)	19636 (81.7)	
BAME	1411	736 (28.7)	675 (23.9)		8875	4480 (18.0)	4395 (18.3)	
Left ventricular ejection fraction				0.42				0.07
Good (≥50%)	6363	3191 (85.0)	3172 (85.1)		56826	29028 (89.2)	27798 (88.6)	
Fair (30%–49%)	991	492 (13.1)	499 (13.4)		5670	2806 (8.6)	2864 (9.1)	
Poor (≤29%)	131	73 (1.9)	58 (1.6)		1418	722 (2.2)	696 (2.2)	
CCS angina grade				<0.001				0.001
No angina	596	300 (8.6)	296 (8.8)		4836	2419 (8.2)	2417 (8.7)	
No limitation of physical activity	908	440 (12.7)	468 (14.0)		5905	2969 (10.1)	2936 (10.6)	
Slight limitation of ordinary activity	3562	1760 (50.6)	1802 (53.8)		23825	12183 (41.5)	11642 (42.0)	
Marked limitation of ordinary activity	1564	861 (24.8)	703 (21.0)		20918	10994 (37.4)	9924 (35.8)	
Symptoms at rest or minimal activity	194	114 (3.3)	80 (2.4)		1586	813 (2.8)	773 (2.8)	
ECG ischemia				0.01				<0.001
No	5901	2906 (81.8)	2995 (84.2)		36199	18126 (65.2)	18073 (68.2)	
On resting ECG	718	368 (10.4)	350 (9.8)		6644	3372 (12.1)	3272 (12.3)	
On stress ECG	260	147 (4.1)	113 (3.2)		6834	3891 (14.0)	2943 (11.1)	
On perfusion scan	232	133 (3.7)	99 (2.8)		4650	2432 (8.7)	2218 (8.4)	
NYHA dyspnea				0.18				<0.001
No limitation of physical activity	2429	1227 (35.5)	1202 (35.4)		23210	11911 (43.0)	11299 (42.8)	
Slight limitation of ordinary activity	3402	1682 (48.7)	1720 (50.6)		20282	10536 (38.0)	9746 (36.9)	
Marked limitation of ordinary physical activity	892	474 (13.7)	418 (12.3)		9257	4737 (17.1)	4790 (18.2)	

(*Continued*)

Table 3. Continued

Variable	Total ORBITA trial–participating centers	Pre-ORBITA trial (October 2016–October 2017)	Post-ORBITA trial (November 2017–November 2018)	*P* value	Total nonparticipating centers	Pre-ORBITA trial (October 2016–October 2017)	Post-ORBITA trial (November 2017–November 2018)	*P* value
Symptoms at rest or minimal activity	132	72 (2.1)	60 (1.8)		1069	516 (1.9)	553 (2.1)	
Smoking status				0.46				<0.001
Nonsmoker	3020	1504 (44.5)	1516 (43.5)		25 680	12 893 (44.2)	12 787 (45.5)	
Current smoker	653	329 (9.7)	324 (9.3)		6470	3263 (11.2)	3207 (11.4)	
Ex-smoker	3192	1546 (45.8)	1646 (47.2)		25 086	13 002 (44.6)	12 084 (43.0)	
Comorbidities								
Prior PCI	3038	1536 (40.9)	1502 (40.3)	0.59	26 211	13 192 (41.1)	13 019 (42.2)	0.008
Prior MI	2302	1143 (30.7)	1159 (31.2)	0.66	22 081	11 046 (34.8)	11 035 (35.9)	0.003
Diabetes	1884	932 (25.6)	952 (25.9)	0.75	15 694	7864 (24.9)	7830 (25.6)	0.041
Hypertension	4661	2297 (63.9)	2364 (64.6)	0.52	40 229	20 501 (64.9)	19 728 (65.5)	0.13
Hypercholesterolemia	4710	2346 (65.2)	2364 (64.6)	0.57	39 657	20 774 (65.8)	18 883 (62.7)	<0.001
Family history of heart disease	3210	1589 (45.9)	1621 (46.4)	0.65	26 244	13 240 (44.7)	13 004 (45.7)	0.014
Renal disease	200	57 (1.5)	143 (3.9)	<0.001	1370	684 (2.2)	686 (2.3)	0.46
Peripheral vascular disease	323	145 (4.0)	178 (4.9)	0.086	2542	1319 (4.2)	1223 (4.1)	0.47
Prior cerebrovascular accident	364	196 (5.5)	168 (4.6)	0.094	2269	1163 (3.7)	1106 (3.7)	0.94
Procedural details								
Femoral	946	521 (14.0)	425 (11.4)	0.004	7873	4445 (14.0)	3428 (11.4)	<0.001
Radial	5738	2828 (75.8)	2910 (78.3)	0.004	49 194	24 916 (78.3)	24 278 (80.7)	<0.001
Glycoprotein IIb/IIIa inhibitor	112	62 (1.7)	50 (1.3)	0.26	1215	629 (2.2)	586 (2.2)	1.00
Clopidogrel	5683	2779 (76.2)	2904 (78.9)	0.007	39 490	20 864 (73.8)	18 626 (71.0)	<0.001
Ticagrelor	597	262 (7.2)	335 (9.1)	0.003	7305	3803 (13.4)	3502 (13.4)	0.85
Prasugrel	70	38 (1.0)	32 (0.9)	0.45	771	429 (1.5)	342 (1.3)	0.035
Warfarin	82	48 (1.3)	34 (0.9)	0.11	773	452 (1.6)	321 (1.2)	<0.001
IVUS	1507	759 (23.3)	748 (22.8)	0.58	5787	2751 (9.5)	3036 (10.9)	<0.001
Pressure wire	1831	867 (26.7)	964 (29.3)	0.016	12 924	5952 (20.5)	6972 (25.0)	<0.001
OCT	178	92 (2.8)	86 (2.6)	0.60	1807	817 (2.8)	990 (3.5)	<0.001
No. of drug-eluting stents				0.55				0.006
0	430	312 (8.6)	118 (9.4)		5117	3688 (11.8)	1429 (13.0)	
1	2174	1620 (44.7)	554 (44.3)		19 878	14 721 (47.0)	5157 (46.9)	
2	1336	984 (27.1)	352 (28.1)		10 858	8095 (25.8)	2763 (25.1)	
≥3	937	710 (19.6)	227 (18.1)		6497	4840 (15.4)	1657 (15.1)	

(*Continued*)

Table 3. Continued

Variable	Total ORBITA trial–participating centers	Pre-ORBITA trial (October 2016–October 2017)	Post-ORBITA trial (November 2017–November 2018)	*P* value	Total nonparticipating centers	Pre-ORBITA trial (October 2016–October 2017)	Post-ORBITA trial (November 2017–November 2018)	*P* value
No. of lesions treated				0.38				0.08
1	3060	2299 (62.5)	761 (60.3)		28 186	20 780 (65.5)	7406 (65.8)	
2	1306	959 (26.1)	347 (27.5)		10 908	8119 (25.6)	2789 (24.8)	
≥3	575	421 (11.4)	154 (12.2)		3873	2815 (8.9)	1058 (9.4)	
No. of stents used				0.76				<0.001
0	422	310 (8.5)	112 (8.9)		5630	3852 (12.2)	1508 (13.6)	
1	2196	1637 (44.6)	559 (44.6)		19.774	14 641 (46.2)	5133 (46.2)	
2	1341	992 (27.0)	349 (27.8)		10955	8162 (25.8)	2793 (25.1)	
≥3	963	729 (19.9)	234 (18.7)		6716	5036 (15.9)	1680 (15.1)	
No. of vessels treated				0.18				0.65
1	5060	2504 (66.7)	2556 (68.6)		47 179	24 062 (75.5)	23 117 (75.6)	
2	1857	955 (25.4)	902 (24.2)		12 505	6423 (20.1)	6082 (19.9)	
≥3	565	297 (7.9)	268 (7.2)		2762	1395 (4.4)	1367 (4.5)	
Target vessel for PCI								
Graft*	191	80 (2.1)	111 (3.0)	0.02	1698	842 (2.7)	856 (2.9)	0.15
LMS*	599	320 (8.5)	279 (7.5)	0.10	3501	1799 (5.7)	1702 (5.7)	0.92
LAD*	4208	2099 (55.9)	2109 (56.7)	0.51	32 921	16 705 (52.9)	16 216 (54.1)	0.003
LCX*	1919	976 (26.0)	943 (25.3)	0.52	15 446	8040 (25.5)	7406 (24.7)	0.03
RCA*	2479	1251 (33.3)	1228 (33.0)	0.77	20 721	10 584 (33.5)	10 137 (33.8)	0.43
Multiple-vessel PCI	2440	1261 (33.6)	1179 (31.7)	0.07	15 881	8088 (25.6)	7793 (26.0)	0.27
Chronic total occlusion	626	464 (12.9)	162 (12.8)	0.96	5042	3765 (12.3)	1277 (11.6)	0.04
Stent length, mm	4524	31.3±19.2	31.9±18.1	0.30	36 141	30.8±18.0	31.1±17.8	0.19
Stent diameter, mm	4420	3.4±0.6	3.4±0.6	0.95	35 344	3.4±0.6	3.4±0.6	0.01
Outcomes								
In-hospital MACCE	53	28 (0.7)	25 (0.7)	0.70	649	324 (1.0)	325 (1.0)	0.60
In-hospital mortality	10	7 (0.2)	3 (0.1)	0.21	84	44 (0.1)	40 (0.1)	0.79
Bleeding complications	22	6 (0.2)	16 (0.4)	0.03	177	100 (0.3)	77 (0.2)	0.14

Data are given as mean±SD or number (percentage). BAME indicates Black, Asian and Minority Ethnic; BMI, body mass index; CCS, Canadian Cardiovascular Society; IVUS, intravascular ultrasound; LAD, left anterior descending; LCX, left circumflex artery; LMS, left main stem; MACCE, major adverse cardiac and cerebrovascular event; MI, myocardial infarction; NYHA, New York Heart Association; OCT, optical coherence tomography; ORBITA, Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina; PCI, percutaneous coronary intervention; and RCA, right coronary artery.

*Not mutually exclusive, cumulative total percentage may be >100%.

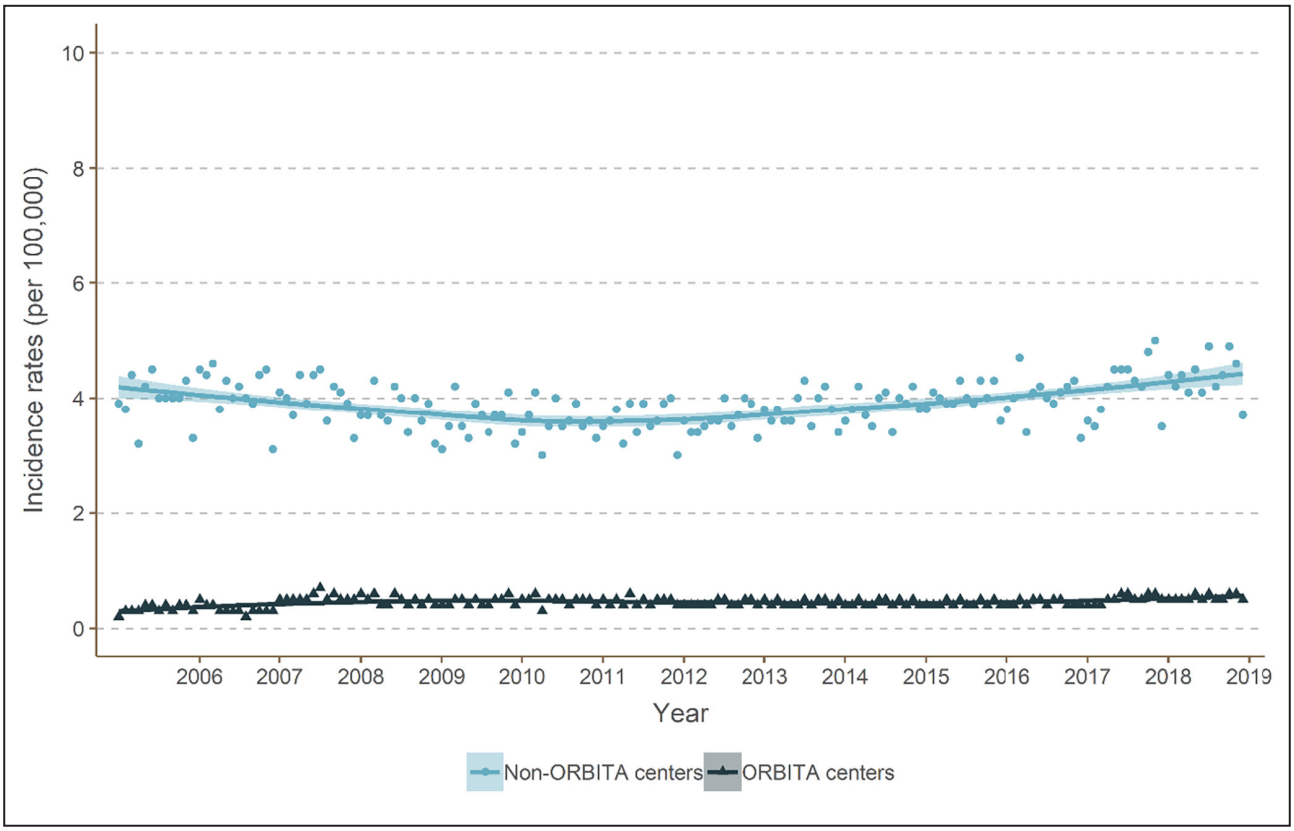

Figure 2. Temporal trends in percutaneous coronary intervention volume for stable angina in ORBITA (Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina) trial vs non-ORBITA trial centers in England and Wales.

infarction, and other interventional therapies.[25–27] In the present study, we leveraged data from a national PCI registry of a universal health care system to study temporal changes in clinical practice and found no meaningful impact of randomized controlled trials, such as COURAGE and ORBITA trials, on elective PCI practice in the United Kingdom.

Several studies have evaluated the trends in the total PCI volume, reporting significant variations in PCI rates over the past decade,[28–32] although they have not studied these changes in relation to publication of landmark trials. An analysis of 26 388 patients undergoing PCI from the Northern New England Cardiovascular Disease PCI registry found that elective PCI rates for stable angina declined from 20.9% to 16.1% between 2006 and 2009.[32] Kataruka et al analyzed all PCI procedures performed in nonfederal hospitals in Washington State between 2005 and 2017, showing an overall increase of 20.0%, with a 30.3% increase in elective PCI.[33] More recently, a binational comparative analysis from Japan and the United States showed similar variations in PCI practice, where increased nonelective PCI procedures mainly drove an increase in PCI volume in the United States.[31] In contrast, higher rates of PCI volume in Japan were primarily driven by increased elective PCI. The present study from a national unified health care system demonstrates an overall stable trend in elective PCI volume and an increased PCI volume for nonelective indications. Interestingly, the temporal trends of elective PCI remained stable both in terms of absolute numbers and the number of PCI procedures per 100 000 population.

The role of PCI in the treatment of stable angina above and beyond optimal medical therapy is contentious, with data from contemporary studies failing to demonstrate any mortality advantage,[11,13,14] despite a subgroup analysis of the COURAGE trial showing that the addition of PCI to optimal medical therapy is associated with a significant reduction in ischemia burden.[34] Consequently, current guidelines and expert consensus advocate offering PCI only to patients who continue to experience angina despite optimal medical therapy.[35,36] Counterintuitively, we observed a significant increase in the proportion of patients undergoing PCI without angina symptoms in the present analysis. Furthermore, almost two-thirds of patients had no objective evidence of ischemia. Data from 500 154 PCI procedures from NCDR (National

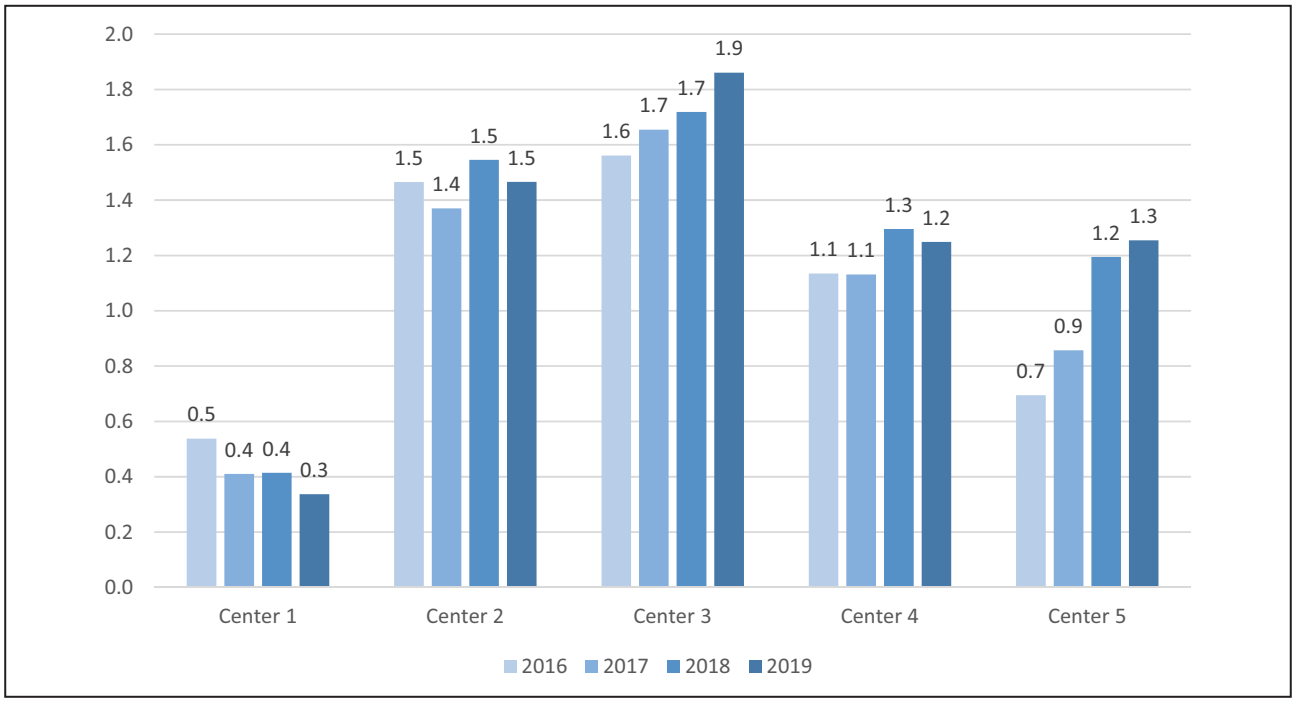

Figure 3. Trends in elective percutaneous coronary intervention activity for stable angina within ORBITA (Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina) trial participating center per 100 000 population.

Cardiovascular Data Registry) between 2009 and 2010 showed that nearly 12% of procedures were inappropriate.[37] Patient preference for PCI over continued medical therapy and a lack of clear consensus among operators about appropriate use of PCI for treatment of stable angina may be responsible for these observations.[38,39]

Our analysis has certain limitations. First, the BCIS registry does not capture pharmacological treatment of stable angina in the form of antianginal medications. Therefore, we were not able to assess whether patients were on optimal medical therapy before undergoing PCI. The BCIS registry database also lacks specific information about the noninvasive assessment of patients before PCI. Also, we did not have information about the improvement in symptoms or functional status after procedure, which would have allowed a more accurate assessment of translation of ORBITA trial results in clinical practice.

CONCLUSIONS

In this large national registry capturing almost all PCIs performed in England and Wales over 14 years, an increase in overall PCI volume was accompanied by stable trends in elective PCI rates. We were unable to detect any significant impact of the COURAGE or ORBITA trial on elective PCI activity nationally or even within the trial participating centers of the ORBITA trial. However, despite increasing case complexity, there was commensurate growth in PCI practice in low-risk cohort without angina symptoms, exertional dyspnea, or evidence of ischemia on ECG.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Figures S1–S2

REFERENCES

1. Brown DL, Redberg RF. Last nail in the coffin for PCI in stable angina? *Lancet*. 2018;391:3–4. doi: 10.1016/S0140-6736(17)32757-5
2. Vos T, Abajobir AA, Abate KH, Abbafati C, Abbas KM, Abd-Allah F, Abdulkader RS, Abdulle AM, Abebo TA, Abera SF. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the global burden of disease study 2016. *Lancet*. 2017;390:1211–1259. doi: 10.1016/S0140-6736(17)32154-2
3. Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis N, Neumann FJ, Robertson DH, DeLucca PT, DiBattiste PM, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med*. 2001;344:1879–1887. doi: 10.1056/NEJM200106213442501
4. Mehta SR, Cannon CP, Fox KA, Wallentin L, Boden WE, Spacek R, Widimsky P, McCullough PA, Hunt D, Braunwald E, et al. Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. *JAMA*. 2005;293:2908–2917. doi: 10.1001/jama.293.23.2908
5. de Winter RJ, Windhausen F, Cornel JH, Dunselman PH, Janus CL, Bendermacher PE, Michels HR, Sanders GT, Tijssen JG, Verheugt FW, et al. Early invasive versus selectively invasive management for acute coronary syndromes. *N Engl J Med*. 2005;353:1095–1104. doi: 10.1056/NEJMoa044259
6. Mehta SR, Granger CB, Boden WE, Steg PG, Bassand JP, Faxon DP, Afzal R, Chrolavicius S, Jolly SS, Widimsky P, et al. Early versus delayed invasive intervention in acute coronary syndromes. *N Engl J Med*. 2009;360:2165–2175. doi: 10.1056/NEJMoa0807986
7. Danchin N, Puymirat E, Steg PG, Goldstein P, Schiele F, Belle L, Cottin Y, Fajadet J, Khalife K, Coste P, et al. Five-year survival in patients with ST-segment-elevation myocardial infarction according to modalities of reperfusion therapy: the French registry on acute ST-elevation and non-ST-elevation myocardial infarction (FAST-MI) 2005 cohort. *Circulation*. 2014:1629–1636. doi: 10.1161/CIRCULATIONAHA.113.005874
8. Damman P, Jernberg T, Lindahl B, de Winter RJ, Jeppsson A, Johanson P, Held C, James SK. Invasive strategies and outcomes for non-ST-segment elevation acute coronary syndromes: a twelve-year experience from SWEDEHEART. *EuroIntervention*. 2016;12:1108–1116. doi: 10.4244/EIJY15M11_05
9. Bhatt DL, Gersh BJ, Steg PG, Harrington RA, Windecker S. Rediscovering the orbit of percutaneous coronary intervention after ORBITA. *Circulation*. 2018;137:2427–2429. doi: 10.1161/CIRCULATIONAHA.118.034596
10. Teoh Z, Al-Lamee RK. COURAGE, ORBITA, and ISCHEMIA: percutaneous coronary intervention for stable coronary artery disease. *Interv Cardiol Clin*. 2020;9:469–482. doi: 10.1016/j.iccl.2020.07.003
11. Sedlis SP, Hartigan PM, Teo KK, Maron DJ, Spertus JA, Mancini GJ, Kostuk W, Chaitman BR, Berman D, Lorin JD. Effect of PCI on long-term survival in patients with stable ischemic heart disease. *N Engl J Med*. 2015;373:1937–1946. doi: 10.1056/NEJMoa1505532
12. Stone GW, Hochman JS, Williams DO, Boden WE, Ferguson TB, Harrington RA, Maron DJ. Medical therapy with versus without revascularization in stable patients with moderate and severe ischemia: the case for community equipoise. *J Am Coll Cardiol*. 2016;67:81–99. doi: 10.1016/j.jacc.2015.09.056
13. Maron DJ, Hochman JS, Reynolds HR, Bangalore S, O'Brien SM, Boden WE, Chaitman BR, Senior R, López-Sendón J, Alexander KP. Initial invasive or conservative strategy for stable coronary disease. *N Engl J Med*. 2020;382:1395–1407. doi: 10.1056/NEJMoa1915922
14. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, Knudtson M, Dada M, Casperson P, Harris CL. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med*. 2007;356:1503–1516. doi: 10.1056/NEJMoa070829
15. Al-Lamee R, Thompson D, Dehbi H, Sen S, Tang K, Davies J, Keeble T, Mielewczik M, Kaprielian R, Malik IS. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomized controlled trial. *Lancet*. 2018;391:31–40. doi: 10.1016/S0140-6736(17)32714-9
16. Julian DG. Translation of clinical trials into clinical practice. *J Intern Med*. 2004;255:309–316. doi: 10.1046/j.1365-2796.2003.01282.x
17. Rashid M, Ludman PF, Mamas MA. British cardiovascular intervention society registry framework: a quality improvement initiative on behalf of the National Institute of cardiovascular outcomes research (NICOR). *Eur Heart J Qual Care Clin Outcomes*. 2019;5:292–297. doi: 10.1093/ehjqcco/qcz023
18. Noman A, Balasubramaniam K, Alhous MHA, Lee K, Jesudason P, Rashid M, Mamas MA, Zaman AG. Mortality after percutaneous coronary revascularization: prior cardiovascular risk factor control and improved outcomes in patients with diabetes mellitus. *Catheter Cardiovasc Interv*. 2017;89:1195–1204. doi: 10.1002/ccd.26882
19. Rashid M, Curzen N, Kinnaird T, Lawson CA, Myint PK, Kontopantelis E, Mohamed MO, Shoaib A, Gale CP, Timmis A, et al. Baseline risk, timing of invasive strategy and guideline compliance in NSTEMI: Nationwide analysis from MINAP. *Int J Cardiol*. 2020;301:7–13. doi: 10.1016/j.ijcard.2019.11.146
20. Wu J, Mafham M, Mamas MA, Rashid M, Kontopantelis E, Deanfield JE, de Belder MA, Gale CP. Place and underlying cause of death during the COVID-19 pandemic: retrospective cohort study of 3.5 million deaths in England and Wales, 2014 to 2020. *Mayo Clin Proc*. 2021:952–963. doi: 10.1016/j.mayocp.2021.02.007
21. Brindle P, Beswick A, Fahey T, Ebrahim S. Accuracy and impact of risk assessment in the primary prevention of cardiovascular disease: a systematic review. *Heart*. 2006;92:1752–1759. doi: 10.1136/hrt.2006.087932
22. Taylor F, Ward K, Moore TH, Burke M, Smith GD, Casas JP, Ebrahim S. Statins for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev*. 2011;19:CD004816. doi: 10.1002/14651858.CD004816.pub4
23. De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z, Jagic N, Möbius-Winkler S, Rioufol G, et al. Fractional flow reserve–guided PCI versus medical therapy in stable coronary disease. *N Engl J Med*. 2012;367:991–1001. doi: 10.1056/NEJMoa1205361
24. Ferreira-González I, Permanyer-Miralda G, Domingo-Salvany A, Busse JW, Heels-Ansdell D, Montori VM, Akl EA, Bryant DM, Alonso-Coello P, Alonso J. Problems with use of composite end points in cardiovascular trials: systematic review of randomized controlled trials. *BMJ*. 2007;334:786. doi: 10.1136/bmj.39136.682083.AE
25. Wennberg DE, Lucas FL, Birkmeyer JD, Bredenberg CE, Fisher ES. Variation in carotid endarterectomy mortality in the Medicare population: trial hospitals, volume, and patient characteristics. *JAMA*. 1998;279:1278–1281. doi: 10.1001/jama.279.16.1278
26. Strom JB, Zhao Y, Shen C, Chung M, Pinto DS, Popma JJ, Cohen DJ, Yeh RW. Hospital variation in the utilization of short-term nondurable mechanical circulatory support in myocardial infarction complicated by cardiogenic shock. *Circ Cardiovasc Interv*. 2019;12:e007270. doi: 10.1161/CIRCINTERVENTIONS.118.007270
27. Secemsky EA, Ferro EG, Rao SV, Kirtane A, Tamez H, Zakroysky P, Wojdyla D, Bradley SM, Cohen DJ, Yeh RW. Association of physician variation in use of manual aspiration thrombectomy with outcomes following primary percutaneous coronary intervention for ST-elevation myocardial infarction: the National Cardiovascular Data Registry CathPCI registry. *JAMA Cardiol*. 2019;4:110–118. doi: 10.1001/jamacardio.2018.4472
28. Yeh RW, Mauri L, Wolf RE, Romm IK, Lovett A, Shahian D, Normand S. Population trends in rates of coronary revascularization. *JAMA Intern Med*. 2015;175:454–456. doi: 10.1001/jamainternmed.2014.7129
29. Alkhouli M, Alqahtani F, Kalra A, Gafoor S, Alhajji M, Alreshidan M, Holmes DR, Lerman A. Trends in characteristics and outcomes of hospital inpatients undergoing coronary revascularization in the United States, 2003–2016. *JAMA Netw Open*. 2020;3:e1921326. doi: 10.1001/jamanetworkopen.2019.21326
30. Bradley SM, Bohn CM, Malenka DJ, Graham MM, Bryson CL, McCabe JM, Curtis JP, Lambert-Kerzner A, Maynard C. Temporal trends in percutaneous coronary intervention appropriateness: insights from the clinical outcomes assessment program. *Circulation*. 2015;132:20–26. doi: 10.1161/CIRCULATIONAHA.114.015156
31. Inohara T, Kohsaka S, Spertus JA, Masoudi FA, Rumsfeld JS, Kennedy KF, Wang TY, Yamaji K, Amano T, Nakamura M. Comparative trends in percutaneous coronary intervention in Japan and the United States, 2013 to 2017. *J Am Coll Cardiol*. 2020;76:1328–1340. doi: 10.1016/j.jacc.2020.07.037
32. Ahmed B, Dauerman HL, Piper WD, Robb JF, Verlee MP, Ryan TJ Jr, Goldberg D, Boss RA Jr, Phillips WJ, Fedele F. Recent changes in practice of elective percutaneous coronary intervention for stable angina. *CircCardiovasc Qual Outcomes*. 2011;4:300–305. doi: 10.1161/CIRCOUTCOMES.110.957175
33. Kataruka A, Maynard CC, Kearney KE, Mahmoud A, Bell S, Doll JA, McCabe JM, Bryson C, Gurm HS, Jneid H. Temporal trends in

percutaneous coronary intervention and coronary artery bypass grafting: insights from the Washington cardiac care outcomes assessment program. *J Am Heart Assoc*. 2020;9:e015317. doi: 10.1161/JAHA.119.015317

34. Shaw LJ, Berman DS, Maron DJ, Mancini GJ, Hayes SW, Hartigan PM, Weintraub WS, O'Rourke RA, Dada M, Spertus JA. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the clinical outcomes utilizing revascularization and aggressive drug evaluation (COURAGE) trial nuclear substudy. *Circulation*. 2008;117:1283–1291. doi: 10.1161/CIRCULATIONAHA.107.743963
35. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, Douglas PS, Foody JM, Gerber TC, Hinderliter AL, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Circulation*. 2012;126:e354–e471. doi: 10.1161/CIR.0b013e318277d6a0
36. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Juni P, et al. ESC/EACTS guidelines on myocardial revascularization. *EuroIntervention*. 2014;2015:1024–1094. doi: 10.4244/EIJY14M09_01
37. Chan PS, Patel MR, Klein LW, Krone RJ, Dehmer GJ, Kennedy K, Nallamothu BK, Weaver WD, Masoudi FA, Rumsfeld JS. Appropriateness of percutaneous coronary intervention. *JAMA*. 2011;306:53–61. doi: 10.1001/jama.2011.916
38. Chan PS, Brindis RG, Cohen DJ, Jones PG, Gialde E, Bach RG, Curtis J, Bethea CF, Shelton ME, Spertus JA. Concordance of physician ratings with the appropriate use criteria for coronary revascularization. *J Am Coll Cardiol*. 2011;57:1546–1553. doi: 10.1016/j.jacc.2010.10.050
39. Rothberg MB, Sivalingam SK, Ashraf J, Visintainer P, Joelson J, Kleppel R, Vallurupalli N, Schweiger MJ. Patients' and cardiologists' perceptions of the benefits of percutaneous coronary intervention for stable coronary disease. *Ann Intern Med*. 2010;153:307–313. doi: 10.7326/0003-4819-153-5-201009070-00005

SUPPLEMENTAL MATERIAL

Figure S1. Study Cohort Selection

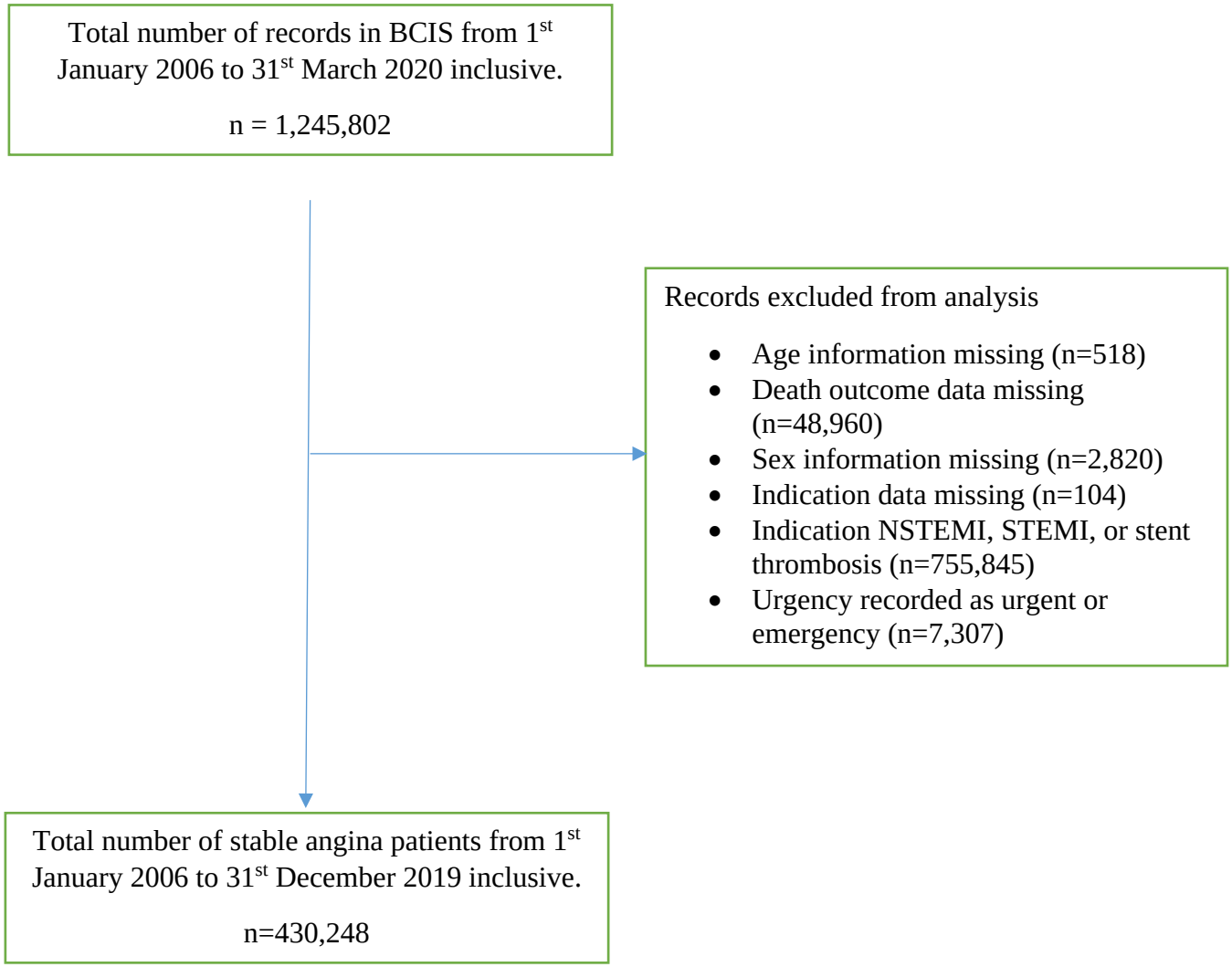

Figure S2. Temporal Trends on PCI volume for stable angina in England Wales between 1st Janaury 2006 to 31st December 2019