

Supplementary data

Supplementary Appendix 1. Study endpoint definitions

MACCE - defined as death, in-hospital CVA or MI.

In-hospital bleeding - defined as either gastrointestinal bleed, intracerebral bleed, retroperitoneal haematoma, blood or platelet transfusion, access-site haemorrhage, or an arterial access-site complication requiring surgery.

Acute coronary procedural complication - defined as no flow, perforation, dissection and major side branch loss.

Access-site complication - defined as either a false aneurysm, haemorrhage (without haematoma), haemorrhage with delayed discharge, retroperitoneal haematoma, arterial dissection, or any access-site complication requiring surgical repair.

Supplementary Appendix 2. Statistical methodology

To adjust for baseline imbalances in order to balance for important covariates that might bias estimates for causal inferences, propensity scores (PS) were calculated using fitted probabilities generated from a logistic regression model by access site which included all covariates described below. These scores were then used to calculate IPTW weights, as previously described, which were utilised to model adjusted outcomes [2]. Prior to performing this, multiple imputations were carried out using the mice package to reduce the potential bias from missing data (**Supplementary Table 1**), assuming missingness at random mechanisms, by using chained equations to impute the data for all variables with missing information generating five data sets to be used in the analyses with satisfactory density plots demonstrating a similar distribution between the imputed and observed data sets (**Supplementary Figure 2**). Covariates included in the adjustment were age, gender, clinical presentation, cardiogenic shock, previous MI, previous CABG, previous PCI, diabetes, baseline disease severity, LV function, smoking status, history of hypertension, stroke, renal failure, valvular heart disease, peripheral vascular disease, left main stem PCI (LMS-PCI), chronic total occlusion PCI (CTO-PCI) attempted, restenosis indication, rotational or laser atherectomy use, use of intracoronary imaging, use of cutting/scoring balloons, use of microcatheter support and mechanical LV support.

Supplementary Table 1. Percent missing values for each variable in the analysed data sets.

Variable	Brachial vs femoral (%)	Brachial vs radial (%)
Age	0.1	0.0
Number of disease lesions	11.7	6.0
Number of vessels attempted	0.9	1.3
Number of lesions attempted	1.3	1.0
Number of CTO attempted	11.0	6.2
Length of stay	0.0	0.0
Female gender	0.2	0.2
Clinical syndrome (ACS)	0.0	0.0
Cardiogenic shock pre procedure	1.7	0.9
Previous MI	11.3	3.7
Previous CABG	4.2	2.0
Previous PCI	4.9	1.9
Diabetes	5.7	2.4
Ejection fraction <30%	51.6	47.8
Smoking history	14.1	8.1
Hypertension	2.6	1.9
Stroke	2.6	1.9
PVD	2.6	1.9
Valve disease	2.6	1.9
Renal disease	8.0	3.7
Ventilated pre procedure	17.4	7.7
LMS	4.0	4.7
Rota	7.0	4.9
Laser	7.0	4.9
Cutting	7.0	4.9
Microcatheter	7.0	4.9
IABP	4.9	2.8
Periprocedural MI	0.0	0.0
Transfusion	0.0	0.0
Periprocedural stroke	0.0	0.0
AKI	0.0	0.0
In-hospital death	0.0	0.0
MACCE	0.0	0.0
Major bleeding	0.0	0.0
Slow flow	0.0	0.0
Side branch loss	0.0	0.0
Dissection	0.0	0.0
Perforation	0.0	0.0
Heart block	0.0	0.0
DCCV	0.0	0.0
Shock induction	0.0	0.0
Arterial complications	0.0	0.0
Arterial haemorrhage	0.0	0.0
Access site	0.0	0.0

Supplementary Table 2. Baseline patient characteristics by access site for PCI in the United Kingdom 2006-2017.

Variable	All (n=861,773)	Brachial (n=1,133)	Femoral (n=329,591)	p-value*	Radial (n=531,049)	p-value†
Age (years), ±SD	65.2±11.9	66.6±11.6	65.7±11.9	0.009	64.9±11.8	<0.001
Female sex, n (%)	222,796 (25.9)	377 (33.4)	92,764 (28.2)	0.001	129,655 (24.5)	<0.001
History of smoking, n (%)	481,911 (62.4)	669 (66.4)	176,142 (62.2)	0.007	305,100 (62.5)	0.012
Diabetes mellitus, n (%)	190,879 (23.3)	353 (32.2)	82,705 (26.4)	<0.001	104,087 (20.1)	<0.001
Previous MI, n (%)	222,831(27.7)	437 (40.9)	93,490 (32.0)	0.001	128,904 (25.2)	<0.001
Hypertension, n (%)	454,553 (53.9)	693 (63.0)	173,763 (54.1)	<0.001	280,097 (53.8)	<0.001
Peripheral vascular disease, n (%)	37,275 (4.4)	277 (25.2)	14,732 (4.6)	<0.001	22,266 (4.3)	<0.001
Previous stroke, n (%)	33,113 (3.9)	98 (8.9)	12,330 (3.8)	<0.001	20,685 (4.0)	<0.001
Chronic renal disease, n (%)	22,012 (2.7)	78 (7.3)	11,733 (3.9)	<0.001	10,201 (2.0)	<0.001
Valvular heart disease, n (%)	12,615 (1.5)	31 (2.8)	4,627 (1.4)	<0.001	7,957 (1.5)	0.001
Previous CABG, n (%)	69,036 (8.2)	163 (14.8)	43,292 (13.7)	0.308	25,581 (4.9)	<0.001
Previous PCI, n (%)	203,019 (24.3)	353 (32.2)	82,705 (26.4)	<0.001	119,961 (23.0)	<0.001
Cardiogenic shock pre, n (%)	17,981 (2.1)	41 (3.7)	10,634 (3.3)	0.509	7,306 (1.4)	<0.001
ACS presentation, n (%)	526,638 (61.1)	672 (59.3)	186,046 (56.4)	0.052	339,920 (64.0)	0.001
Ejection fraction <30%, n (%)	25,282 (5.8)	55 (8.9)	11,498 (7.2)	0.120	13,729 (5.0)	<0.001
Ventilated pre procedure, n (%)	12,359 (1.9)	28 (2.8)	7,231 (2.7)	0.923	5,100 (1.0)	<0.001

* p-value brachial vs femoral. † p-value brachial vs radial.

Supplementary Table 3. Procedural variables by access site for PCI in the United Kingdom 2006-2017.

Variable	All (n=861,773)	Brachial (n=1,133)	Femoral (n=329,591)	p-value*	Radial (n=531,049)	p-value†
Number of diseased vessels ±SD	1.36±0.8	1.51±0.9	1.41±0.8	0.001	1.32±0.7	<0.001
No. of vessels attempted ±SD	1.19±0.7	1.26±0.6	1.20±0.6	0.019	1.18±0.6	0.001
No. of lesions attempted ±SD	1.35±0.6	1.42±0.6	1.39±0.6	0.772	1.31±0.6	<0.001
No. of CTO PCI attempted, ±SD	0.07±0.3	0.10±0.3	0.09±0.3	0.906	0.06±0.3	<0.001
Rotational atherectomy, n (%)	15,250 (1.9)	51 (4.8)	7,225 (2.4)	<0.001	7,974 (1.6)	<0.001
Circulatory support, n (%)	9,700 (1.5)	14 (1.3)	6,729 (2.2)	0.040	2,957 (0.7)	0.018
Pressure wire, n (%)	88,569 (10.7)	94 (8.8)	20,793 (6.6)	0.005	67,682 (13.3)	<0.001
Intracoronary imaging, n (%)	54,819 (6.6)	78 (7.3)	15,488 (4.9)	0.001	39,253 (7.7)	0.668
Target vessels, n (%)						
Left main	34,027 (4.3)	96 (8.8)	15,525 (4.9)	<0.001	18,406 (3.6)	<0.001
Left anterior descending	398,693 (48.1)	495 (45.4)	145,063 (45.8)	0.821	253,135 (50.0)	0.003
Circumflex	202,846 (24.6)	291 (26.7)	76,985 (24.3)	0.071	125,570 (24.8)	0.157
Right	295,309 (35.9)	392 (36.0)	113,790 (36.0)	1.000	181,127 (35.8)	0.918
Atherectomy balloon, n (%)	25,058 (3.1)	68 (6.4)	9,936 (3.2)	<0.001	15,054 (3.0)	<0.001
Microcatheter, n (%)	12,348 (1.5)	28 (2.6)	4,404 (1.4)	0.001	7,916 (1.6)	0.013
Glycoprotein inhibitor, n (%)	163,895 (20.3)	181 (17.3)	68,251 (22.2)	<0.001	95,463 (19.0)	0.175
Longest stent (mm) ±SD	25.8±14.5	25.6±14.2	24.1±13.7	0.005	27.2±15.2	<0.001
No. of stents used ±SD	1.46±1.0	1.50±1.0	1.48±1.0	0.679	1.43±1.0	0.239

* p-value brachial vs femoral. † p-value brachial vs radial.

Supplementary Table 4. Baseline patient characteristics by access site for PCI in the United Kingdom 2006-2017 for default radial operators.

Variable	All (n=43,605)	Femoral (n=43,050)	Brachial (n=555)	<i>p</i>- value
Age (years), \pm SD	67.3 \pm 12.1	67.3 \pm 12.1	66.2 \pm 11.4	0.02
Number of disease lesions, \pm SD	1.6 \pm 0.9	1.6 \pm 0.9	1.5 \pm 0.9	0.15
Female gender, n (%)	15,052 (34.6)	14,863 (34.6)	189 (34.2)	0.87
Clinical syndrome (ACS), n (%)	27,335 (62.7)	26,978 (62.7)	357 (64.3)	0.46
Cardiogenic shock pre procedure, n (%)	3,296 (7.6)	3,275 (7.7)	21 (3.8)	0.00
Previous MI, n (%)	17,202 (41)	16,955 (41)	247 (45.7)	0.03
Previous CABG, n (%)	9,598 (22.3)	9,512 (22.4)	86 (15.8)	0.00
Previous PCI, n (%)	14,693 (34.4)	14,508 (34.4)	185 (34.1)	0.91
Diabetes, n (%)	11,056 (26.1)	10,900 (26.1)	156 (28.8)	0.17
Ejection fraction <30%, n (%)	2,701 (10.8)	2,673 (10.8)	28 (9.2)	0.43
Smoking history, n (%)	23,907 (61.3)	23,555 (61.2)	352 (69.3)	0.00
Hypertension, n (%)	25,418 (59.7)	25,074 (59.7)	344 (63.2)	0.10
Stroke, n (%)	2,672 (6.3)	2,612 (6.2)	60 (11)	0.00
PVD, n (%)	3,384 (8)	3,252 (7.7)	132 (24.3)	0.00
Valve disease, n (%)	1,119 (2.6)	1,101 (2.6)	18 (3.3)	0.38
Renal disease, n (%)	2,640 (6.4)	2,597 (6.3)	43 (8.1)	0.11
Ventilated pre procedure, n (%)	2,236 (5.5)	2,220 (5.6)	16 (3.1)	0.02
Q-wave on ECG, n (%)	6,326 (15.8)	6,260 (15.8)	66 (13)	0.10

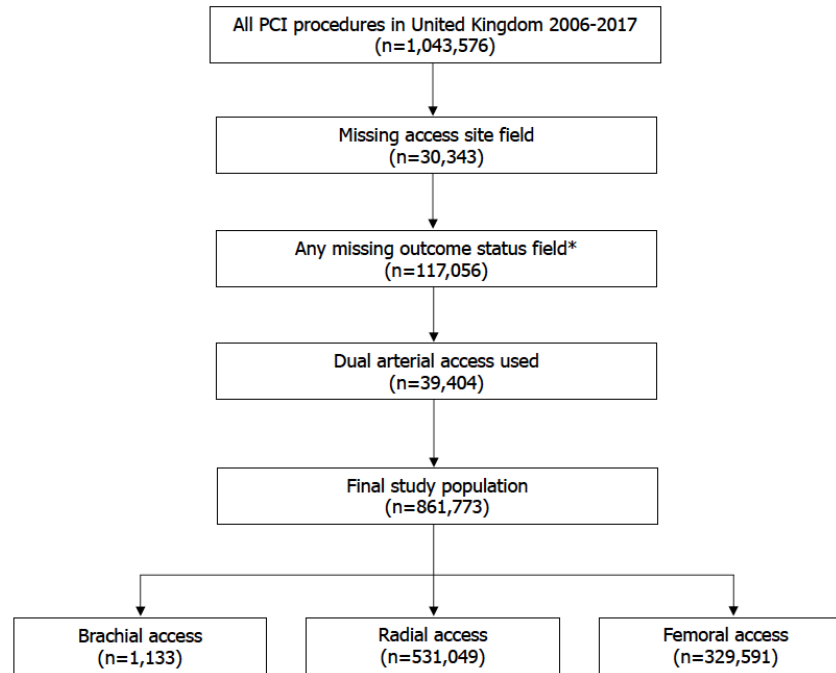
Supplementary Table 5. Procedural characteristics by access site for PCI in the United Kingdom 2006-2017 for default radial operators.

Variable	All (n=43,605)	Femoral (n=43,050)	Brachial (n=555)	<i>p</i>-value
No. of vessels attempted, \pm SD	1.3 \pm 0.6	1.3 \pm 0.6	1.2 \pm 0.6	0.81
No. of lesions attempted, \pm SD	1.4 \pm 0.8	1.4 \pm 0.8	1.4 \pm 0.8	0.33
No. of chronic total occlusions attempted, \pm SD	0.1 \pm 0.3	0.1 \pm 0.3	0.1 \pm 0.3	0.20
LMS disease pre PCI, n (%)	3,894 (9.3)	3,843 (9.3)	51 (9.6)	0.87
Rotational atherectomy, n (%)	1,932 (4.6)	1,903 (4.6)	29 (5.3)	0.50
Laser, n (%)	217 (0.5)	217 (0.5)	0 (0)	-
Cutting balloon use, n (%)	1,287 (3.1)	1,257 (3)	30 (5.5)	0.00
Microcatheter use, n (%)	1,590 (3.8)	1,570 (3.8)	20 (3.7)	0.99
Intra-aortic balloon pump use, n (%)	1,488 (3.5)	1,480 (3.5)	8 (1.5)	0.02

Supplementary Table 6. Crude unadjusted outcomes by access site for PCI in the United Kingdom 2006-2017.

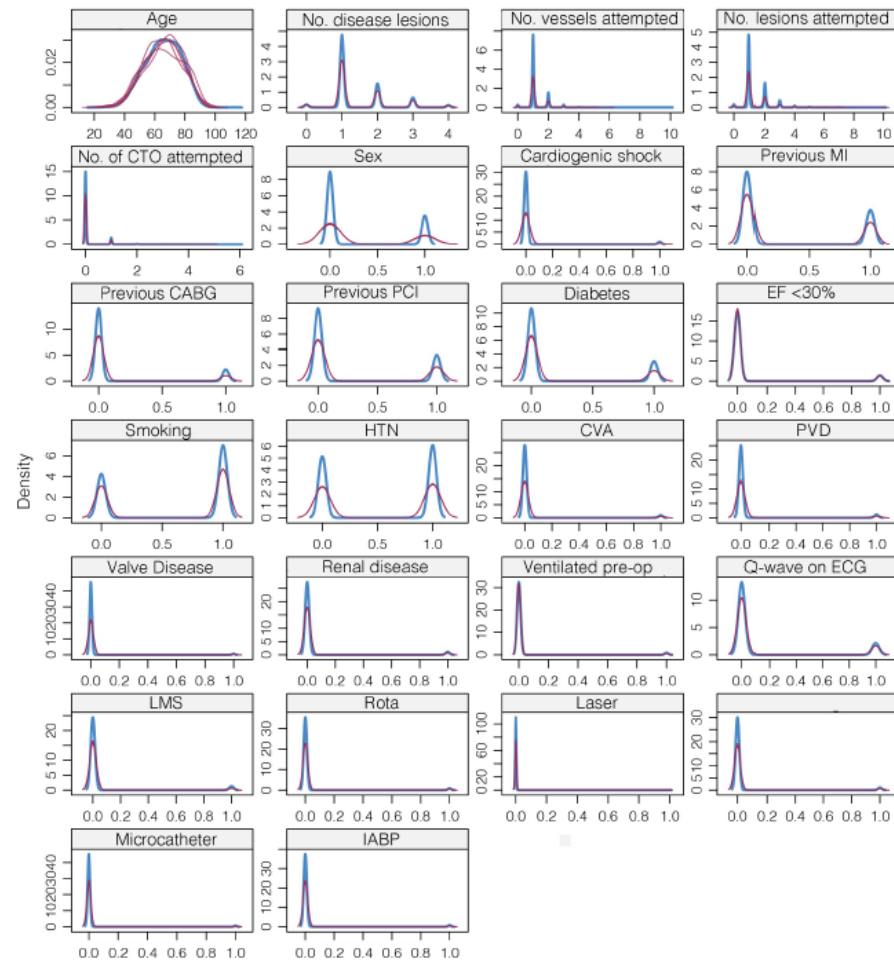
Outcome	All (n=861,773)	Brachial (n=1,133)	Femoral (n=329,591)	p-value*	Radial (n=531,049)	p-value†
Procedural success, n (%)	716,877 (92.0)	943 (91.0)	265,452 (91.2)	0.885	450,482 (92.5)	0.0283
Number of successful vessels, ±SD	1.05±0.49	1.09±0.57	1.05±0.50	0.002	1.06±0.48	0.009
Number of successful lesions, ±SD	1.27±0.77	1.33±0.85	1.31±0.80	0.298	1.25±0.75	<0.001
Major side branch loss, n (%)	5,042 (0.6)	9 (0.8)	1,753 (0.6)	0.501	3,280 (0.6)	0.500
Slow flow, n (%)	7,698 (0.9)	9 (0.8)	2,948 (1.0)	0.601	4,741 (0.9)	0.844
Coronary dissection, n (%)	12,455 (1.5)	11 (1.0)	4,777 (1.6)	0.143	7,657 (1.5)	0.215
Coronary perforation, n (%)	2,417 (0.3)	2 (0.2)	955 (0.3)	0.773	1,460 (0.3)	0.773
Acute kidney injury, n (%)	790 (0.1)	4 (0.4)	316 (0.1)	0.012	470 (0.1)	0.014
Access-site complication, n (%)	11,311 (1.3)	35 (3.1)	6,020 (1.8)	0.002	5,256 (1.0)	<0.001
Transfusion, n (%)	1,690 (0.2)	1 (0.1)	1,165 (0.4)	0.211	524 (0.1)	1.000
Access-site haemorrhage, n (%)	2,205 (0.3)	5 (0.4)	1,818 (0.6)	0.465	382 (0.1)	0.004
In-hospital major bleeding, n (%)	4,926 (0.6)	10 (0.9)	3,284 (1.0)	0.855	1,632 (0.3)	0.001
In-hospital mortality, n (%)	13,036 (1.5)	50 (4.4)	7,577 (2.3)	<0.001	5,409 (1.0)	<0.001
Periprocedural CVA, n (%)	970 (0.1)	6 (0.5)	444 (0.1)	<0.001	524 (0.1)	<0.001
Periprocedural MI, n (%)	2,537 (0.3)	3 (0.3)	1,280 (0.4)	0.803	1,254 (0.2)	0.724
In-hospital MACCE, n (%)	16,305 (1.9)	58 (5.1)	9,134 (2.8)	<0.001	7,113 (1.3)	<0.001
Length of stay (days), ±SD	2.7±8.0	3.7±14.8	3.0±8.7	0.032	2.5±7.3	<0.001

* p-value brachial vs femoral. † p-value brachial vs radial.



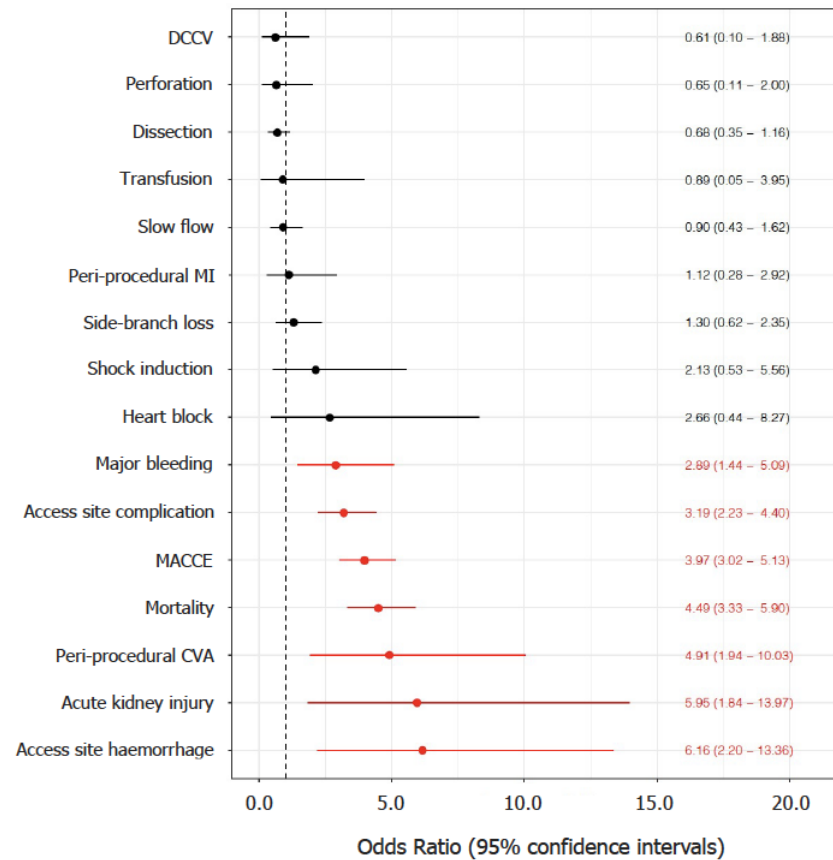
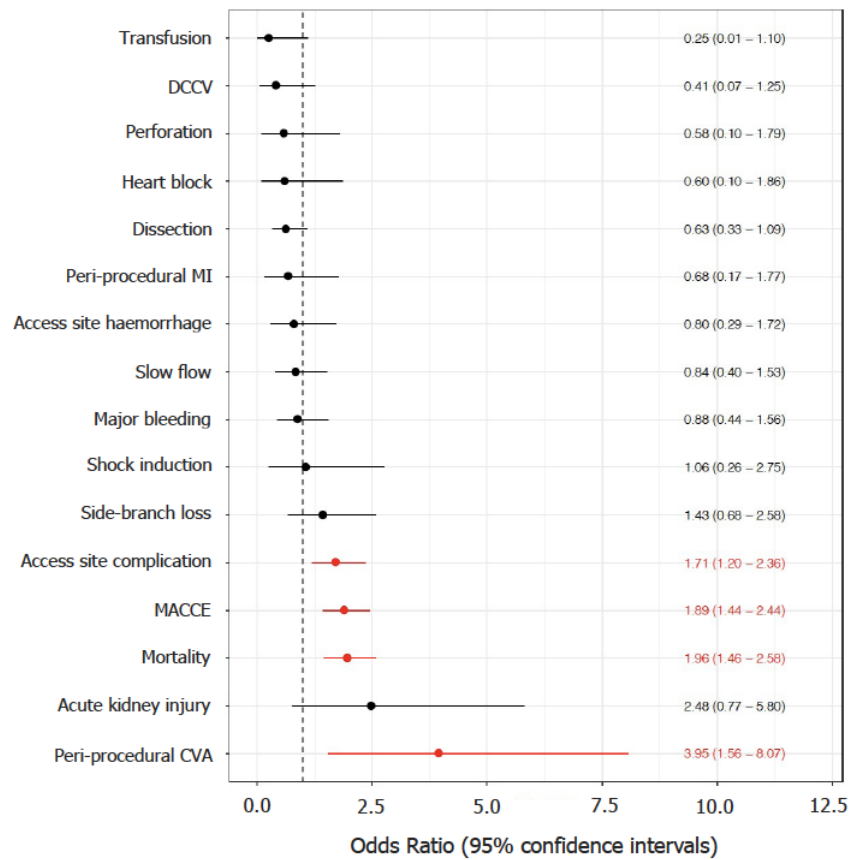
Supplementary Figure 1. Patient number flow for study.

*Fields included were MACCE, mortality, arterial complication and major bleeding.



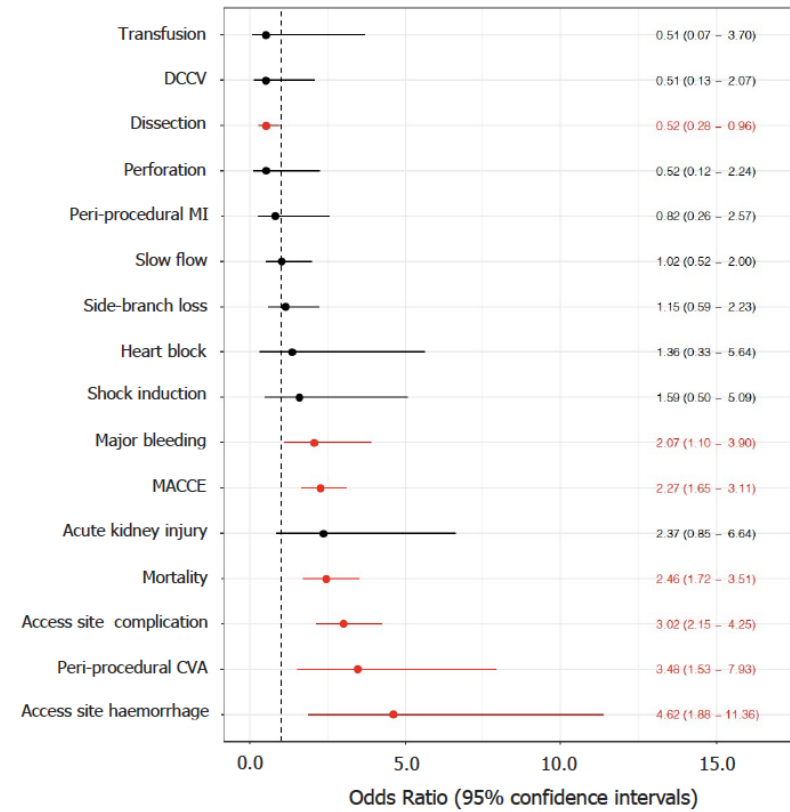
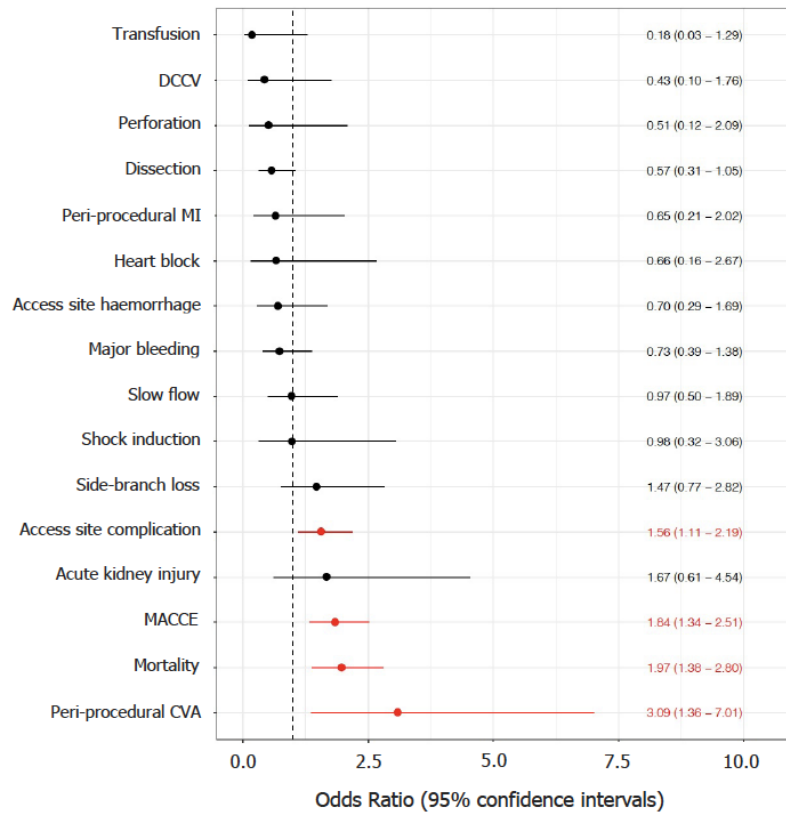
Supplementary Figure 2. Density plot.

Density plot of all imputed variables demonstrating that the imputed data set distribution (red curves; one from each of the five imputed data sets) is similar to the observed data set distribution (blue curves) indicating that the multiple imputation with chained equations (mice) process has successfully imputed values that are “plausible”. X-axis indicates the range of values for each variable. Y-axis is the density distribution.



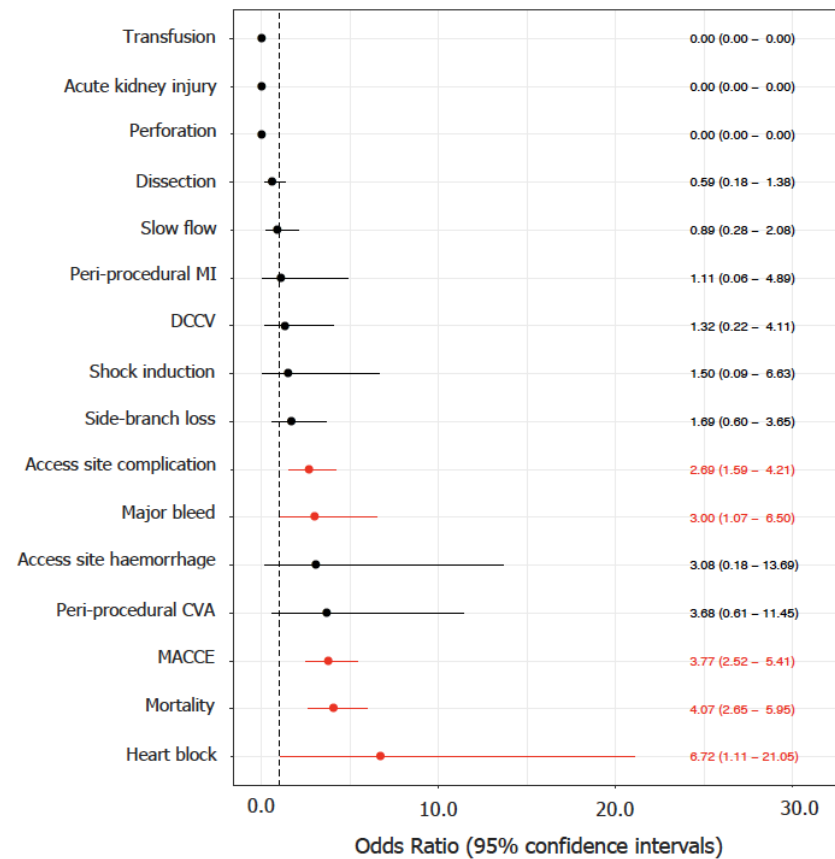
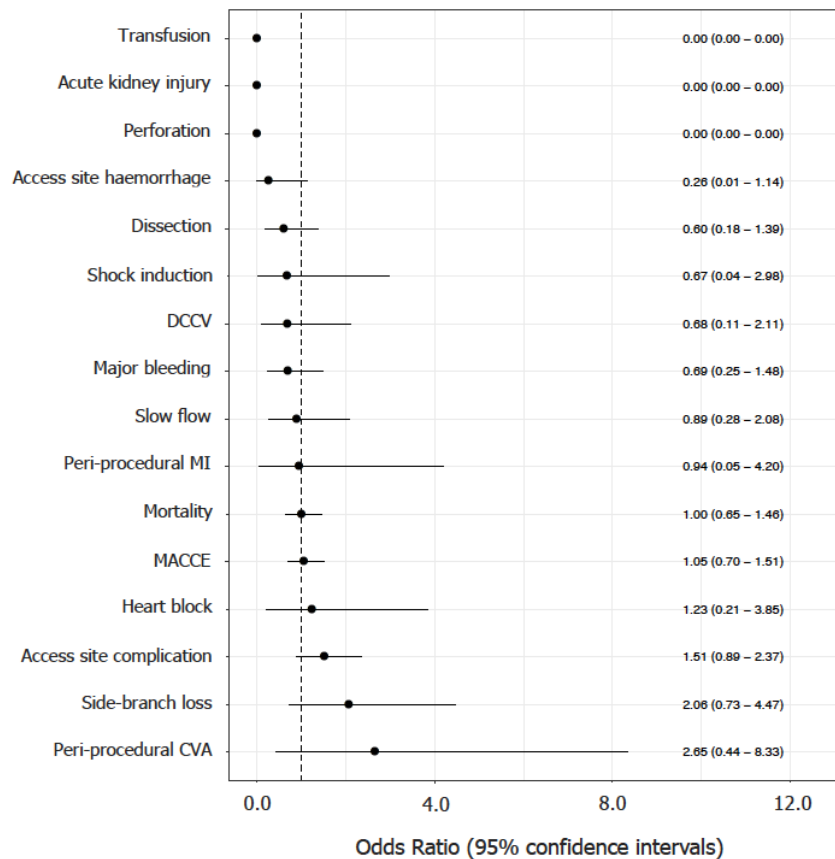
Supplementary Figure 3. Weight-adjusted procedural and clinical outcomes.

Left panel - IPTW weight-adjusted procedural and clinical outcomes of brachial access procedures compared to femoral access for PCI in the United Kingdom 2006-2017. Right panel - IPTW weight-adjusted procedural and clinical outcomes of brachial access procedures compared to radial access for PCI in the United Kingdom 2006-2017.



Supplementary Figure 4. Multivariate-adjusted procedural/clinical outcomes.

Left panel - Multivariate-adjusted procedural/clinical outcomes of brachial access procedures compared to femoral access for PCI in the UK 2006-2017. Right panel - Multivariate-adjusted procedural/clinical outcomes of brachial access procedures compared to radial access for PCI in the UK 2006-2017.



Supplementary Figure 5. IPTW weight-adjusted procedural and clinical outcomes.

Left panel - IPTW weight-adjusted procedural and clinical outcomes of brachial access procedures compared to femoral access for PCI in the United Kingdom 2013-2017. Right panel - IPTW weight-adjusted procedural and clinical outcomes of brachial access procedures compared to radial access for PCI in the United Kingdom 2013-2017. IPTW: inverse probability of treatment weighting