Supplementary data

Supplementary Appendix 1

Methods.

Angiographic classification system for coronary vessel calcification

Coronary vessel calcification grade	Angiographic findings
None	No radiopacity
Mild	Faint radiopacities noted during the cardiac cycles
Moderate	Dense radiopacities noted only during the cardiac cycle
Severe	Dense radiopacities noted without cardiac motion before contrast injection generally compromising both sides of the arterial lumen

Supplementary Appendix 2

List of variables considered by the LASSO model

Age, body mass index (BMI), sex, diabetes mellitus, hypertension, hypercholesterolaemia, smoking status, acute coronary syndrome (ACS) presentation, multi-vessel disease, previous MI, previous CABG, restenosis morphology (focal or non-focal), left circumflex (LCx) coronary artery, ostial LCx coronary artery, distal vessel, vessel calcification, ostial lesion, bifurcation lesion, chronic total occlusion (CTO) lesion, restenosis severity ≥90%, maximum device diameter (stent or balloon) and short restenosis interval (<6 months between the initial DES implantation and the initial treatment of the DES-ISR)

Supplementary Table 1. TRIPOD Checklist: Prediction Model Development and Validation

Section/Topic			Checklist Item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	4
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	4
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	4,5
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	4
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	4
	5b	D;V	Describe eligibility criteria for participants.	4
	5c	D;V	Give details of treatments received, if relevant.	22
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	5
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	6, 33
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	6
Sample size	8	D;V	Explain how the study size was arrived at.	4
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	6
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	5-7
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	5-7
	10c	V	For validation, describe how the predictions were calculated.	5-7
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	5-7
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	5-7
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	5-7
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	5-7
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	8, 23
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	8, 20
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	20, 21, 22
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	23
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	8, 24
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	24
	15b	D	Explain how to the use the prediction model.	8-10
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	9
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	9
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	14
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	9
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	12-14
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	14
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	15
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	15

Supplementary Table 2. Indication for repeat PCI for recurrent DES-ISR through to 1 year and 5 years follow up*

Indication for Repeat PCI for recurrent DES-ISR	All Patients (N=341)	Training Population (N=250)	Validation Population (N=91)	p value
Through to 1-year follow-up				
STEMI	4 (1.2%)	2 (0.8%)	2 (2.2%)	0.27
NSTEMI	43 (12.6%)	27 (10.8%)	16 (17.6%)	
Unstable Angina	44 (12.9%)	35 (14.0%)	9 (9.9%)	
Stable Angina	232 (68.0%)	174 (69.6%)	58 (63.7%)	
Positive Ischemia Stress Testing	18 (5.3%)	12 (4.8%)	6 (6.6%)	
Indication for Repeat PCI for recurrent DES-ISR	**All Patients (N=178)**	**Training Population (N=129)**	**Validation Population (N=49)**	**p value**
From 1- to 5-year follow-up				
STEMI	4 (2.3%)	4 (3.1%)	0 (0.0%)	0.35
NSTEMI	19 (10.7%)	12 (9.3%)	7 (14.3%)	
Unstable Angina	34 (19.1%)	26 (20.2%)	8 (16.3%)	
Stable Angina	111 (62.4%)	78 (60.5%)	33 (67.3%)	
Positive Ischemia Stress Testing	10 (5.6%)	9 (7.0%)	1 (2.0%)	

*Indication for repeat PCI for recurrent DES-ISR is reported at a patient level. Some patients had repeat PCI for recurrent DES-ISR in more than one lesion.

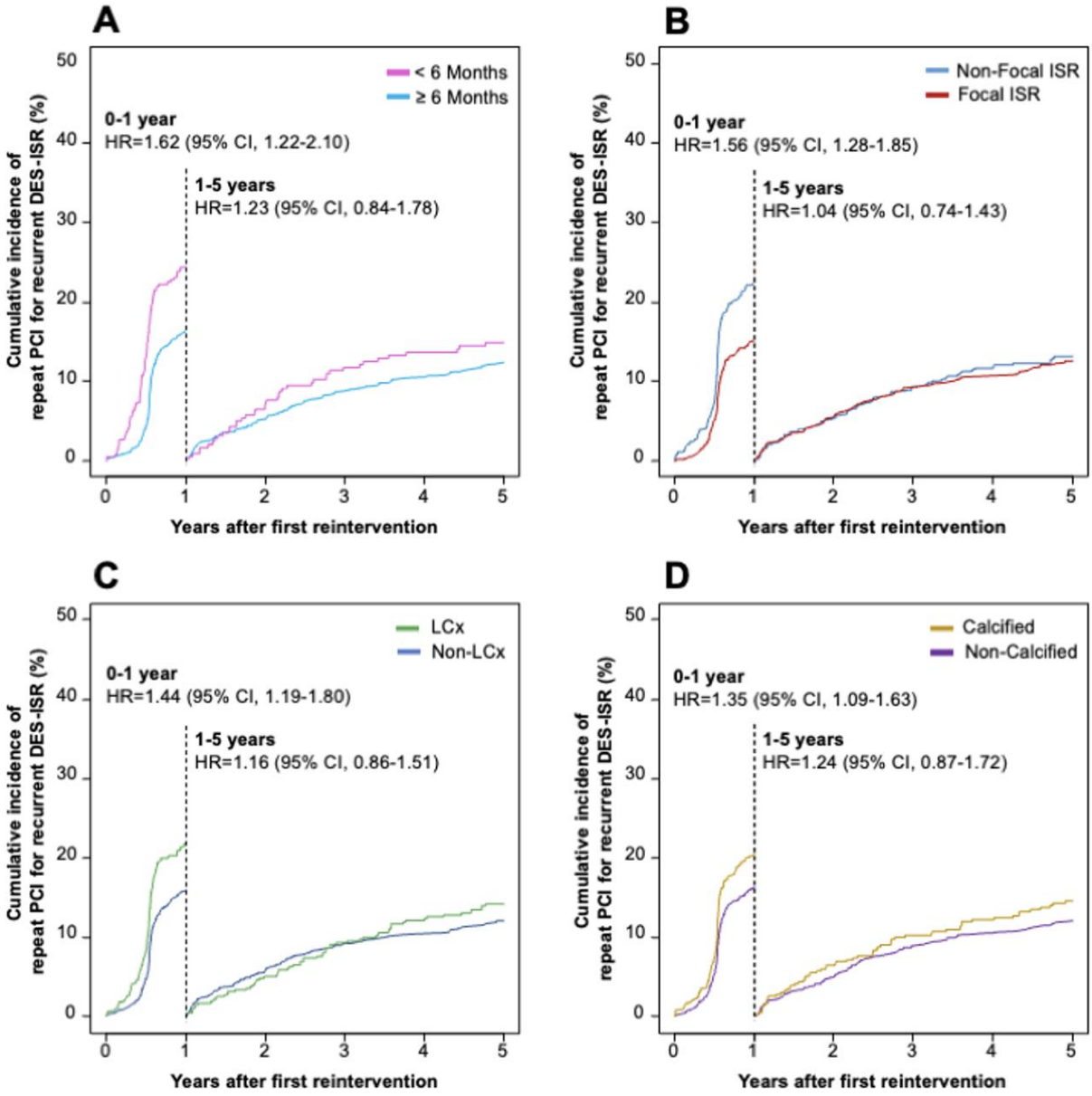
DES = drug-eluting stent, ISR = in-stent restenosis, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction

Supplementary Table 3. Repeat PCI for recurrent DES-ISR from 0 to 1 year and from 1 to 5 years as per ISR interval and morphology

		Restenosis Interval				
	All Training Population Lesions (N=1,778)	**6 months** (N=284)	**6-12 months** (N=711)	**>12-24 months** (N=238)	**>24 months** (N=545)	**P value**
Repeat PCI for recurrent DES-ISR from 0 to1 year – no. (%)	299 (16.8)	69 (24.3)	117 (16.5)	45 (18.9)	68 (12.5)	<0.001
Repeat PCI for recurrent DES-ISR from 1 to 5 years – no. (%)	155/1,284 (12.1)	29/195 (14.9)	62/546 (11.4)	12/176 (6.8)	52/367 (14.2)	0.050
		ISR Morphology				
	All Training Population Lesions (N=1,778)	**Focal** (N=1,163)	**Diffuse intra-stent** (N=420)	**Diffuse proliferative** (N=40)	**Total occlusion** (N=155)	**P value**
Repeat PCI for recurrent DES-ISR from 0 to 1 year – no. (%)	299 (16.8)	165 (14.2)	90 (21.4)	11 (27.5)	33 (21.3)	0.001
Repeat PCI for recurrent DES-ISR from 1 to 5 years – no. (%)	155/1,284 (12.1)	108/886 (12.2)	37/279 (13.3)	1/22 (4.6)	9/97 (9.3)	0.475

Supplementary Table 4. Results of logistic regression analysis for repeat PCI for recurrent DES-ISR from 1 to 5 years after first reintervention for DES-ISR.

Variable	Regression coefficient	p value
Age	-0.018	0.060
Diabetes	0.195	0.376
Hypertension	0.822	0.809
Hypercholesterolemia	0.256	0.308
Acute coronary syndrome	-0.056	0.801
Multivessel disease	0.258	0.512
Previous myocardial infarction	0.033	0.873
Left circumflex coronary artery	0.004	0.984
Chronic total occlusion	-0.111	0.774
Vessel calcification	0.336	0.143
Bifurcation lesion	0.273	0.136
Restenosis interval <6 months	0.263	0.322



Supplementary Figure 1. Landmark analysis demonstrating the cumulative incidence of repeat PCI for recurrent DES-ISR from 0 to 1 year and from 1 to 5 years for lesions with and without the four predictor variables identified in the logistic regression model.

(Panel A) Restenosis interval <6 months versus restenosis interval ≥6 months, (Panel B) Restenosis morphology: non-focal versus restenosis morphology: focal (Panel C) Artery involved: left circumflex artery versus non-left circumflex artery, (Panel D) Vessel calcification: calcified vessel versus non-calcified vessel.