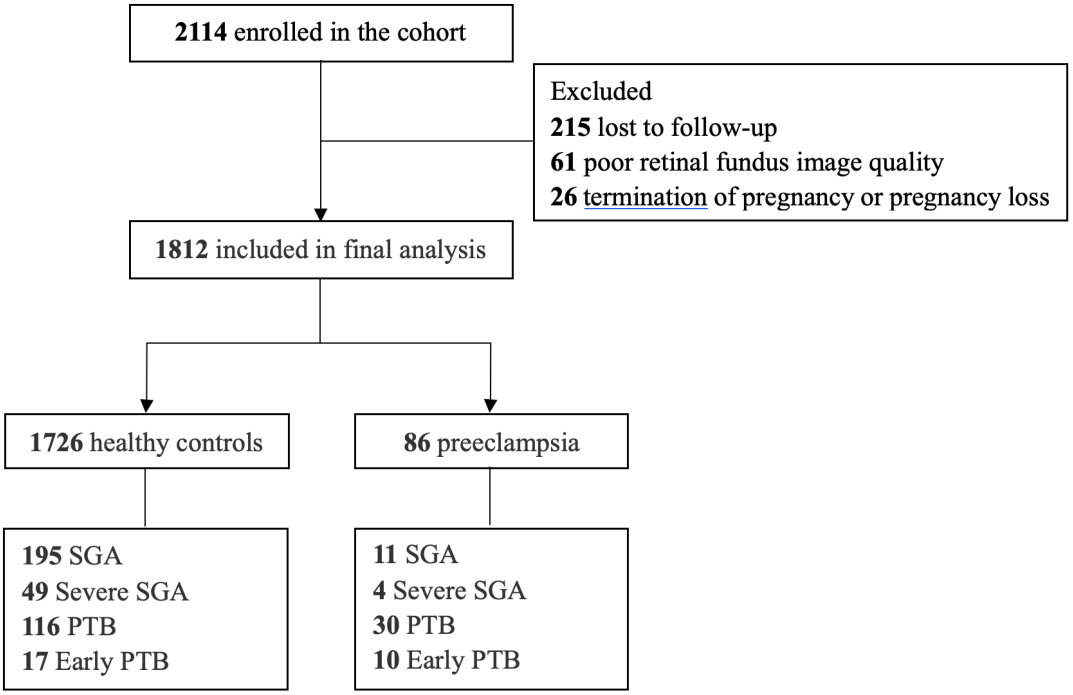
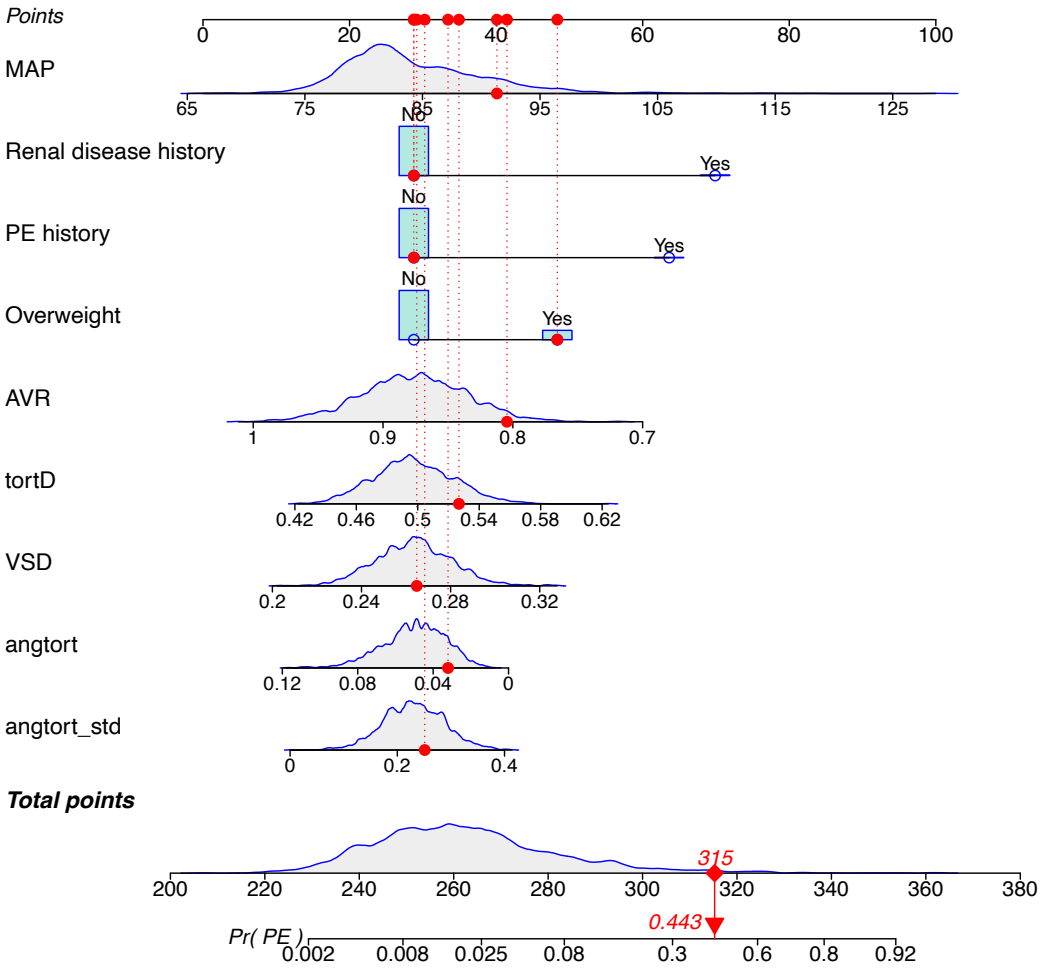
Supplementary Figure 1. Study workflow



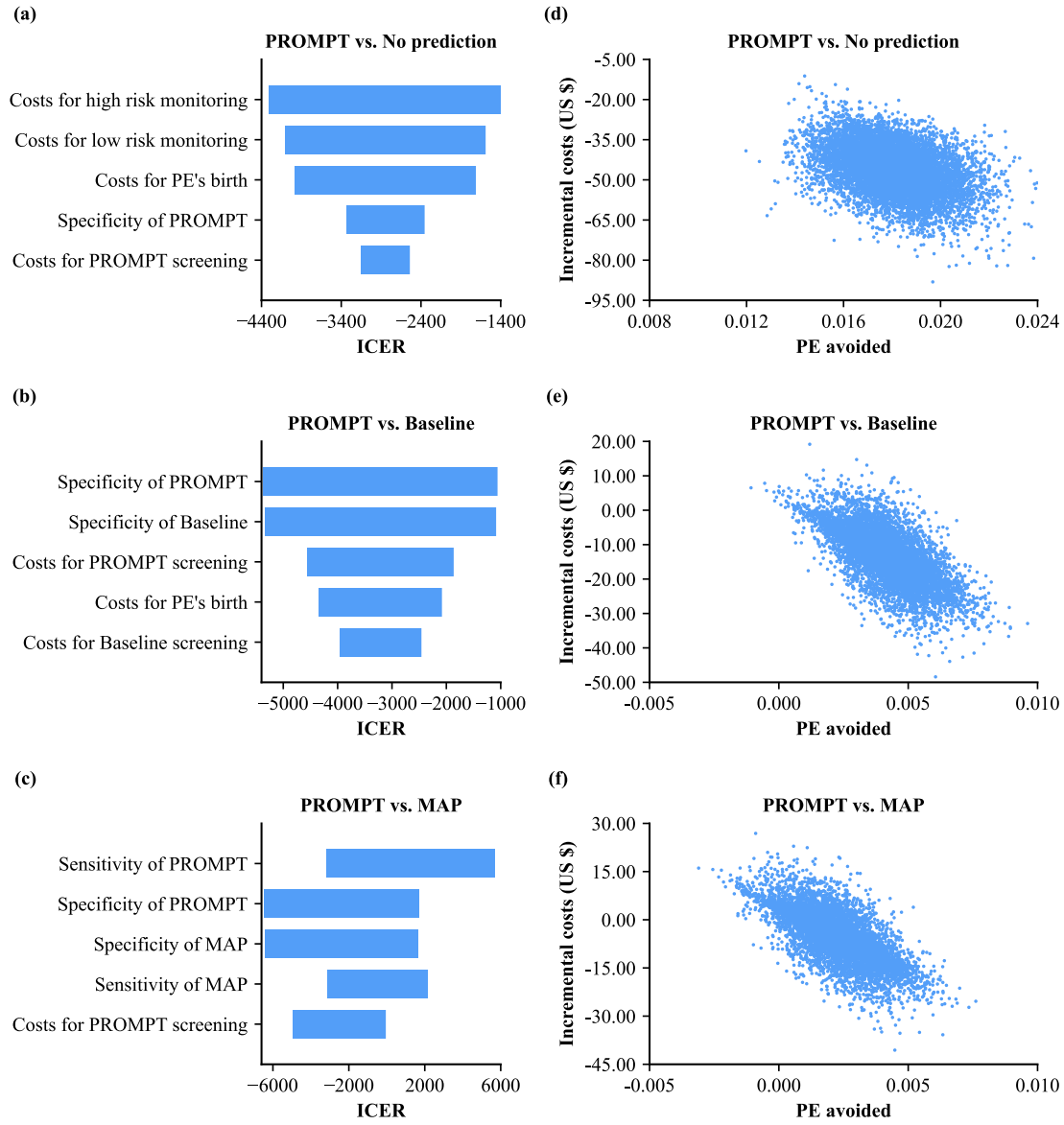
Notes: Flowchart summarizing enrollment of study population and pregnancy outcomes. HC=healthy controls. PE=preeclampsia. SGA=small-for-gestational age (SGA < 10th percentile; severe SGA < 3rd percentile). PTB=preterm birth (<37 weeks' gestation; early PTB < 34 weeks' gestation).

Supplementary Figure 2. The nomogram of the PROMPT model for PE prediction



Notes: Nomogram of the PROMPT model and an example of PE case was illustrated. Abbreviations: MAP=mean arterial pressure. PE=preeclampsia. AVR=artery-to-vein ratio. TortD=tortuosity density. VSD=vessel skeleton density. Angtort=angle-based tortuosity. Std=standard deviation.

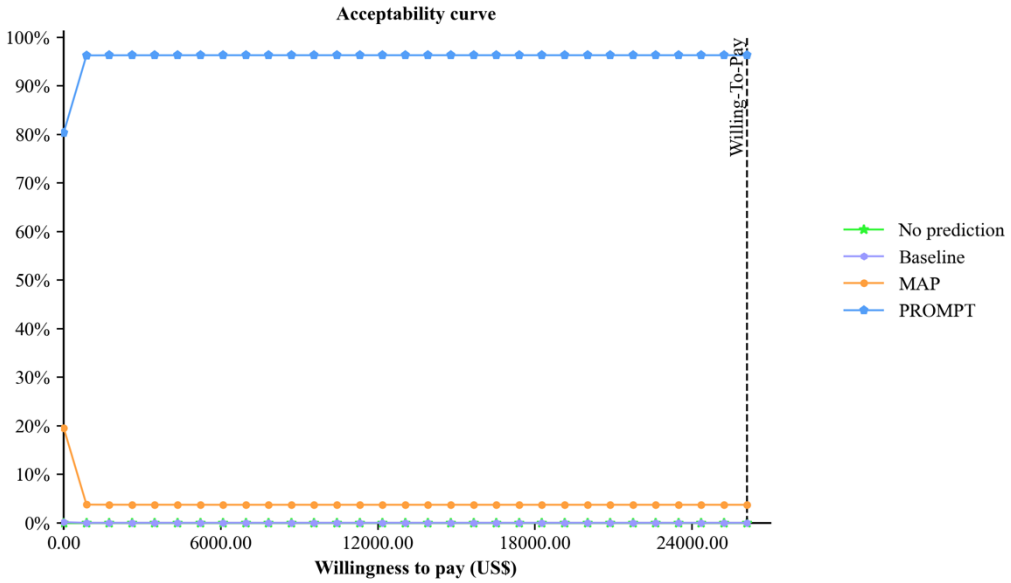
Supplementary Figure 3. Deterministic one-way and probabilistic sensitivity analysis



Notes: One-way (a, b, c) and probability (d, e, f) sensitivity analysis of the PROMPT model Vs. no prediction (a, d), baseline model (b, e), and MAP model (c, f). Costs are expressed in US dollars.

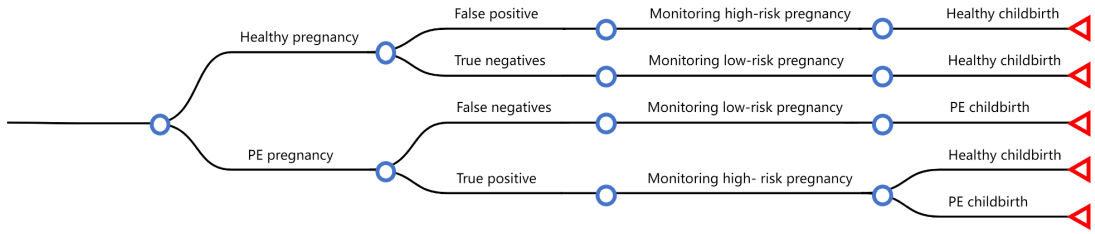
Abbreviations: PE=preeclampsia. ICER= incremental cost effectiveness ratio. MAP= mean arterial pressure.

Supplementary Figure 4. Cost-effectiveness acceptability curves of prediction models



Notes：Cost-effectiveness acceptability curves of the PROMPT model Vs. no prediction, baseline and MAP models. The curve of each color represents a prediction strategy, and its acceptability probability represents the ratio by which the corresponding strategy outperforms other strategies as WTP changes in the probabilistic sensitivity analysis. Costs are expressed in US dollars. WTP=willingness to pay. MAP= mean arterial pressure.

Supplementary Figure 5. The decision tree model of cost-effectiveness analysis



Notes: Decision tree model of PE prediction in the first trimester. Monitoring of low- and high-risk pregnancies and pregnancy outcomes in which the true positives and true negatives are determined by, respectively, the sensitivity and specificity of different prediction models. Abbreviations: PE=preeclampsia.

Supplementary Table 1. Performances of different machine learning models of PE prediction

Algorithms	Training	Validation
LR	0.889±0.006	0.863±0.049
RF	1±0	0.863±0.060
XGBoost	0.963±0.002	0.858±0.059
GBM	0.977±0.001	0.860±0.059
SVM	0.879±0.005	0.867±0.063

Notes: AUC are expressed in (mean ± SD).

Abbreviations: LR=logistic regression. RF=random forest. XGBoost=extreme gradient boosting. GBM=gradient boosting method. SVM: support vector machine. AUC=area under the curve. SD=standard deviation.

Supplementary Table 2. Detailed detection rate of adverse maternal and neonatal outcomes of different models

Model/	SGA n=206		Severe SGA n=53		PTB n=146		Early PTB n=27	
FPR for PE	DR %	aDR n=115	DR %	aDR n=34	DR %	aDR n=73	DR %	aDR n=12
Baseline model								
5%	2.9 (1.3, 6.2)	2.6 (1.1, 5.9)	0 (0, 6.8)	0 (0, 7.3)	13.0 (8.5, 19.4)	8.6 (4.7, 15.1)	25.9 (13.2, 44.7)	23.5 (9.6, 47.3)
10%	9.2 (6.0, 14.0)	7.7 (4.7, 12.3)	5.7 (1.9, 15.4)	6.1 (2.1, 16.5)	20.5 (14.8, 27.8)	14.7 (9.4, 22.2)	33.3 (18.6, 52.2)	29.4 (13.3, 53.1)
15%	14.6 (10.4, 20.0)	12.8 (8.8, 18.2)	13.2 (6.5, 24.8)	14.3 (7.1, 26.7)	30.8 (23.9, 38.7)	21.6 (15.0, 29.9)	51.9 (34.0, 69.3)	41.2 (21.6, 64.0)
MAP model								
5%	5.8 (3.4, 9.9)	3.6 (1.7, 7.2)	7.5 (3, 17.9)	6.1 (2.1, 16.5)	17.8 (12.5, 24.8)	7.8 (4.1, 14.1)	22.2 (10.6, 40.8)	11.8 (3.3, 34.3)
10%	12.6 (8.8, 17.9)	9.2 (5.9, 14.1)	13.2 (6.5, 24.8)	10.2 (4.4, 21.8)	26.7 (20.2, 34.4)	15.5 (10, 23.2)	37 (21.5, 55.8)	23.5 (9.6, 47.3)

15%	17.5 (12.9, 23.2)	14.4 (10.1, 20)	17.0 (9.2, 29.2)	14.3 (7.1, 26.7)	33.6 (26.4, 41.6)	23.3 (16.5, 31.7)	51.9 (34, 69.3)	41.2 (21.6, 64)
PROMPT model								
5%	6.8 (4.1, 11.1)	5.6 (3.2, 9.8)	7.5 (3, 17.9)	6.1 (2.1, 16.5)	21.9 (16, 29.3)	11.2 (6.7, 18.2)	40.7 (24.5, 59.3)	29.4 (13.3, 53.1)
10%	14.1 (10, 19.5)	11.8 (8, 17.1)	9.4 (4.1, 20.3)	8.2 (3.2, 19.2)	28.8 (22, 36.6)	15.5 (10, 23.2)	55.6 (37.3, 72.4)	41.2 (21.6, 64)
15%	20.4 (15.5, 26.4)	18.5 (13.6, 24.5)	15.1 (7.9, 27.1)	14.3 (7.1, 26.7)	34.2 (27, 42.3)	21.6 (15, 29.9)	63.0 (44.2, 78.5)	47.1 (26.2, 69)

Notes: Values in parentheses are 95% CI. Adverse outcome (AO) was defined as any one or more of the following maternal and neonatal outcomes: PE, SGA (birth weight < 10th percentile) and PTB (< 37 weeks). Severe AO was defined as any one or more of the following maternal and neonatal outcomes: PT PE, severe SGA (birth weight < 3rd percentile) and early PTB (< 34 weeks).
Abbreviations: PE= preeclampsia. MAP=mean arterial pressure. SGA= small-for-gestational age. PTB=preterm birth. FPR=false positive rate. DR=detection rate. aDR=additional detection rate of adverse outcomes other than PE (i.e. after exclusion of PE screen-positive cases).

Supplementary Table 3. Recent PE prediction models for comparisons

Source	Population	Timing	Input	Output	Algorithm	Sample size	Non-invasive	AUC
Marić et al.[1] 2020	USA	<16w	maternal factors, lab results	PE	EN/GB/LR	5245	No	0.79
Hu et al.[2] 2021	China	11-13^{+6}w	maternal factors and different biomarker combinations	Preterm PE	FMF competing-risks model	10899	No	0.86
Li et al.[3] 2021	China	<20w	EHR	PE	LR/RF/SVM/XGBoost	3759	No	0.96
Manoochehri et al.[4] 2021	Iran	All pregnancy	Maternal factors	PE	LR/RF/LDA/KNN/SVM/DT	1452	Yes	ACC 0.79
Ansbacher-Feldman et al.[5] 2022	UK	11-13^{+6}w	maternal factors and different biomarker combinations	PE	NN	30437	No	0.82
Liu et al.[6] 2022	China	11-13^{+6}w	maternal factors, lab and ultrasound results	PE	LR/RF/DT/DNN/SVM	11152	No	0.86
Khalil et al.[7] 2024	UK	<14w	maternal factors and cfDNA	PE	NN	17520	No	0.71
Adil et al.[8] 2025	USA	≤16 w	maternal factors, PDNAS	PE	LR/XGBoost	1854	No	0.85
Our study, 2025	China	11-13^{+6}w	maternal factors and retinal parameters	PE	LR/RF/SVM/XGBoost/GBM	1812	Yes	0.86

Abbreviations: AUC=area under the curve. EN=elastic net. GB=gradient boosting. LR=logistic regression. FMF= Fetal Medicine Foundation. RF=random forest. SVM= supporting vector machine. EHR=electronic health records. XGBoost=extreme gradient boosting. LDA= linear

discriminant analysis. KNN=k-nearest neighbors. DT=decision tree. NN=neural network. DNN= deep neural network. cfDNA= cell free DNA. PDNAS= prenatal cell-free DNA screening. GBM= gradient boosting method.

Supplementary Table 4. Clinical diagnosis criteria of adverse pregnancy outcomes

Disease	Definition	Source
PE	A disorder of pregnancy occurs after 20 weeks of gestation associated with new-onset hypertension（systolic blood pressure ≥140mmHg and (or) diastolic blood pressure ≥ 90mmHg）, accompanied by any one of the following: urine protein ≥ 0.3g/24h, or urine protein/creatinine ratio ≥ 0.3, or random urine protein ≥ (+) (examination method when protein quantification is unavailable); no proteinuria but accompanied by any one of the following organs or systems involved: heart, lung, liver, kidney and other important organs, or abnormal changes in the blood system, digestive system, nervous system, placenta-fetus involvement, etc. PE can also occur after delivery.	[9]
Preterm PE	PE with delivery at $<37^{+0}$ weeks of gestation.	[10]
SGA	Newborn with birth weight less than the 10th percentile of the Chinese reference.	[11]
Severe SGA	Newborn with birth weight less than the 3rd percentile of the Chinese reference.	[11]
PTB	Birth between 24^{+0} weeks of gestation and 36^{+7} weeks of gestation.	[12]
Early PTB	Birth between 24^{+0} weeks of gestation and 33^{+7} weeks of gestation.	[12]

Abbreviations: PE=preeclampsia. SGA=Small for gestational age. PTB= Preterm birth.

Supplementary Table 5. Definition and significance of the retinal fundus parameters

Name	Full name	Vessel	Definition and calculation	Significance
AVR	Artery-to-vein ratio	A/V	The ratio calculated from CRAE/CRVE.	Changing in AVR is associated with a variety of systemic diseases including hypertension, CKD, and immune disorders, etc.[13–15]
VSD	Vessel skeleton density	V	The ratio of the total length of vessels to total area of the image at 1 pixel, a measure of overall vessel length within a fundus image	VSD is a sensitive biomarker to the perfusion changes at the capillary levels.[16]
tortD	Tortuosity density	A	This tortuosity measure has a dimension of 1/length	Tortuosity demonstrates pathological microvascular remodeling and/or ischemia-induced arterialization in collateral micro vessels.[17]
angtort	Angle-based tortuosity	V	This tortuosity measure has a dimension of rad^2/length	
angtort_std	Angle-based tortuosity_ standard deviation	A	The standard deviation of artery angle-based tortuosity	Demonstrates the fluctuation of vessel tortuosity[17]

Abbreviations: CRAE= central retinal artery equivalent. CRVE=central retinal vein equivalent. CKD=chronic kidney disease. A=artery. V=vein. Std=standard deviation.

Supplementary Table 6. Parameters and variation range in cost-effectiveness analysis

Parameters	Base-case value (% or $)	Source	Ranges for sensitivity analysis	Probability distribution for sensitivity analysis
PE prevalence	4.7%	a	±10%	Beta
PE prevalence reduction using ASA	48%	[18]	±10%	Beta
ASA side effect prevalence	10%	[18]	±10%	Beta
PROMPT model sensitivity	74%	a	±10%	Beta
PROMPT model specificity	83%	a	±10%	Beta
MAP model sensitivity	65%	a	±10%	Beta
MAP model specificity	82%	a	±10%	Beta
Baseline model sensitivity	57%	a	±10%	Beta
Baseline model specificity	82%	a	±10%	Beta
PROMPT screening costs	11.27	FAH	±50%	Gamma
MAP screening costs	6.34	FAH	±50%	Gamma
Baseline screening costs	6.34	FAH	±50%	Gamma
High risk monitoring costs	674.23	FAH	±20%	Gamma
Low risk monitoring costs	579.86	FAH	±20%	Gamma
Side effect medication costs	192.25	FAH	±20%	Gamma
Healthy birth costs	1352.11	FAH	±20%	Gamma
PE birth costs	5699.30	FAH	±20%	Gamma

Abbreviations: PE=preeclampsia. ASA=aspirin. MAP=mean arterial pressure. PROMPT= PE risk factor + ophthalmic data + mean arterial pressure prediction test. The “a” means the data were from this study. FAH= The First Affiliated Hospital, Sun Yat-sen University.

Supplementary Table 7. Explanations and calculations of classification metrics

	Explanation	Calculation
NRI	The continuous NRI is calculated for biomarker and PROMPT models in our analysis. The 'upward' movement in categories for subjects with the outcome highlights better classification, and any 'downward movement' highlights worse reclassification. The sum of proportions of cases and non-cases with improved reclassification for cases denoted by P[up|case] {where P indicates probability} and lower for non-cases denoted by P[down|non-case]) minus the sum of proportions with P[up|non-case] and P[down|case].[19]	NRI = P(up|case) − P(down|case) − P(up|non-case) + P(down|non-case)
IDI	It is proposed as a measure that integrates the NRI over all possible cut-offs for the probability of the outcome. The higher the IDI, the more discriminant the additional retinal variables.[20]	IDI=P_{PROMPT} (case) −P_{PROMPT} (non-case) − P_{MAP} (case) + P_{MAP} (non-case)

Abbreviations: NRI= net reclassification index. IDI= integrated discrimination improvement.

Supplementary Table 8. STROBE Checklist

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	 P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P3
Objectives	3	State specific objectives, including any prespecified hypotheses	P3
Methods			
Study design	4	Present key elements of study design early in the paper	P7-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	P7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P8 and Supplementary Table 4

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Exposed group: P8 and Table 1 Unexposed group: P8 and Table 1
Bias	9	Describe any efforts to address potential sources of bias	P8
Study size	10	Explain how the study size was arrived at	P9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	P8-9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Exposed group: P4 and Supplementary Figure 1 Unexposed group: P4 and

		(b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	Supplementary Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	Exposed group: Table 1 and P7-8 Unexposed group: Table 1 and P7-8
Outcome data	15*	Report numbers of outcome events or summary measures over time	P8

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	P4-5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	P5
Discussion			
Key results	18	Summarise key results with reference to study objectives	P5
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P5-7
Generalisability	21	Discuss the generalisability (external validity) of the study results	P5-7
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P10

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at

http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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