ASSESSING LONG-TERM EFFECTIVENESS AND COST-EFFECTIVENESS OF STATIN THERAPY IN THE UK: A MODELLING STUDY USING INDIVIDUAL PARTICIPANT DATASETS

SUPPLEMENTARY MATERIAL

Contents

TRIPOD Checklist: Prediction Model Development and Validation in Chapters 2 and 3

Section/Topic	Item	Development (D) or Validation (V)	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.	Chapter 2 title. Chapter 3 title. Chapter 2/3 Introduction and methods
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	Not directly applicable. Chapters 2 and 3 are chapters in a larger report with a single abstract. Abstract pg.3 includes some of summary.
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.	Chapters 2 and 3 aims and objectives.
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	Chapters 2 and 3 aims and objectives.
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately	Chapter 2 Methods 'Data' section. Chapter 3 Methods UK Biobank cohort and Appendix 2.

			for the development and validation data sets, if applicable.	
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	Chapter 2 Methods 'Data' section. Chapter 3 Methods CVD model development in UK Biobank and Appendix 2.
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.	Chapter 2 Methods 'Data' section includes a reference to details for each individual trial. Chapter 3 Methods UK Biobank cohort, Table 4 and Appendix 2.
	5b	D;V	Describe eligibility criteria for participants.	Chapter 2 Aims and Objectives and Methods 'Data' section includes a reference to details for each individual trial. Chapter 3 Methods UK Biobank cohort and Appendix 2.
	5c	D;V	Give details of treatments received, if relevant.	Chapter 2 Methods 'Data' section includes a reference to details for each individual trial. Chapter 3 is an observation cohort study and does not involve active treatment.
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	Chapter 2 Aims and Objectives and Methods. Chapter 3 Methods CVD model development in UK Biobank.
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	Not relevant. The work is based on secondary analysis of already completed studies. Protocol of current study was prospectively completed and versions documented at https://fundingawards.nihr.ac.uk/award/17/140/02.
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	Chapter 2 Methods 'Risk equations' section. Chapter 3 Methods CVD model development in UK Biobank.
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	Not relevant. The work is based on secondary analysis of already completed studies. Protocol of current study was prospectively completed and versions documented at

				https://fundingawards.nihr.ac.uk/award/17/140/02.
Sample size	8	D;V	Explain how the study size was arrived at.	Not relevant. The work is based on secondary analysis of already completed studies.
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.	Chapter 2 Methods 'Handling of missing data' section. Appendix 1.
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	Chapter 2 Methods 'Risk equations' section. Chapter 3 Methods 'CVD model development in UK Biobank' section.
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	Chapter 2 Methods 'Risk equations' and 'Internal model validation' sections. Chapter 3 Methods 'CVD model development in UK Biobank' and 'Further model validation in UK Biobank and Whitehall II studies' sections.
	10c	V	For validation, describe how the predictions were calculated.	Chapter 2 Methods 'Microsimulation model' section. Chapter 3 Methods 'Executing model predictions' section.
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	Chapter 2 Methods 'Risk equations' and 'Internal model validation' sections. Chapter 3 Methods 'Further model validation in UK Biobank and Whitehall II studies' section.
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	Chapter 3 Methods 'CVD model development in UK. Biobank' section gives the reason for calibrating the model.
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	NA
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	Chapter 3 'UK Biobank cohort' section.
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the	Chapter 2 Table 3.

			number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	Chapter 3 Results paragraph 1.
	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.	Chapter 2 Table 2. Chapter 2 Methods 'Handling of missing data' section. Chapter 3 Table 4.
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	Chapter 3 Table 4 and Appendix 2.
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	Chapter 2 Table 3. Chapter 2 Figure 3. Chapter 3 Table 5.
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	NA
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).	Chapter 2 Figures 1(a)-1(f). Chapter 3 Figure 4, Appendix 3 Table 28.
	15b	D	Explain how to the use the prediction model.	Chapter 3 Results, Chapter 8.
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	Chapter 3 Figures 5-6.
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	Chapter 3.
Discussion				

Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	Chapter 9 'Limitations of the assessment' section.
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	Chapter 3 Summary.
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	Chapter 9 'Cardiovascular disease microsimulation policy model' section.
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	Chapter 9 'Cardiovascular disease microsimulation policy model' and 'Statin cost-effectiveness findings' sections.
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Protocol of current study was prospectively completed and versions documented at https://fundingawards.nihr.ac.uk/award/17/140/02. Chapter 8; and in 'Data sharing statement' on page 97.
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	Pg. 1 and Pg. 4

D, model development; V, model validation

Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS2022) Checklist for Chapters 6 and 7

Topic	No.	Item	Location where item is reported
Title			
	1	Identify the study as an economic evaluation and specify the interventions being compared.	The report title; Title of Chapter 6 (analyses 40-70 years old); Title of Chapter 7 (analyses for ≥70 years old)
Abstract			
	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Abstract and scientific summary
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	Chapter 1. Introduction
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	Study protocol available at https://fundingawards.nihr.ac.uk/award/17/140/02
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Chapter 3, Table 4 (analyses 40-70 years old); Chapter 7, Table 16 (analyses for ≥70 years old)
Setting and location	6	Provide relevant contextual information that may influence findings.	Chapter 1; Aims and objectives in Chapter 6 (analyses 40-70 years old); and Chapter 7 (analyses for ≥70 years old).
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Methods in Chapter 6 (same for analyses in 40-70 and ≥70 years old).
Perspective	8	State the perspective(s) adopted by the study and why chosen.	First paragraph of Chapter 4 and Chapter 6 (same for analyses in 40-70 and ≥70 years old)

Topic	No.	Item	Location where item is reported
Time horizon	9	State the time horizon for the study and why appropriate.	First paragraph of Methods in Chapter 6 (same for analyses in 40-70 and ≥70 years old)
Discount rate	10	Report the discount rate(s) and reason chosen.	Methods in Chapter 6 (same for analyses in 40-70 and ≥70 years old)
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Methods in Chapter 6 (same for analyses in 40-70 and ≥70 years old)
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Results, Chapter 3 and Chapter 5 Methods, Chapters 6 and 7
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Chapter 3 and Chapter 5 (same for analyses in 40-70 and ≥70 years old)
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Chapter 4 (same for analyses in 40-70 and ≥70 years old)
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Methods, Chapter 4 (same for analyses in 40-70 and ≥70 years old)
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	Rationale for the study in Chapter 1; Chapter 2; Chapter 3; Chapter 4; Chapter 5; Methods in Chapter 6; Chapter 8 (same for analyses in 40-70 and ≥70 years old)
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Methods in Chapter 3 and Appendix 3 (same for analyses in 40-70 and ≥70 years old)
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	Risk equations, methods in Chapter 2; CVD model development in UK Biobank in Chapter 3 (same for analyses in 40-70 and ≥70 years old)
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	Study population, Methods in Chapter 6 (analyses in 40-70 years old); study population, Methods in Chapter 7 (analyses in ≥70 years old)

Topic	No.	Item	Location where item is reported
Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	Methods, Chapters 6 and 7 (same for analyses in 40-70 and ≥70 years old)
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	Patient and public involvement and engagement in Chapter 9 (same for analyses in 40-70 and ≥70 years old)
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Table 4, Chapter 3 Table 13, Chapter 6 (analyses in 40-70 years old); Table 16, Chapter 7 (analyses in ≥70 years old)
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	Results in Chapter 6 (analyses in 40-70 years old); Results in Chapter 7 (analyses in ≥70 years old)
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Results in Chapter 6 (analyses in 40-70 years old); Results in Chapter 7 (analyses in ≥70 years old)
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	Equality, diversity and inclusion and Patient and public involvement and engagement, Chapter 9 (same for analyses in 40-70 and ≥70 years old)
Discussion			
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Chapter 9 and Chapter 10 (same for analyses in 40-70 and ≥70 years old)

Topic	No.	Item	Location where item is reported
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	Title page and abstract
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	Title page and ICMJE disclosure forms

GRIPP2 Short Form

Section and topic	Item	Reported on page No
1: Aim	Report the aim of PPI in the study	90
2: Methods	Provide a clear description of the methods used for PPI in the study	90
3: Study results	Outcomes - Report the results of PPI in the study, including both positive and negative outcomes	90
4: Discussion and conclusions	Outcomes - Comment on the extent to which PPI influenced the study overall. Describe positive and negative effects	90-91
5: Reflections/critical perspective	Comment critically on PPI input in the study, reflecting on the things that went well and those that did not, so others can learn from this experience	91