STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	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	(a) Page 2: paragraph 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	(b) Page 2: paragraph 1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 3: paragraph 1
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 3: paragraph 1
Methods			
Study design	4	Present key elements of study design early in the paper	Page 3: paragraph 1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 6-7: Methods: Patient Recruitment
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	(a) Page 6-7: Methods: Patient Recruitment; Fig. 1; Fig. S1
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	(b) N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6-7: Methods: Patient Recruitment; Fig. 1; Fig. S1
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	Page 6-8: Methods; Supplementary Methods; Fig. 1; Fig. S1
Bias	9	Describe any efforts to address potential sources of bias	Page 8: Methods: Statistical Analysis; Supplementary Methods: Power and Statistical Analyses
Study size	10	Explain how the study size was arrived at	Supplementary Methods: Power and Statistical Analyses
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 8: Methods: Statistical Analysis; Supplementary Methods: Machine Learning Model; Power and Statistical Analyses
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	(a) Page 8: Methods: Statistical Analysis; Supplementary Methods: Machine Learning Model; Power and Statistical Analyses
		(*b*) Describe any methods used to examine subgroups and interactions	(b) Page 8: Methods: Statistical Analysis;

			Supplementary Methods: Machine Learning Model; Power and Statistical Analyses
		(*c*) Explain how missing data were addressed	(c) Supplementary Methods: Power and Statistical Analyses
		(*d*) If applicable, explain how loss to follow-up was addressed	(d) Supplementary Methods: Power and Statistical Analyses
		(*e*) Describe any sensitivity analyses	(e) Supplementary Methods: Machine Learning Model; Power and Statistical Analyses
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	(a) Page 6-7: Methods: Patient Recruitment; Fig. 1; Fig. S1
		(b) Give reasons for non-participation at each stage	(b) Page 6-7: Methods: Patient Recruitment; Fig. 1; Fig. S1
		(c) Consider use of a flow diagram	(c) Fig. 1; Fig. S1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	(a) Supplementary Tables 1, 2 and 6
		(b) Indicate number of participants with missing data for each variable of interest	(b) Fig S1; Supplementary Table 2
		(c) Summarise follow-up time (eg, average and total amount)	(c) Supplementary Table 1
Outcome data	15*	Report numbers of outcome events or summary measures over time	Fig 1 and 2; Fig S2-S3 and S5-S7; Supplementary Tables 1, 2, 6, 7 and 8

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	(a) Pages 3-6; Fig 1 and 2; Fig S2-S3 and S5-S7; Supplementary Tables 1, 2, 6, 7 and 8 (b) Supplementary Methods: Single Nucleotide Variant Analysis; Machine Learning Model; Power and Statistical Analyses (c) N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Supplementary Methods: Machine Learning Model; Power and Statistical Analyses; Fig S4
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 3-6
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	Page 6
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 6
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 6
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	Page 9: Acknowledgements

*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.