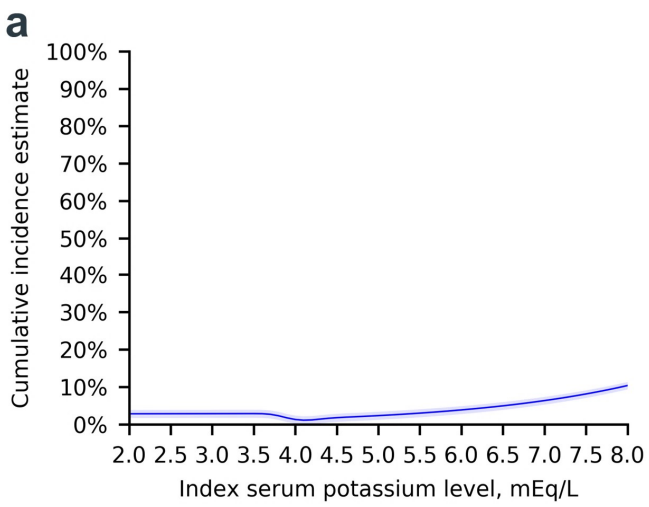
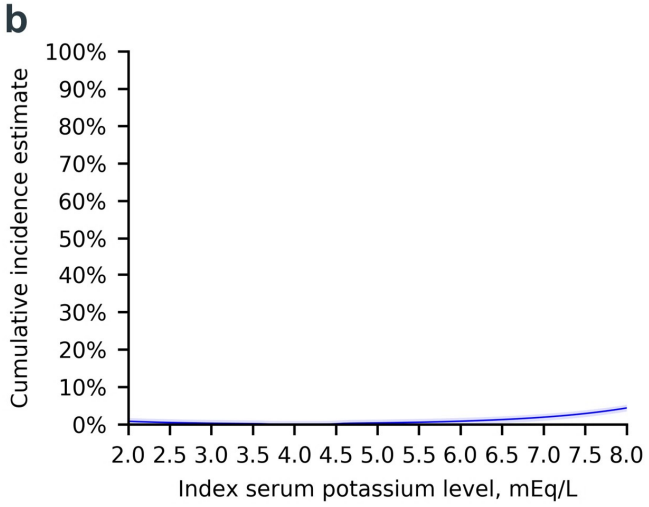
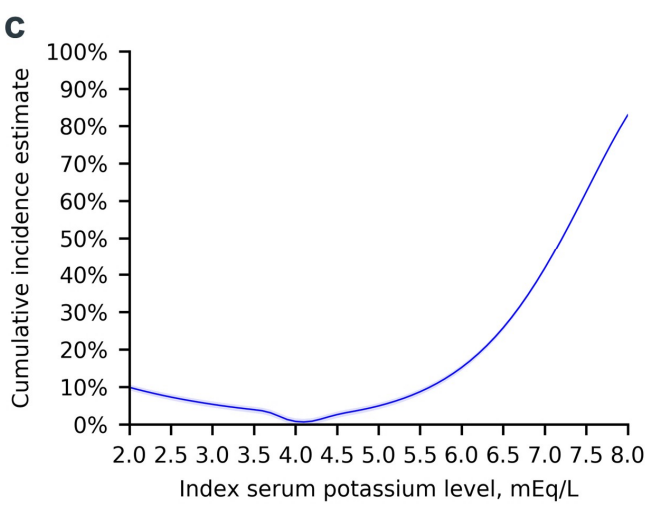
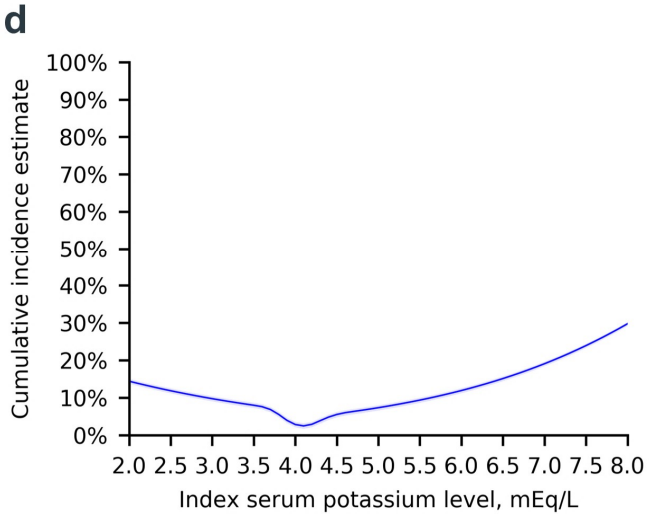
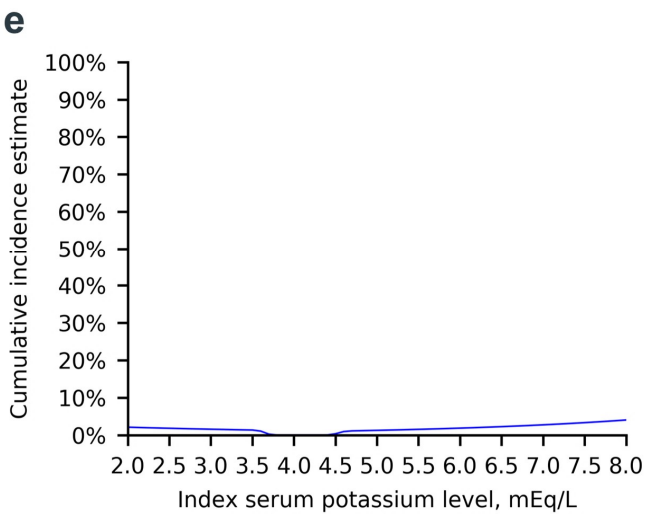

a
Cumulative incidence estimate
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0
Index serum potassium level, mEq/L


b
Cumulative incidence estimate
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0
Index serum potassium level, mEq/L


c
Cumulative incidence estimate
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0
Index serum potassium level, mEq/L


d
Cumulative incidence estimate
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0
Index serum potassium level, mEq/L


e
Cumulative incidence estimate
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0
Index serum potassium level, mEq/L

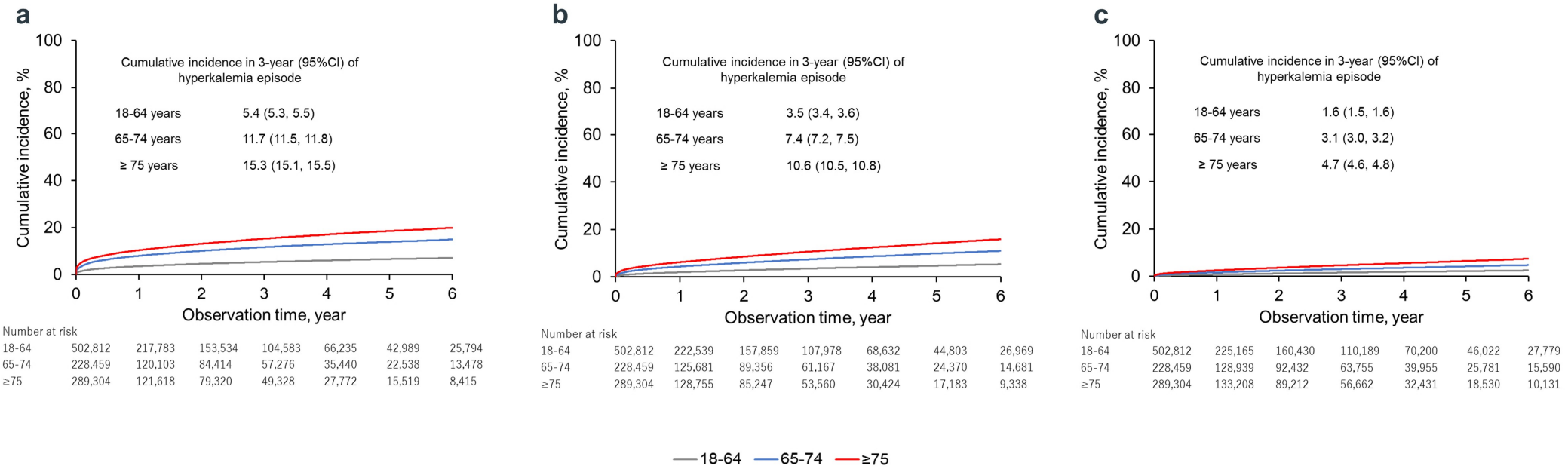

a
Cumulative incidence, %
100
80
60
40
20
0
Cumulative incidence in 3-year (95%CI) of hyperkalemia episode
18-64 years 5.4 (5.3, 5.5)
65-74 years 11.7 (11.5, 11.8)
≥ 75 years 15.3 (15.1, 15.5)
0 1 2 3 4 5 6
Observation time, year
Number at risk
18-64 502,812 217,783 153,534 104,583 66,235 42,989 25,794
65-74 228,459 120,103 84,414 57,276 35,440 22,538 13,478
≥75 289,304 121,618 79,320 49,328 27,772 15,519 8,415
b
Cumulative incidence, %
Cumulative incidence in 3-year (95%CI) of hyperkalemia episode
18-64 years 3.5 (3.4, 3.6)
65-74 years 7.4 (7.2, 7.5)
≥ 75 years 10.6 (10.5, 10.8)
Observation time, year
Number at risk
18-64 502,812 222,539 157,859 107,978 68,632 44,803 26,969
65-74 228,459 125,681 89,356 61,167 38,081 24,370 14,681
≥75 289,304 128,755 85,247 53,560 30,424 17,183 9,338
c
Cumulative incidence, %
Cumulative incidence in 3-year (95%CI) of hyperkalemia episode
18-64 years 1.6 (1.5, 1.6)
65-74 years 3.1 (3.0, 3.2)
≥ 75 years 4.7 (4.6, 4.8)
Observation time, year
Number at risk
18-64 502,812 225,165 160,430 110,189 70,200 46,022 27,779
65-74 228,459 128,939 92,432 63,755 39,955 25,781 15,590
≥75 289,304 133,208 89,212 56,662 32,431 18,530 10,131
18-64 65-74 ≥75

Table S1. Definitions of high-risk subgroups

Subgroup	Definition
Chronic kidney disease	Defined as either a diagnosis of chronic nephritic syndrome (ICD-10 code: N03), glomerular disease (N05-N08), chronic kidney disease/chronic renal failure (N18-N19), diabetic nephropathy (E102, E112, E122, E132, E142), or hypertension with renal failure (I120, I13), or the presence of an average eGFR of <60 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$ CKD stage 1: eGFR ≥90 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$, stage 2: eGFR 60-89 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$, stage 3a: eGFR 45-59 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$, stage 3b: eGFR 30-44 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$, stage 4: eGFR 15-29 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$, and stage 5: eGFR <15 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$
Diabetes mellitus	Defined as a diagnosis of DM (E10-E14)
Heart failure	Defined as a diagnosis of heart failure (I50, I110)
Hypertension	Defined as a diagnosis of hypertension (I10-I15)

ICD-10, International Classification of Diseases 10th revision; eGFR, estimated glomerular filtration rate; DM, diabetes mellitus

Table S2. Definitions of clinical outcomes

Outcome	Definition
In-hospital death	Based on death information in the hospital discharge summary
Cardiac events	Hospitalizations with ICD-10 codes of I21, I22, I23, I44, I45, I46, I47, I48, or I49
Hospitalization due to HF	ICD-10 code I50 or I110 as the main reason for hospitalization
Introduction of renal replacement therapy	Presence of a national receipt code for dialysis or renal transplant
CG-GI therapy	[Regular insulin or intermediate-acting insulin] and glucose injection prescribed on the same date, or prescriptions of calcium gluconate
Rehospitalization	Readmission within 30 days after discharge from previous hospitalization
Recurrence of hyperkalemia episode	An S-K level of ≥5.1 mEq/L following a normal S-K level (3.6-5.0 mEq/L)

ICD-10, International Classification of Diseases 10th revision; HF, heart failure; CG-GI, calcium gluconate and glucose-insulin; S-K, serum potassium

Table S3. List of comorbidities

Condition	ICD-10 code
Myocardial infarction	I21; I22; I23; I24
Peripheral vascular disease	I70; I71; I72; I73; I74; I77
Cerebrovascular disease	I60-I69; G45
Chronic pulmonary disease	J40-J47; J60-J67; J684; J701; J703; J841; J920; J961; J982; J983
Moderate to severe liver disease	B150; B160; B162; B190; K704; K72; K766; I85
Atrial fibrillation or atrial flutter	I48
Valvular heart disease	I00-I02; I05-I09; I34; I35; I36; I37; Q20-Q25;
Alcoholism-related or other substance-abuse related disorders	T36-T65; F10-F19; G312; G612; G721; I426; K292; K860; K70; R780; T51; Z714; Z721
Acute kidney injury	N17
Sepsis	A021, A207, A227, A241, A267, A282, A327, A394, A400-A403, A409-A415, A418-A419, A427, A548, B007, B349, B377, D71, I301, I330, J020, J209, J950, L029, L080, M8699, O080, O753, O85, O883
Gastrointestinal bleeding	K250, K252, K254, K256, K260, K262, K264, K266, K284, K290, K571, K573
Gastrointestinal perforation	K251, K252, K255, K256, K261, K265, K266, K285, K570, K572
Peripheral edema	R600

ICD-10, International Classification of Diseases 10th revision;

Table S4. Comorbidities stratified by high-risk subgroups

	Overall n=25 395	CKD n=14 322	DM n=12 101	HF n=8 570	HTN n=16 463
Comorbidity, n (%)					
Myocardial infarction	1 073 (4.2)	597 (4.2)	593 (4.9)	699 (8.2)	816 (5.0)
Peripheral vascular disease	3 790 (14.9)	2 458 (17.2)	2 248 (18.6)	1 792 (20.9)	3 112 (18.9)
Cerebrovascular disease	5 795 (22.8)	3 440 (24.0)	3 217 (26.6)	2 431 (28.4)	4 657 (28.3)
Chronic pulmonary disease	4 196 (16.5)	2 336 (16.3)	2 025 (16.7)	1 924 (22.5)	3 059 (18.6)
Moderate to severe liver disease	491 (1.9)	211 (1.5)	222 (1.8)	112 (1.3)	283 (1.7)
Atrial fibrillation or atrial flutter	3 496 (13.8)	2 081 (14.5)	1 608 (13.3)	2 530 (29.5)	2 722 (16.5)
Valvular heart disease	2 371 (9.3)	1 528 (10.7)	1 179 (9.7)	1 809 (21.1)	1 911 (11.6)
Alcoholism-related or other substance-abuse related disorders	641 (2.5)	296 (2.1)	303 (2.5)	159 (1.9)	376 (2.3)
Acute kidney injury	1 145 (4.5)	598 (4.2)	431 (3.6)	521 (6.1)	592 (3.6)
Sepsis	2 796 (11.0)	1 429 (10.0)	1 371 (11.3)	1 196 (14.0)	1 825 (11.1)
Gastrointestinal bleeding	915 (3.6)	469 (3.3)	407 (3.4)	321 (3.7)	611 (3.7)
Gastrointestinal perforation	72 (0.3)	28 (0.2)	22 (0.2)	16 (0.2)	36 (0.2)
Peripheral edema	575 (2.3)	398 (2.8)	303 (2.5)	284 (3.3)	484 (2.9)

CKD, chronic kidney disease; DM, diabetes mellitus; HF, heart failure; HTN, hypertension

Table S5. Prescription coverage of potassium binder prescribed on index date

	Overall n=1 468	CKD n=1 308	DM n=825	HF n=543	HTN n=1 171
MPR (%)					
Mean±SD	77.2±29.0	78.1±28.6	78.5±27.7	77.2±29.9	78.4±28.7
Median	91.6	92.6	92.2	92.1	93.3
PDC (%)					
Mean±SD	54.8±41.0	58.8±39.9	58.0±39.8	53.0±40.7	58.6±40.3
Median	61.7	71.4	69.6	52.5	71.9

CKD, chronic kidney disease; DM, diabetes mellitus; HF, heart failure; HTN, hypertension; MPR, medication possession ratio; PDC, proportion of days covered; SD, standard deviation

PDC was the proportion of days covered with potassium binder treatment supplied during a 1-year fixed follow-up period.

MPR was the number of days with potassium binder treatment supplied within the refill interval.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant part from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2	Title and abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Abstract section
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3	Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	3	Line 64 "Herein, …"
Methods				
Study design	4	Present key elements of study design early in the paper	4	Study design and patient selection
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4	Study design and patient selection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4	Study design and patient selection Line 82 "Hyperkalemia was defined…"
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N.A.	N.A.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6	Study design and patient selection and statistical analysis We used the ICD-10 codes for disease diagnoses and the relevant codes used in this study

				is summarized in the supplementary materials.
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	4	Data source
Bias	9	Describe any efforts to address potential sources of bias	6	Statistical analysis
Study size	10	Explain how the study size was arrived at	4	Study design and patient selection

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5	Covariates and statistical analysis We set high-risk subgroups to study the patient at risk of developing hyperkalemia. Rationale of choosing the criteria is summarized in the covariates section.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6	Statistical analysis Line 115 “The associations between…”
		(*b*) Describe any methods used to examine subgroups and interactions	6	Statistical analysis Line 124 “Subgroup analyses of prevalence…”
		(*c*) Explain how missing data were addressed	N.A.	N.A.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N.A.	N.A.
		(*e*) Describe any sensitivity analyses	6	Statistical analysis Line 122 “Although an S-K reading…”
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	7	Results Line 134 “We extracted 1 022 087 patients…”
		(b) Give reasons for non-participation at each stage	7	Results Line 136 “After excluding 16 033 patients…”
		(c) Consider use of a flow diagram	7	Results Summarized in the figure1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	24	Results Table 2. Patient characteristics

		(b) Indicate number of participants with missing data for each variable of interest	N.A.	N.A.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	21	Results Table 3. Patient characteristics
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	7-8	Results We summarized measures of the prevalence, incidence, treatment patterns, potassium control status, and results of cubic spline analyses in the results.
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N.A.	N.A.
		Cross-sectional study—Report numbers of outcome events or summary measures	N.A.	N.A.
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	7-8	Results We presented the estimated precision range (95% confidence interval) of the outcomes of interest. The confounder adjusted in the study is explained in the method section.
		(*b*) Report category boundaries when continuous variables were categorized	7-8	Results We applied a category boundary when we studied the cumulative incidence of hyperkalemia by age groups. The results are summarized in the main text as well as Figure S2.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N.A.	N.A.

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9	Results We applied different cut-off value of S-K for the analysis of recurrent hyperlalemia. The results are summarized in the main text as well as Figure 9.
Discussion				
Key results	18	Summarise key results with reference to study objectives	9	Discussion Line 197 “To our knowledge…”
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	12	Discussion Line 269 “This study has several limitations…”
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12	Discussion Line 243 “This study has several limitations…”
Generalisability	21	Discuss the generalisability (external validity) of the study results	12	Discussion Line 280 “Second, the data were mostly…”
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	13	Acknowledgements

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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 www.strobe-statement.org.