# BMJ Open Consistency of causal claims in observational studies: a review of papers published in a general medical journal

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#### ABSTRACT

Objective To evaluate the consistency of causal statements in observational studies published in *The BMJ*. **Design** Review of observational studies published in a general medical journal.

Data source Cohort and other longitudinal studies describing an exposure-outcome relationship published in The BMJ in 2018. We also had access to the submitted papers and reviewer reports.

Main outcome measures Proportion of published research papers with 'inconsistent' use of causal language. Papers where language was consistently causal or non-causal were classified as 'consistently causal' or 'consistently not causal', respectively. For the 'inconsistent' papers, we then compared the published and submitted version.

Results Of 151 published research papers, 60 described eligible studies. Of these 60, we classified the causal language used as 'consistently causal' (48%), 'inconsistent' (20%) and 'consistently not causal' (32%). Eleven out of 12 (92%) of the 'inconsistent' papers were already inconsistent on submission. The inconsistencies found in both submitted and published versions were mainly due to mismatches between objectives and conclusions. One section might be carefully phrased in terms of association while the other presented causal language. When identifying only an association, some authors jumped to recommending acting on the findings as if motivated by the evidence presented.

**Conclusion** Further guidance is necessary for authors on what constitutes a causal statement and how to justify or discuss assumptions involved. Based on screening these papers, we provide a list of expressions beyond the obvious 'cause' word which may inspire a useful more comprehensive compendium on causal language.

#### INTRODUCTION

Many researchers remain tempted to draw causal conclusions from observational data despite acknowledging that mere association is not causation because causal inference is the ultimate goal of most clinical and public health research.<sup>1 2</sup> Gold-standard answers are typically sought through randomised controlled trials (RCTs). The unique ability of RCTs to avoid confounding bias<sup>3</sup> has led to demands that empirical research must

#### Strengths and limitations of this study

- By evaluating published observational studies in a general medical journal, we provided relevant examples of (ambiguous) causal statements.
- We focused on the abstract where clear messages are especially important, as many readers start by screening the abstract of the study.
- Comparing the submitted and published versions of the abstract allowed us to identify whether any causal claims were made or not as a result of the peer-review process.
- The focus on the use of causal language rather than the specific methods avoided discussion on the validity of underlying assumptions justifying causal inference in the setting studied.
- Assessing observational studies from a single journal allowed us to flag the inconsistent use of causal claims in this context, but not to estimate its prevalence more generally.

be drawn from randomised studies to justify causal statements. 4-6 RCTs are mainly used to assess the effect of a treatment or intervention but are not easily adapted to evaluate prognostic or risk factors rather than interventions.

There are however good reasons to look beyond RCTs for evidence on treatment effects. In many settings, RCTs are not feasible, ethical or timely and thus observational data are all that is available for some time, as in the recent COVID-19 crisis. Furthermore, observational studies typically involve broader realworld contexts than RCTs, where the costs and risks of experimentation suggest studying high-risk patients without major comorbidities.<sup>7</sup> This selection challenges generalisation to the target population. Highly selected populations with a usually short follow-up, render RCTs inappropriate to evaluate (longterm) unintended side effects. Trials further suffer from treatment non-compliance which complicates analysis, as treatment-specific populations lose the benefit of randomisation.



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Recent International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E9 guidelines therefore emphasise the importance of causal estimands beyond intention-to-treat, such as perprotocol and as-treated analysis.<sup>8 9</sup>

Deliberately avoiding causal statements on a hoped-for causal answer brings ambiguity and contrived reporting. <sup>10</sup> <sup>11</sup> Instead, authors should openly discuss the likely distance in meaning and magnitude between the data-based measure they are able to estimate and the desired targeted causal effect. Arguments would consider study design with additional assumptions in context. <sup>12</sup> Owing to decades of progress in statistical science (involving potential outcomes, directed acyclic graphs, propensity scores and more), <sup>13</sup> this allows for results, often unreachable by randomised trials, with a justified causal interpretation. <sup>14</sup>

In 2010, Cofield  $et\,at^0$  assessed the use of causal language in observational studies in nutrition but deemed causal language inappropriate for all observational studies. In 2017, Adams  $et\,at^{15}$  also considered that only RCTs allowed for causal inference, in their study assessing how people understand causal expressions in the news. From a different angle, Haber  $et\,at^{16}$  examined whether the tone and strength of causal claims made in a given paper matched the language describing the findings in social media. Not surprisingly, they found stronger causal statements in the media in half of the cases, emphasising the importance of clear scientific messages.

To promote this, Lederer *et al*<sup>17</sup> recently published a guide for authors and editors on how to report causal studies in respiratory, sleep and critical care journals. Rather than circumventing the problem by asking to avoid causal language, they provide key elements that ensure valid causal claims. Besides briefly explaining causal inference, they provide a definition of a confounder, outline how to identify confounding through so-called directed acyclic graphs and discuss how p values are often misinterpreted and how their value does not reflect the magnitude, direction or clinical importance of a given association. All these elements empower their target audience to critically assess observational studies.

To find out whether and how statements in study reports present confusing use of causal language (or lack thereof), we examined research papers concerned with exposures and outcomes published in *The BMJ* in 2018. Our focus was on the causal message *The BMJ* readers receive from these papers, particularly from the abstract. We evaluate the consistency of causal statements in the published abstracts of observational studies, whether this consistency was a reflection of the full text and if any a priori changes had been made as a result of the peer-review process.

#### **METHODS**

#### Sampling and inclusion criteria

COP identified all original research articles published in *The BMJ* in 2018 described as either cohort or longitudinal

studies in the study design section of the abstract. The eligible studies were identified by statements in this section of the abstract such as 'cohort', 'longitudinal' or 'registry-based'. Those identified as 'observational' were included if they suggested a period of follow-up rather than being cross-sectional. Articles described as case cohorts were excluded as their interpretation and analysis differs from other studies with follow-up assessing the exposure-outcome relationship.

#### **Assessment of published abstracts**

Two reviewers (COP, LB) independently screened the published abstracts of the eligible papers. For the text included under each of the subheadings in the abstract (objective, design, setting, participants, outcome, results, conclusion), the reviewers assessed whether there was an (implicit) causal (cl)aim using a yes/no/unclear response. After assessing each separate subheading, each reviewer then gave an overall assessment of the main claims in the paper's abstract as either 'consistently causal', 'inconsistent' or 'consistently not causal'. After the independent assessments, the overall rating of the abstract was compared between both reviewers; where there was disagreement, a third reviewer (EG) was consulted and a consensus reached.

#### Assessment of published full text

We further evaluated the full published text of all eligible papers to identify the statistical methods applied and any further causal claims. In particular, we looked for statements that would support or undermine a causal aim, including confounding adjustment, discussing residual confounding, exchangeability and issues of transportability. We randomly divided the papers between the two reviewers (COP, LB) for this assessment. For each paper, we extracted statements where authors described the statistical method and method for confounding adjustment, if any. We then extracted the sentences summarising the results and conclusions to highlight any causal claims.

#### **Assessment of initially submitted abstract version**

As the focus of this paper is to highlight ambiguous use of causal language, we further assessed those articles judged as 'inconsistent' to see if there were changes introduced to the manuscript between submission and publication, leading to this inconsistent use of causal language. For this subset, we obtained the submitted version of the manuscripts and the associated peer reviewers' comments from *The BMJ*'s manuscript tracking system. We then compared the published version with the first submitted version of the abstract to identify whether the same wording related to causal claims appeared in the submitted version and whether changes occurred as a result of comments from peer reviewers and editors, as indicated in the corresponding peer-review reports.

The same reviewers (COP, LB) independently evaluated the submitted versions of the abstracts. The reviewers assessed whether the content under each subheading of



the submitted abstract differed from the published version. Where there were discrepancies between versions, each reviewer indicated the presence of a causal claim as yes/no/unclear for each abstract subheading (title, objective, design, setting, participants, outcome, results, conclusion) and made an overall assessment of the submitted abstract as either 'consistently causal', 'inconsistent' or 'consistently not causal'. As before, the assessments were compared and, in cases of disagreement, a third reviewer (EG) was consulted and consensus reached.

#### Patient and public involvement

Patients were not involved in the design, analysis or interpretation of the study. Patients were not participants in this study; it was a methodological study (research on research). Patients' opinions of causal statements and the use of ambiguous language in research papers is important and further work in this area partnered by patients is important.

#### **RESULTS**

#### **Assessment of published abstracts**

In 2018, 151 research papers were published in *The BMJ*, of which 60 (40%) were eligible for inclusion in our study. We identified 29 studies (48%) reporting causal language consistently. A further 12 (20%) studies were considered inconsistent mainly because the objective stated the evaluation of an association while the conclusion presented a causal finding (9/12) or the opposite (3/12). Finally, there were papers that described studies aiming for prediction or reporting associations without (implicitly) suggesting that they had a causal nature that were considered consistently not causal (n=19, 32%). Table 1 shows sample excerpts from the published abstracts that were evaluated. Each row corresponds to statements from the same study. The first column indicates the assigned category, based on the type of association it describes. The last column explains why a given abstract was considered to belong to the assigned category. As the assessment pertains to causal claims in general, the words referring to the particular topic of the corresponding study were removed from the statements. The examples shown are not an exhaustive list, but were chosen to illustrate the different phrasing of statements belonging to the different categories. It is worth noting that the statements presented correspond to the objective and conclusion subheadings of the abstract. When assessing the abstracts, we identified that these were the subheadings under which the information to classify the abstract was mainly found. Other subheadings like design, setting and participants were not as relevant for this purpose, but were also assessed.

To further illustrate how statements in these two sections can be misleading, we tabulated a few examples in a 2 by 2 table showing mismatches between what was reported in the objectives and conclusion resulting in

the paper being categorised as either 'consistently (not) causal' or 'inconsistent' (table 2).

#### **Assessment of published full text**

Table A in online supplemental material presents statements found in both the published abstract and published full text of each of these papers (n=60) regarding the statistical method used and considerations suggesting a causal aim or otherwise. Each row corresponds to a different study. The papers are grouped according to the category to which the corresponding abstract was assigned to. The particular causal or non-causal wording is highlighted in bold. A brief description on the consistency of causal language is provided in the last column of table, labelled 'Comment'.

We found that all papers classified as 'consistently causal' based on the abstract, also used causal language and contained causal statements in the full text. This was additionally the case with more than half (11/19) of the abstracts classified as 'consistently not causal', where even though the abstract was carefully phrased in terms of association, the authors applied causal methods, discussed residual confounding, biological plausibility or a doseresponse relationship suggesting a causal aim.

In the previous section, we referred to three abstracts that had a clear causal objective but a non-causal conclusion. In the full text of these papers, the authors discussed concerns of residual confounding which explains why they decided to play down the conclusion.

Looking at the 'Methods' section in the full text of the abstracts classified as 'inconsistent', we found that 11 of the 12 provided adjusted estimates. Most of the studies (8/12, 67%) used outcome regression models, mainly Cox proportional hazard models, or (propensity score) matching (3/12, 25%).

#### **Assessment of submitted abstract version**

Of the 12 published abstracts classified as 'inconsistent', we further classified 11/12 (92%) as also inconsistent on submission. There was only one study where the submitted version of the abstract described a different type of association. In this case, the conclusion of both the submitted and published versions was rather conservative by stating that the intervention was 'independently associated' with the outcome. The submitted version expressed a causal objective, stating the aim of evaluating the 'impact' of a particular intervention with corresponding methods: providing adjusted estimated effects and including sensitivity analysis using propensity score matching. However, in the published version the term 'impact' was replaced by 'association' making the abstract less clear about a causal aim because both the abstract's objectives and the conclusion described an association but the authors still provided adjusted HRs and resorted to propensity score matching.

#### DISCUSSION

#### **Statement of principal findings**

We found that the majority (80%) of the published research abstracts reporting on observational studies had



**Table 1** Examples of statements found in the objectives and conclusions sections of abstracts of observational studies published in *The BMJ* in 2018 and their corresponding assigned category

Assigned category	Abstract objectives	Abstract conclusions	Comment
Consistently	"assess the effectiveness of"	'Little evidence was found of a direct impact of'	When discussing associations, words like
causal	'To determine the effect of in'	'has led to risk'	effect, contribution or role are similar to cause and then (direct) impact and effect will be their consequence.
	'To describe the contributions of'	' an important role in'	will be their consequence.
	'To evaluate the impact of'	'impacts are'	
	'To investigate whether improving adherence to'	"the beneficial effect of improved"	Evaluates taking an action 'improving adherence' and concludes that the effect is beneficial.
	'benefit of in reducing risk'	' is an overlooked risk factor for'	Evaluates how a given intervention can reduce the risk of an outcome and then labels it as an 'overlooked risk factor'.
	'To determine outcomes and safety of'	' is at least as effective and safe as'	Evaluates and determines that a certain intervention is as safe as the comparator.
	'to quantitatively decompose this joint association to only, to only, and to their interaction'.	'excess risk ofThese findings suggest that most cases of could be prevented by'	Suggests interest in direct and indirect effect, that is, mediation analysis, and concludes consequently.
Consistently not causal	"is associated withcompared with"	'is associated withcompared with'	Describes associations without labelling them as causal or prediction.
(associations)	'To describe trends in'	'rates were high during the study period of with the highest rates in vs'	Limits to describe frequency.
	'To assess how often'	'One in adults were'	
	'To examine the association between'	'could increase $\dots$ confirmation of these findings are warranted, preferably in an intervention setting'.	Suggests further research to determine the nature of the association.
	'compared withis associated with'	'Additional studies, with long term follow-up, are needed to investigate the effects of'	
Consistently not causal (prediction)	'To develop and validate a set of practical prediction tools that reliably estimate the outcome of'	"prediction models reliably estimate the outcome"	Describes developing and validating prediction models.
	'To prospectively validate the algorithm to'	'accurately classified'	
Inconsistent	"evaluate safety of"	'associated with'	Phrasing the objective as causal and
	"analyse the effect of"		limiting to describing an association in the conclusion.
	"critical determinant"		
	"association with"	'is safe'	Phrasing the objective as just to explore
		" had no substantial effect on long term survival"	an association and presenting a causal claim in the conclusion.
		" was determined by may be largely explained by"	
		' was found to be the safest drug, with reduced risks of'	
		'These results emphasise the benefit of'	
	"association with"	"tackling all these risk factors might substantially"	Phrasing the objective and conclusion as if just to assess an association but
		"Targeting prevention strategies among these patients should be considered".	then suggesting to take action given the findings.
		'Systematically addressing $\dots$ may be an important public health strategy to reduce the incidence of'	
		'present findings encourage the downward revision of such guidelines'	

a consistent use of causal language in the abstract. Still 20% of abstracts contained inconsistent messages on the causal nature of the key 'effect'. Inconsistencies showed up in two directions: an intentional quest for causality ending in uncriticised non-causal conclusions or carefully phrased mere associations ending with recommendations to act and intervene based on the exposure outcome association.

Beyond the wording, readers can learn much about the sought, after interpretation from described statistical methods, and assumptions made explicit in the paper. On a case-by-case basis, one could then assess whether additional assumptions, for example, involving 'no-unmeasured confounders', would justify the causal assessment derived from these approaches. Identifying key elements like the ones presented in the online supplemental

Examples of (mis)matching causal and non-casual statements found in the objectives and conclusions sections of abstracts of observational studies published in The BMJ in 2018

		Abstract conclusions	
		Causal	Not causal
Abstract objectives	Causal	Consistent 'assess the effectiveness of'and 'Little evidence was found of a direct impact of' 'benefit of in reducing risk' and ' is an overlooked risk factor for'	Inconsistent  'evaluate safety of' and 'associated with'  'analyse the effect of' and 'associated with'  'critical determinant' and 'associated with'
	Not causal	Inconsistent 'association with' and 'is safe' 'association with' and ' had no substantial effect on long term survival' 'association with' and 'tackling all these risk factors might substantially' 'association with' and 'Systematically addressing may be an important public health strategy to reduce the incidence of'	Consistent 'To describe trends in' and 'rates were high during the study period of with the highest rates in vs' 'To assess how often' and 'One in adults were' 'To develop and validate a set of practical prediction tools that reliably estimate the outcome of' and ' prediction models reliably estimate the outcome'

material would help to assess if causal inference is possible. If in doubt, a sensitivity analysis may be in order. It seems better to be transparent about the ultimate aim to draw a causal conclusion and to acknowledge to fall short of that, than to generate confusion.

When assessing the full text of the 'consistently causal' papers, we identified that authors often discussed these assumptions and resorted to conducting a sensitivity analysis. This was also the case for those papers that were classified as 'inconsistent' or 'consistently not causal'. In these papers, there was a concern for residual confounding because of the observational nature of the study or due to specific missed confounders. Therefore, the abstract's objective avoided suggesting a causal aim instead of being explicit of such concern or limitations in the abstract.

#### **Comparison with other studies**

This is not the first study to evaluate the use of causal language in the medical literature. Cofield et  $al^p$  assessed the use of causal language in observational studies in nutrition. However, they focus only on assessing whether authors included causal language or not, as it was deemed inappropriate due to the observational nature of the study. We have made the case that merely avoiding explicit causal terms is not a real solution. Even without them, a causal conclusion is implicit when the take home message encourages interventions based on the presented findings. Avoiding inconsistency is important but equally one

should be able to trust that the use of consistent causal language is not in vain. This requires a more in-depth look at methods and assumptions validating the causal claims.

#### Strengths and weaknesses of the study

Accurate abstracts are important. In just a few brief paragraphs, the authors summarise key elements of design, methods and results, and come to a conclusion. Many readers only read the abstract. However, a powerful abstract opens the door to readers and sets the scene for any study. It serves the different roles of informing the audience about its main findings while motivating the reader to further explore the full text, all within the constraints of brevity. This demands authors to give special attention to ensure that every word in the abstract is required. All of the above makes the assessment of the abstract relevant but also challenging.

Further research is needed to explore how causal claims presented in the abstract and full text are supported by the design and methods applied, which entails assessing the methods used and evaluating whether the underlying assumptions were met. 19 The optimal conclusion should not simply label a study as black or white in causal terms. In the present study, we used a convenient limited number of classifications for short statements. In practice, a continuous degree of confidence in a potential causal relationship is likely to emerge based on the observed association.

True nature of the main exposure effect							
		Causal	Not causal				
Reported nature of the studied exposure	Causal	A true causal effect has been discovered. Recommendation to act on this should be considered. Language in the context of a study intended for causal inference.	Type I error: there is no causal effect, but it is claimed. Causal language used or suggestion to take action made when the purpose/ability was to find associations.				
effect	Not causal	Type II error: hiding the true causal objective/result by avoiding use of causal language.	No causal language when the objective is prediction or t explore associations.				

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## **Table 4** Examples of words and study elements that could point to causality or otherwise

Words expressing a causal relationship

- ▶ Affect
- Attributable
- ▶ Benefit
- ▶ Cause/Causal pathway
- ▶ Contribute
- Determinant
- ▶ Effect
- ▶ Efficacy
- ► Impact
- ► Improve
- Leads to
- Mediates
- ► Responsible for
- Results in
- Safety

Words that could suggest causality in a given context

- ► Independently associated
- ► Induce
  - Higher (lower) probability
- Modify
- ► Risk (factor)
- ► Trajectory (quantitatively) decompose

Specific expressions avoiding suggestions of

causal effects

- Association
- Correlation
- ► Less (more) likely link
- ► Predict
- Pattern

Key aspects suggesting causal aim

- ► Adjusting for confounders
- Discussing biological plausibility, doseresponse and/or temporal relationship
- Discussing 'unmeasured confounders' assumption
- Mediation analysis
- Propensity score adjustment (propensity score) matching
- Providing estimates of (population) attributable risks
- ► Suggesting/Recommending intervention
- ► Target trial emulation design
- Using directed acyclic graphs to identify confounders and mediators
- Using negative controls
- ► Using instrumental variables

We are aware that by limiting our assessment to the consistency of causal language, we may have missed the discussion of the extent to which the underlying assumptions that enable causal inference were met. This requires subject-matter knowledge in each particular case. <sup>13</sup> Indeed, when there was a clear causal aim but the authors considered that these assumptions were not fulfilled, they may have decided that a causal claim was inappropriate and phrased their conclusion in terms of association rather than causation. If this is the case, the apparent inconsistency would no longer hold. On the contrary, any undue causal claims can be viewed as a form of spin. <sup>20</sup> <sup>21</sup>

#### **Policy implications**

As observational data resources abound, methods for causal inference from observational data have surged in tandem with the call for real-world evidence. The new

opportunities bring new challenges and the responsibility for clear and well-supported statements on the evidence. In this spirit and motivated by novel guidelines as proposed by International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E9 and Food and Drug Administration, Hernán et al have embarked on a project entitled 'Developing Guidelines for the Analysis of Randomised Controlled Trials in Real-World Settings'. 22 The importance of such initiatives supports a shift towards being explicit and discussing assumptions underlying causal methods that allow for causal interpretations in context, with or without an RCT.<sup>13</sup> In the meantime, uncritical ambiguous phrasing in observational studies remains prevalent. 14 Those searching for the best possible evidence supporting future treatment decisions are best served by transparent reports of observational studies.

Faced with uncertainty when concluding on the nature of the observed exposure outcome relationship, a justifiable balance between the type I and II error rate is a natural guide for action. The cost of errors must be weighed in context, for instance, as in clinical trials emphasising control of the type I error to avoid introducing new unhelpful drugs at a potentially large cost. Alternative weights are typical in screening programmes where false positives will be caught in follow-up examinations, but false negatives are lost forever. In a crisis, such as the current COVID-19 pandemic, we must act before long-term randomised trials have materialised. It becomes undeniably important to learn as much as we can from observational data, be aware of the types of risk when acting or not, as displayed in table 3.

A prerequisite for good causal language practice includes awareness of which language implies a causal statement and which does not. To support correct phrasing and raise awareness, we have compiled a short list of words and expressions with dedicated (non) causal meaning (table 4). The list draws on phrases found in our study and in the references cited, particularly Hernán<sup>10</sup> and Thapa *et al.*<sup>6</sup> This list is a suggestion as a starting point and further studies can test and validate it. We consider that a definition of causal language that is generally recognised by the research community is needed.<sup>23</sup> <sup>24</sup>

Words like 'effect', 'impact', 'determinant of'..., inevitably point in the causal direction and their use should come with the requirement of at least stating and ideally critically evaluating the necessary assumptions. Uncertainty on the causal nature of the conclusion should tone down any suggestion for intervening on the studied exposure. Specifying the corresponding level of evidence rather than hiding the ultimate causal aim of a study is what we recommend, while acknowledging a margin of error in any empirical study.

#### **Conclusion**

In summary, we have found that causal messages are embedded in studies otherwise carefully phrased in terms of association. Further guidance for authors is needed on



what constitutes a causal statement, similar to the one published by Lederer *et al*<sup>17</sup> for respiratory, sleep and critical care journals. We look forward to similar guidance for other disease groups. From the screened BMJ abstracts, we provided a list of expressions with clear interpretation which may inspire a useful more comprehensive compendium that can be derived from a consensus meeting, for instance. We argue that such awareness and special attention among authors and reviewers would serve our communication on the best available evidence for conceived interventions.

Correction notice The affiliation for Agnès Dechartres has been corrected to Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, AP-HP. Sorbonne Université, Hôpital Pitié Salpêtrière, Département de Santé Publique, F75013, Paris, France

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#### **REFERENCES**

- Begg MD, March D. Cause and association: missing the forest for the trees. *Am J Public Health* 2018;108:620.
- 2 Hernán MA. A definition of causal effect for epidemiological research. J Epidemiol Community Health 2004;58:265–71.
- 3 Kunz R, Oxman AD. The unpredictability paradox: review of empirical comparisons of randomised and non-randomised clinical trials. BMJ 1998;317:1185–90.
- 4 Ruich P. The use of cause-and-effect language in the JAMA network journals 2017.
- 5 Cofield SS, Corona RV, Allison DB. Use of causal language in observational studies of obesity and nutrition. *Obes Facts* 2010;3:353–6.
- 6 Thapa DK, Visentin DC, Hunt GE, et al. Being honest with causal language in writing for publication. J Adv Nurs 2020;76:1285–8.
- 7 Pinsky PF, Miller A, Kramer BS, et al. Evidence of a healthy volunteer effect in the prostate, lung, colorectal, and ovarian cancer screening trial. Am J Epidemiol 2007;165:874–81.
- 8 Permutt T, Scott J, Food Drug Administration (FDA). E9(R1) statistical principles for clinical trials: addendum: estimands and sensitivity analysis in clinical trials 2017;9.
- 9 European Medicine Agency (EMA). ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials 2020 17 February 2020.
- 10 Hernán MA. The C-Word: scientific euphemisms do not improve causal inference from observational data. Am J Public Health 2018;108:616–9.
- 11 Glymour MM, Hamad R. Causal thinking as a critical tool for eliminating social inequalities in health. Am J Public Health 2018:108:623.
- 12 Green MJ. Calculating versus estimating causal effects. Am J Public Health 2018;108:e4–5.
- 13 Hernán M, Robins J. Causal inference: what if. Boca Raton: Chapman & Hall/CRC, 2020.
- 14 Goetghebeur E, le Cessie S, De Stavola B, et al. Formulating causal questions and principled statistical answers. Stat Med 2020;39:4922–48 https://onlinelibrary.wiley.com/doi/full/10.1002/sim. 8741 doi:10.1002/sim.8741
- 15 Adams RC, Sumner P, Vivian-Griffiths S, et al. How readers understand causal and correlational expressions used in news headlines. J Exp Psychol Appl 2017;23:1–14.
- 16 Haber N, Smith ER, Moscoe E, et al. Causal language and strength of inference in academic and media articles shared in social media (claims): a systematic review. PLoS One 2018;13:e0196346.
- 17 Lederer DJ, Bell SC, Branson RD, et al. Control of confounding and reporting of results in causal inference studies. guidance for authors from editors of respiratory, sleep, and critical care journals. Ann Am Thorac Soc 2019;16:22–8.
- 18 Harhay MO, Au DH, Dell SD, et al. Methodologic guidance and expectations for the development and reporting of prediction models and causal inference studies. Ann Am Thorac Soc 2020;17:679–82.
- 19 Hernán MA, Robins JM. Estimating causal effects from epidemiological data. J Epidemiol Community Health 2006:60:578–86.
- 20 Boutron I, Dutton S, Ravaud P, et al. Reporting and interpretation of randomized controlled trials with statistically nonsignificant results for primary outcomes. *JAMA* 2010;303:2058.
- 21 Ghannad M, Olsen M, Boutron I, *et al.* A systematic review finds that spin or interpretation bias is abundant in evaluations of ovarian cancer biomarkers. *J Clin Epidemiol* 2019;116:9–17.
- 22 Developing guidelines for the analysis of randomized controlled trials in real-world settings. Available: https://www.pcori.org/sites/default/ files/PCORI-Hernan270-English-Abstract.pdf
- 23 Doan S, Yang EW, Tilak SS, et al. Extracting health-related causality from Twitter messages using natural language processing. BMC Med Inform Decis Mak 2019;19:79.
- 24 Chiolero A. Causality in public health: one word is not enough. Am J Public Health 2019;109:1319–20.

#### **Supplementary Material**

Table A. Statements in each of the included observational studies published in the BMJ in 2018

Published Abstract		Published Full text					
Objective	Conclusion	Method	Confounder adjustment	Estimates provided	Authors Considerations	Comment	
CONSISTENTLY CA	USAL						
"To evaluate the impact of [] on [] in []"	"[] is associated with negative effects on []. Given the relatively low prevalence of [], population level impacts are currently modest. Nevertheless, as [] has doubled in the US over the past generation, further investigation is warranted of the impact on	"To estimate the adjusted odds ratio for each [] outcome by [] group, we created logistic regression models with [] as the reference group. [] The population attributable risk was calculated using the standard formula"	"Other subgroup analyses were done to ensure that [] association was not confounded by []"	"[] had 14% higher odds of [] compared with [] (adjusted odds ratio 1.14, 99% confidence interval 1.13 to 1.15). [] 14.5% (13.6% to 15.4%) of [] (under the assumption of a causal relation) can be attributed to []"	"The pooling of all [] during this period minimizes the risk of confounding from yearly fluctuations in [] outcomes. Finally, despite attempts to adjust [] using regression analysis and stratification, some residual confounding effects from [] could remain. [] As more than 12% of [] might have been	Both abstract and main text use causal language: they state that their aim is to assess the impact of the exposure on the outcome, adjust for confounders, provide population attributable risks and discuss residual confounding.	

"To examine the [...] risks of [...] initiation compared with initiation of other traditional [...] drugs, initiation of [...], and no initiation."

					[]. The	
					cumulative risk	
					over [] is also	
					likely to be	
					important in	
					terms of both	
					economic	
					burden and	
					overall public	
					health"	
	"[] poses a	"[W]e conducted a series	"We calculated	"[] initiators	"We performed	The use of
	[] risk	of cohort studies, each	the <b>propensity</b>	had a 50%	the following	causal
	compared with	mimicking the strict design	score for all	increased rate of	sensitivity	language
	non-use, []	criteria of a clinical trial (a	eligible	[] events	analyses, [] to	appears in
r	use, and use of	so-called emulated trial	individuals	compared with	estimate how	both abstract
	other	design), to compare rates	initiating [] at	[] non-initiators	strongly a single	and main text.
	traditional []	of [] among [] with	enrolment by	(incidence rate	unmeasured	They apply
	drugs."	rates among []. [] We	fitting a logistic	ratio 1.5, 95%	binary	causal
		estimated an	regression model	confidence	confounder	methods
		observational analogue of	including	interval 1.4 to	would need to be	including
		the intention to treat	covariates on	1.7)."	associated with	target trial
		hazard ratio, as a measure	sex, age, year,		[] to fully	emulation and
		of the incidence rate ratio,	comorbidity, and		explain our	propensity
				l .		

prevented were

[...], the importance of these data are most relevant to

	by fitting a Cox	drug treatment	findings. []	score
	proportional hazards	use. We then	Finally, an	matching and
	model, using time since	matched non-	unmeasured	discuss
	start of follow-up as the	initiators to []	confounder that	residual
	time scale and a time	initiators (1:1) by	was twice as	confounding.
	independent covariate for	propensity score	frequent among	
	treatment assignment. We	within a	[] initiators	
	pooled data from all trials	maximum	versus among	
	into one model and	matching range	non-initiators	
	included each trial as a	of 0.025 and	would still need	
	stratum in the regression	without	to increase the	
	(using values from 1 to	replacement."	risk of [] by a	
	252)."		factor of nine or	
			more to fully	
			explain the	
			results, if no	
			increased risk	
			actually existed	
			(eFigure 3). []	
			Still, the	
			emulated trial	
			design lacked	
			baseline	
			randomisation,	
			and therefore,	
			unmeasured	
			confounding	
			cannot be	
			excluded."	ļ

"To explore	"[] was	"We used Cox regression	"We considered	"Women with a	"We did	Causal
associations	associated with	with age as the underlying	[] as a priori	history of [] had	sensitivity	language is
between [] and	an <b>increased</b>	time to estimate hazard	confounders."	a 53% increase in	analyses []	present in
later[], overall	risk of [],	ratios for [] comparing		risk of []	using the array	abstract and
and by []	particularly	women with and without		overall,	approach for	main text.
subtype and	[subtype]. []	a history of [] We used		compared with	testing the effect	They apply
timing of onset."	were unlikely	competing risk methods		women with no	of an	mediation
	to <b>mediate</b> the	when analysing		history of []	unmeasured or	analysis,
	associations	associations with []		(incidence rate	incompletely	adjust for
	substantially,	subtypes. [] We		for women with a	measured	confounders,
	suggesting that	evaluated potential		history of []:	confounder. []	and discuss
	[] and []	mediation by []"		11.6 per 100 000	Sensitivity	the
	may share			person years;	analyses	unmeasured
	underlying			incidence rate for	suggested that	confounding
	mechanisms or			women with no	confounding by	assumption
	susceptibility			history of []:	[] was unlikely	and residual
	pathways.			8.33 per 100 000	to explain the	confounding.
	Asking about a			person years;	observed	
	history of []			hazard ratio 1.53,	associations for	
	could help			95% confidence	[]; in contrast,	
	physicians to			interval 1.26 to	[] could	
	identify			1.85)."	conceivably	
	women who				explain a	
	might benefit				considerable part	
	from screening				of the association	
	for early signs				between [] and	
	of disease,				[]. [] we also	
	allowing for				cannot rule out	
					the possibility of	

	early clinical intervention."				residual confounding by other unmeasured covariates"	
"To investigate	"Severe and	"We used Cox regression	"For each patient	"Table 3 shows	"Limitations of	The causal aim
whether adults	predominantly	stratified by <b>matched</b> set	with [], we	that in the	the study,	is evident in
with [] are at an	active [] are	[] with current age as the	randomly	primary analysis,	inherent to most	the abstract
increased risk of	associated with	underlying timescale to	matched up to	there was	large	because they
[] and whether	an increased	generate hazard ratios for	five patients by	evidence of	observational	intend to
the risk varies by	risk of []	the association between	age (within 15	associations	studies, include	assess how the
[] severity and	outcomes.	[] and each [] outcome	years), sex,	between [] and	the possibility for	risk of the
condition activity	Targeting []	(the unadjusted model).	general practice,	all [] outcomes,	confounding,	outcome
over time."	prevention	Subsequent multivariable	and calendar	except for [].	bias, and missing	varies when
	strategies	analyses adjusted for []	time at cohort	Associations	data. [] We	the exposure
	among these	(the <b>adjusted</b> model). The	entry. These	were strongest	have shown a	is modified
	patients should	adjusted model was	unexposed	with [] (hazard	clinically	and the
	be considered."	further adjusted for	patients were	ratio 1.25, 99%	relevant increase	conclusion is
		variables which may have	required to have	confidence	in the risk of []	to take action
		been on the causal	at least one year	interval 1.11 to	outcomes in	given the
		pathway (ie, mediators)	of follow-up in	1.41 in the	patients with	findings. The
		between [] and []	CPRD and no	adjusted model)	[].This	main text uses
		outcomes [] (the	history of []	and [] (1.19,	increased risk is	causal
		mediation model). [] The	when matched.	1.10 to 1.30),	largely confined	language,
		population attributable	[] We used a	with <b>partial</b>	to patients with	discusses
		risk of each [] outcome	directed acyclic	attenuation in	severe or more	DAGs,
		was estimated by using	graph to inform	the mediation	active [] and	mediators,
		the estimated hazard ratio	the identification	model. [] The	persists despite	collider bias

		and assuming the prevalence of [] to be 10%."	of covariates and mediators and to avoid collider bias"	greatest population attributable risks were estimated for [] (2.4%, 1.1% to 3.9%) and [] (1.9%, 1.0% to 2.9%)."	adjusting for potential mediators, including conventional risk factors for [] outcomes. Consideration should be given to developing prevention strategies to reduce the risk of [] among patients with severe or predominantly []"	and provides population attributable risks.
"To determine the effect of []	"This study did	"We used a <b>change point analysis</b> to study the	"The <b>risk factors</b> included in this	"The 90 day mortality in	"If we assume that the decrease	Causal language is
outcome	evidence that	change over time in	logistic	patients	in mortality can	present in
reporting in []	the	adjusted 90 day mortality	regression model	undergoing an	be causally	abstract and
on risk averse	introduction of	after [] and after []. We	are []. An	[] fell during the	linked to [], the	main text as
clinical practice,	[] in [] has	used a multivariable	adjusted	study period	process of []	they state that
"gaming" of	led to risk	logistic regression model	outcome was	from 952/33 638	This team	their aim is to
clinical data, and	averse clinical	for 90 day mortality, with	then produced by	(2.8%) before the	response could	determine the
90 day	practice	a slope for calendar time	indirect	introduction of	have been	effect of the
	behaviour or	and an interaction	standardisation"	[] to 552/25		exposure on

postoperative	"gaming" of	between time pre-		905 (2.1%) after	mediated	the outcome
mortality."	data. However,	introduction versus post-		(fig 4). Therefore,	through []"	and conclude
	its introduction	introduction of [], in		we carried out		that the
	coincided with	addition to all of the <b>risk</b>		change point		exposure has
	a significant	adjustment variables. This		analysis which		not led to the
	reduction in 90	modelled a change in the		showed a steeper		outcome. The
	day mortality."	slope of mortality at the		decline in 90 day		main text
		point that [] was		mortality after		explains that
		introduced but no		the introduction		confounder
		immediate change in		of [] (P=0.03).		adjustment
		mortality."		The change point		was made
				analysis also		through
				found a		standardisatio
				significant effect		n and discuss
				<b>of</b> [] when it		possible
				was modelled as		mediators for
				an immediate		this
				shift in 90 day		relationship.
				mortality		
				(P=0.01) and		
				when it was		
				modelled as both		
				an immediate		
				shift and a		
				change in slope		
				(P=0.04)."		
"To assess the	"Little evidence	"We estimated one year	"Survival	"One year	"The lack of	Causal
effectiveness of	was found of a	net survival for each []	estimates for all	survival	consistent results	language is

the [] policy	direct impact	by sex, year of diagnosis	ages combined	improved for 20	between men	present in
initiatives <b>in</b>	of [] on one	(1996 to 2013), and	were age	of the 21 []	and women, as	both abstract
improving []	year survival,	deprivation category.	standardised	examined in	well as the lack of	and main text.
and reducing []	and no	Patients with a diagnosis	with the	women and 16 of	general patterns	The aim is to
in survival in	evidence for a	between 1996 and 2013	International	the 20 []	across [] types,	evaluate the
England."	reduction in []	had the potential to be	Cancer Survival	examined in	provide <b>little</b>	effectiveness
	in cancer	followed up for at least	Standard	men. [] For	evidence for any	of a policy on a
	survival. These	one year, so we used the	weights. [] We	these [], the	strong impact of	given
	findings	classic cohort approach.	used	average annual	the [] policies	outcome, they
	emphasise that	[] We estimated net	multivariable	absolute increase	on short term []	provide
	[] in survival	survival using the	linear regression	in one year age	survival. The	standardised
	remain a major	consistent nonparametric	to investigate the	standardised net	evidence is even	net survival
	public health	estimator defined by	survival patterns	survival was	weaker for their	and suggest to
	problem for a	Pohar-Perme."	for each [] and	often greater	impact on the	take action
	healthcare		by sex"	than 1% over the	[] in []	given the
	system			whole study	survival. []	findings.
	founded on			period"	These findings	
	equity."				should be taken	
					into	
					consideration by	
					[] policy makers	
					and inform	
					future	
					initiatives."	
<u> </u>						

To investigate whether improving adherence to [] interacts with the genetic predisposition to [] in relation to long term changes in [] and []."	"These data indicate that improving adherence to [] could attenuate the genetic association with []. Moreover, the beneficial effect of improved [] on [] was particularly pronounced in people at high genetic risk for [].	"We used multivariable generalized linear models with repeated measures analyses to assess the main associations of the [] and changes in the [] with change in []"	"We used multivariable models to adjust for []"	"In general, the [] was associated with increases in [] every four years: in the two cohorts combined, each additional [] was associated with 0.02 (SE 0.01) increase in [] and 0.05 (SE 0.03) kg increase in []"	"[] unmeasured or unknown confounders may also exist. Secondly, because adherence to [] was not randomized, the association between [] and [] may not imply a causal relation. Thirdly, the results could be underestimated by potential reverse causality. [] Our study provides reproducible evidence from two prospective cohorts of US men and women that improving	Assessing if improving adherence has an effect translates to an intervention that is being assessed. They conclude that there is a beneficial effect and suggest to take action. The main text discusses unmeasured confounding assumption and reverse causality. All of the above is consistent with a causal aim.
					men and women	

					association with	
"To assess the	"[] is an	"We calculated the time	"[] adjusting for	"A statistically	"More evidence	Causal
independent and	overlooked <b>risk</b>	to event from the date of	[]."	significantly	was needed to	language is
joint associations	factor for [],	enrollment to the date of		increased risk of	clarify whether	present in
of [] and []	as important as	[] incident or [] death,		incident [] was	the inverse	abstract and
with [] risk and	five major	death due to causes other		observed for the	association was	main text.
to explore the	lifestyle factors	than [], or the end of		eight diseases	causal or related	They identify
benefit of [] in	combined. In	cohort follow-up (31		and markers.	to []. [] the	that the
reducing the []	this study, []	December 2008),		Specifically, []	dose-response	exposure
risk associated	contributed to	whichever came first. We		was inversely	relation, the	contributes to
with [] and [].	more than one	used Cox proportional		associated with	exclusion of []	the outcome,
	fifth of the risk	hazards model to estimate		risk of incident	during recent	after adjusting

	for incident [] and more than one third of the risk for [] death. [] is associated with a nearly 40% reduction in the [] risk associated with []."	hazard ratios and 95% confidence intervals"		[] in a dose- response manner"	follow-up, and further adjustment for [] minimize the likelihood of reverse causation and lend support for causality. [] Our study uncovered a substantial impact of [] jointly on [] risk, which were equally as important as five lifestyle factors combined."	for covariates. They discuss dose-response relationship and reverse causality.
"To examine the association between [] and [] in later life, and determine whether the maintenance of [] will offset age related []"	"These results show that [] is not associated with the trajectory of [] in late life, but is associated with the acquisition of ability during	"The raw scores from the [] tests were standardised to a mean of 100 and a standard deviation of 15 to produce an [] scale. Age at testing was the number of years after participants' 60th birthdays. We modelled age in this form so that	"Because our sample were all born in the same year and tested at a similar age, a confounder for age at entry was not used. We modelled cognitive	"The typical intellectual engagement models for each domain are shown in table 2 and indicated an expected significant decline in []	"In our statistical models, we introduced possible confounders available from early life and life course, including []. We also controlled for []	The causal aim is suggested when the goal is to establish temporal relationship between exposure and outcome, describing the

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	the life course. Overall, findings suggest that high performing adults engage and those that engage more being protected from relative decline."	the intercept occurred at age 60 years rather than zero years, such that the calculation for the intercept would represent a realistic adult value rather than one extrapolated 64 years earlier. [] For each model, a probability value of P<0.05 was considered significant."	performance with a linear mixed model, as a combination of []."	with age, ranging from –1.09 to –1.31 standard points per year for the [] test and –0.77 to –1.69 for the [] test. [] None of the age×TIE interaction terms were significant, indicating that [] did not influence the trajectories of age decline."	associated with repeated testing. [] significant associations remained after adjustment for age, sex, and test practice effects. [] is an independent contributor to late life [] and has a unique effect over and above the effect of other life course variables. [] It is, however, impossible for a causal effect to	exposure as a trajectory, providing standardised and adjusted estimates and considering whether it is possible to infer a causal link.
"To evaluate the associations of a [] and [] with	"In this cohort study, [] were independently	"To test the <b>association</b> of [] and [] with [] we used Cox proportional	"Cox proportional hazards models	"In Cox proportional hazards analysis,	"The present study provides further support	The abstract describes that the goal is to
incident []."	associated with incident []. These results	hazards models. The duration of follow-up was calculated as time	included adjustment for age and sex for	the <b>risk of</b> [] was higher for those with []	that common [] are implicated in the development	establish a temporal relationship

	emphasise the benefit of entire populations adhering to [], independent of [] risk."	between the baseline assessment and the first event of either [] or 1 March 2016, which was the end of follow-up for the current data release. Participants who had a [] before a [] occurred were censored at the time of the respective event."	the lifestyle score models. For the models including the genetic score we additionally adjusted for the first 10 principal components of ancestry and genotyping batch."	(hazard ratio 1.20, 95% confidence interval 1.08 to 1.34) and [] (1.35, 1.21 to 1.50) compared with those with a low genetic risk score"	of []. [] The [] was also associated with [], which suggest that the effect of the [] on risk of incident [] might at least in part be mediated by []. The effects of [] might differ according to the cause of [], although some [] factors are shared between two or more causal factors"	between the exposure and the outcome and suggest to take action given the findings. The main text describes adjusting for covariates and discusses mediation.
"To determine the longitudinal association between [] and []."	"In older adults, a higher cumulative level of [] was associated with a higher likelihood of []. These	"We used a Cox proportional hazards model to evaluate the association between time-varying [], adjusting for time-varying covariates (updated at [] measurement), and the	"We selected covariates and potential mediators based on biological interest, current or previously observed	"Figure 1 shows that after multivariable adjustment for demographic, lifestyle, cardiovascular risks, dietary	"[] we excluded participants [] who reported baseline [] (to avoid reverse causality; n=195). [] The community	The abstract describes that the goal is to establish a temporal relationship between the exposure and

	findings	likelihood []. Time at risk	associations with	habits, and other	based design	the outcome
	support	was from the first []	[], and	[], higher []	improves	and suggest to
	guidelines for	measurement until the	meaningful	levels were	generalizability,	take action
	increased	first [] event or	changes in the	associated with a	and regular	given the
	dietary	censoring [] or the latest	exposure risk	lower likelihood	physical	findings. The
	consumption of	date of adjudicated	estimate (±5%).	of unhealthy	examinations	main text
	[] in older	follow-up in June 2015."	Minimal	ageing. Overall,	ensured that	describes
	adults."		adjustments	participants in	demographics	adjusting for
			included age and	the highest group	and other risk	covariates and
			sex.	of [] had an	factors were well	discusses
			Multivariable	18% (95%	measured, which	mediation,
			adjustments	confidence	may help to	residual
			additionally	interval 3% to	minimize	confounding
			included []. We	30%; P=0.001)	confounding.	and reverse
			used the	lower risk of	[]The possibility	causality. The
			potential	[].Findings were	of <b>residual</b>	statement in
			mediators to	not appreciably	confounding by	italic is a clear
			explore what	altered after	imprecisely	causal
			additional	adjustment for	measured or	statement.
			associations	potential	unknown factors	
			could exist to	mediators (not	also cannot be	
			these potential	shown)."	excluded for an	
			pathways."		observational	
					study. [] <i>Any</i>	
					unmeasured	
					confounders	
					would have to be	
					strongly	
					associated with	

					both the exposure and the outcome, conditional on all the variables already in the model. Thus, it seems unlikely that either poorly measured or unmeasured confounders could fully account for our findings."	
"To prospectively	"Among female	"Participants contributed	"Information on	"We observed a	"From a public health	Their aim is to establish a
evaluate the joint association of	nurses, both [] were	person time from the return of the baseline	potential confounders was	positive association	standpoint,	temporal
[] and [] with	associated with	questionnaire [] until the	assessed and	between	because 71% of	relationship
risk of type 2	a higher risk of	date of diagnosis of [],	updated every	duration of []	the joint effect	exposure-
diabetes risk, and	[]. The excess	death, loss to follow-up,	other year via the	and risk of [] in	could be	outcome, they
to quantitatively	risk of [] was	or the end of the follow-	questionnaires	both cohorts.	attributed to an	discuss
decompose this	higher than the	up period (30 June 2012	throughout	Compared with	[], our findings	adjusting for
joint association	addition of risk	for the NHS and 30 June	follow-up. This	women without	underscore the	confounders,
to []"	associated with	2013 for NHS II),	information	rotating night	importance of	provide excess
	each individual	whichever came first. We	included [] In	shift work, the	maintaining	risk and
	factor. These	used <b>multivariable time</b>	multivariable	pooled	[].Our findings	suggest to
	findings	dependent Cox	analysis, we	multivariable	suggest that	take action

most cases of [] could be prevented by [], and the benefits could be greater in []."	
prevented by [], and the benefits could be greater in []."    Intervals for the associations between [] alone and in combination with []."    Intervals for the associations between [] alone and in combination with []."    Intervals for the associations between [] alone and in combination with []."    Intervals for the associations between [] alone and in combination with [] we also examined the decomposition of the joint effect: the proportion (1.22), 1.28 (1.10 effect: the proportion (1.33 to 1.62) (P for trend <0.001) [] (table 3). [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
[], and the benefits could be greater in []."    [] associations between [] alone and in combination with []."    [] We also examined the decomposition of the joint effect: the proportion attributable to []"    [] were 1.11 (95% confidence interval 1.00 to 1.22), 1.28 (1.10 to 1.49), and 1.46 (1.33 to 1.62) (P for trend < 0.001) [] (table 3). []    The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to 1.40%	
benefits could be greater in []."  alone and in combination with []."  be larger in [] "  decomposition of the joint effect: the proportion attributable to []"  []"    The attributable proportions of the joint effect were 17.1% (95% confidence interval 1.00 to 1.22), 1.28 (1.10 to 1.49), and 1.46 proportion (1.33 to 1.62) (P for trend <0.001) [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to 1.22), 1.28 (1.10 to 1.22), 1.28	
be greater in []."    decomposition of the joint   1.22), 1.28 (1.10   1.33 to 1.62) (P   1.33 to 1.62) (P   1.34 to 1.46   1.35 to 1.62) (P   1.36 to 1.36	
I]."	
effect: the proportion (1.33 to 1.62) (P attributable to []" [](table 3). [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
proportion attributable to []"  [](table 3). [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
attributable to []"  for trend <0.001) [](table 3). [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
[]"  [](table 3). []  The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
the joint effect were 17.1% (95% confidence interval 14.0% to	
were 17.1% (95% confidence interval 14.0% to	
confidence interval 14.0% to	
interval 14.0% to	
20.8%) for []	
alone, 71.2%	
(66.9% to 75.8%)	
for [] alone, and	
11.3% (7.3% to	
17.3%) for their	
interaction."	
"To assess the "In this analysis "Patients were followed "We used an "Use of [], as "The findings The goal is t	)
association of nationwide from cohort entry to active compared with should be evaluate the	
between [] and registers from treatment cessation, comparator new- [], was interpreted in the association	

seven serious	two countries,	crossover to the other	user study design	associated with	context of	with the
adverse events	use of [], as	study drug [], the	and controlled	an increased risk	limitations of	exposure to
of current	compared with	outcome event, death,	for a wide range	of [] (hazard	observational	adverse events
concern."	[], was	emigration, or the end of	of potential	ratio 2.32, 95%	studies and the	which
concern.			confounders	confidence		translates into
	associated with	the study period (31		interval 1.37 to	uncertainty of	
	an increased	December 2016). We used	(patient		the <b>effect</b>	assessing
	risk of [], but	Cox proportional hazards	characteristics	3.91) and []	estimates. []	safety. They
	not with other	regression to calculate	that might be	(2.14, 1.01 to	Therefore, the	discuss
	serious <b>adverse</b>	hazard ratios, analysing	associated with	4.52) but not	studies could	adjusting for
	events of	each outcome	both the	with [] (1.11,	suffer from	confounding,
	current	independently. The	outcome and the	0.93 to 1.33), []	compromised	resort to
	concern."	absolute risk difference	decision to	(0.69, 0.45 to	confounding	propensity
		was calculated as hazard	initiate a drug)	1.05), [] (0.89,	control, as	score
		ratio-1 multiplied by the	through a non-	0.67 to 1.19), []	indicated by the	matching and
		rate in the comparator	parsimonious	(0.99,	imbalance in []	consider
		group."	propensity score	0.71to 1.38), or	at baseline	residual
			model to	[] (1.16, 0.64 to	between users of	confounding.
			minimise the risk	2.12)."	[] versus	
			of bias, including		comparators,	
			confounding by		even after	
			indication [].		propensity score	
			We estimated		matching []	
			propensity		Finally, residual	
			scores by using		and unmeasured	
			logistic		confounding	
			regression for the		affecting the	
			probability of []		findings in our	
			conditional on		study cannot be	
			the status of 66		ruled out."	
			514143 01 30			

covariates,
defined and
selected a priori,
including
sociodemographi
c characteristics,
comorbidities,
comedications,
and healthcare
utilisation [] We
matched [] and
[] users (1:1
ratio, by country)
according to
propensity score,
by using the
nearest
neighbour
matching
algorithm (caliper
width 0.2 of the
standard
deviation of the
logit score).
Analyses were
performed in a
pooled dataset of
the two
countries."

"To determine	**In results:	"For all outcome	"We examined	"Patients []	"A confirmatory	The abstract
whether patients	"Per 100 000	comparisons we report	hospital type and	were <b>less likely</b>	time-to-event	and main text
[] have <b>fewer</b>	patients, there	unadjusted and adjusted	several	to have follow-up	analysis in a	use causal
[] and higher	were 2999	odds ratios (with 95%	characteristics of	with a physician	propensity score	language: they
rates of [] than	fewer follow-	confidence intervals).	patients and	within seven days	matched cohort	discuss risk
patients [].	up	Adjusted odds ratios were	admissions: year	(36.3% v 47.8%,	(see	attributed to
	appointments	obtained with logistic	of Charlson	adjusted odds	supplementary	the exposure,
	within 14 days,	regression models	comorbidity	ratio 0.61, 95%	appendix table 5)	provide
	26 excess	estimated using	index score,	confidence	showed	adjusted
	deaths, []	generalised estimating	socioeconomic	interval 0.60 to	consistent results	estimates
	attributable to	equations methods and	status (measured	0.62) and 14 days	(death or	using
	[]."	including all measured	using median	(59.5% v 68.7%,	readmission	propensity
	"Patients []	patient and hospital	neighbourhood	0.65, 0.64 to	hazard ratio 1.08,	score
	are less likely	characteristics."	income), length	0.66). []	95% confidence	matching and
	to have [] and		of hospital stay,	Patients	interval 1.07 to	discuss
	are at higher		arrival by	discharged	1.09). [] The	residual
	risk of []."		ambulance,	during the	differences in	confounding.
			diagnosis,	holiday period	outcomes <b>could</b>	
			discharged with	were at	not be explained	
			home support or	increased risk of	<b>by</b> observed	
			against medical	death or	hospital or	
			advice, and	readmission	patient	
			previous	within 30 days	characteristics,	
			healthcare usage	(25.9% v 24.7%,	including	
			(emergency	1.09, 1.07 to	admission	
			department	1.10). This was	diagnosis. [] the	
			visits, hospital	explained by an	possibility of	
			stays, outpatient	increased risk of	confounding due	
			visits, home care	return to the	to unmeasured	

			visits). hospital discharge, age, sex, rural residence, "	emergency department (24.3% v 23.0%, 1.09, 1.07 to 1.10), rehospitalisation (11.8% v 11.4%, 1.06, 1.04 to 1.08), and death (1.5% v 1.5%, 1.06, 1.02 to 1.10) within 30 days"	differences remains"	
"To investigate	"Use of [] is	"We calculated age	"Adjusted	"The age	"The data linkage	When
the <b>association</b>	associated with	standardised incidence	incidence rate	adjusted	study design also	assessing the
between [] and	a reduction in	rates of [] per 100 000	ratios (referred	incidence of []	enabled us to	exposure-
overall and	[] risk in	person years, using the	to here as	was highest in	adjust for several	outcome
specific types of	women of	age distribution of the	relative risks) and	women who	important	relationship,
[]."	reproductive	cohort as standard. Risk of	their surrounding	were never users	confounding	they provide
	age—an <b>effect</b>	[] among users of the	95% confidence	of [] (7.5 per	variables. We	standardised
	related to	different product groups	intervals were	100 000 person	were not able to	estimates,
	duration of	was analysed by a Poisson	calculated for	years; table 2).	adjust for some	discuss
	<b>use</b> , which	regression model in SAS	each model, with	Among ever	factors, such as	residual
	diminishes	version 9.3 (SAS Institute).	never users as	users of [],	[] Our findings,	confounding,
	after stopping	[] We calculated the	the reference	reduction in the	therefore, could	dose-response
	use. These data	population prevented	group. The	age standardised	be subject to	and provide
	suggest no	fraction (population	adjusted models	absolute rate of	residual	attributable
	protective	prevented fraction =	included the	[] was 3.2 per	confounding."	fraction.

	effect from []."	prevalence <sub>exposure</sub> (1-relative risk)) associated with ever use of [] by using the relative risk of never use versus ever use of []. The population prevented fraction is the proportion (expressed as a percentage) of the [] in the cohort that has been prevented by ever use of []."	following time varying covariates []"	100 000 person years. Overall, ever users of [] had a reduced risk of [] compared with never users (relative risk 0.66 (95% confidence interval 0.58 to 0.76)). [] use of [] prevented 21% of [] in the study population"		
"To assess whether [] is	"In participants older than 74	"To prevent survivor bias and covariate	"We explored the variables	"In participants without [], the	"To prevent residual	They use causal
associated with a	years without	measurement bias, we	associated with	hazard ratios for	confounding we	language and
reduction in []	[], [] was	selected a "new users	[] to determine	[] were 0.94	performed	causal
and mortality in	not associated	design" over "all [] users.	candidate	(95% confidence	additional	methods. To
old and very old	with a	[] Using Cox proportional	variables for the	interval 0.86 to	regression	estimate the
adults with and	reduction in	hazard regression models	propensity score	1.04) for [] and	adjustments after	effect of the
without []."	[] or in all-	adjusted by propensity	of []. From	0.98 (0.91 to	adjustment of	exposure on
	cause	score, we calculated the	SIDIAPQ we	1.05) for all cause	propensity score.	the outcome.
	mortality, even	hazard ratios of statin use	obtained data on	mortality in 75-	Variables that	They use
	when the	for the outcome events.	age, sex, []	84 year olds. []	remained	propensity
	incidence of []	Participants were	Because of non-	The one year	imbalanced after	score methods
	was	censored at the date of	random	number needed	propensity score	to adjust for

atatiatiaall	tue meters from CIDIADO - :	tue etue e ut	4- 44 1C4	a aliakus a usk :	f
statistically	transfer from SIDIAPQ or	treatment	to treat was 164	adjustment were	confounding,
significantly	at the end of the study	allocation, we	for [] and 306	also included in	provided a
higher than the	period. "	used a logistic	for all cause	the models. []	NNT and
risk thresholds		model based on	mortality."	Despite these	consider
proposed for		potential		efforts, we	residual
[]. In the		confounding		acknowledge	confounding.
presence of		covariates to		that some	
[], [] was		calculate the		residual	
statistically		propensity score		confounding	
significantly		of []. We		might exist."	
associated with		calculated the			
reductions in		propensity score			
the incidence		separately for			
of [] and in		participants with			
all-cause		and without []			
mortality. This		and also within			
effect		each age group,			
decreased after		and standardised			
age 85 years		differences			
and		before and after			
disappeared in		adjustment for			
nonagenarians.		propensity score.			
"		Variables with			
		standardised			
		differences < 0.10			
		were considered			
		to be <b>well</b>			
		balanced."			

role of [...] in the association

					between [] and increased []"	
"To assess	"[] as second	"The study cohort was	"[] exposed and	"Compared with	"Based on a post-	The aim is to
whether adding	line drugs are	formed by identifying all	reference	the use of [],	hoc analysis, the	assess the
or switching to	associated with	subjects from the base	subjects were	adding or	findings of the	effect of the
[] is associated	an increased	cohort of [] initiators	matched on	switching to []	primary analysis	intervention
with an increased	risk of []	who subsequently added	high-dimensional	was associated	on [] unlikely to	strategy of
risk of [],	compared with	or switched to a [] as	propensity score.	with an increased	be the result of	adding or
compared with	remaining on	second line treatment.	The high-	risk of [] (7.8 v	an <b>unmeasured</b>	switching to a
remaining on []	[]. Continuing	Patients who added or	dimensional	6.2 per 1000	confounder	particular
in patients with	[] when	switched to other []	propensity score	person years,	under most	drug, they
[]."	introducing []	were censored. For each	method	hazard ratio 1.26,	plausible	emulate a
	appears to be	patient adding or	empirically	95% confidence	exposure-	target trial,
	safer than	switching to a [], we	selects covariates	interval 1.01 to	confounder and	use propensity
	switching."	identified a matched	based on their	1.56), all cause	confounder-	score
		reference patient who	prevalence and	mortality (27.3 v	outcome	matching,
		also was a [] initiator but	potential for	21.5, 1.28, 1.15	associations. []	discuss
		remained on metformin,	confounding. For	to 1.44), and []	For our study, we	residual
		using a prevalent new-	each member of	(5.5 v 0.7, 7.60,	used the recently	confounding
		user design. [] we	each matched	4.64 to 12.44).	developed	and conclude
		constructed a Cox	set, we identified	There was also a	prevalent new-	that the
		proportional hazards	all available	trend towards	user design. To	strategy is
		regression model for each	information from	increased risks of	emulate the	safe.
		outcome that estimated	seven data	[] (6.7 v 5.5,	randomised	
		the hazard ratio and the	dimensions (five	1.24, 0.99 to	controlled trial,	
		95% confidence intervals	dimensions from	1.56) and [] (9.4	this design	
		for [] versus []."	the CPRD: drug	v 8.1, 1.18, 0.98	identifies (at the	
			prescriptions,	to 1.43)."	doctor visit that	

			procedures,		led to the patient	
			diagnoses,		on [] adding or	
			disease history,		being switched to	
			and		[]) a	
			administrative		comparable	
			information; two		· ·	
			dimensions form		patient with the	
					same history of	
			the HES:		[] use and of	
			diagnoses and		other	
			procedures) in		characteristics,	
			the one year		but who on that	
			period before the		visit continued	
			date of the		on []. [] owing	
			matched set. We		to its	
			then applied		observational	
			conditional		nature there is	
			logistic		the potential for	
			regression to		residual	
			estimate the		confounding."	
			propensity of			
			receiving a []			
			drug, thereby			
			considering the			
			500 most likely			
			confounders."			
"To investigate	"Overall, []	"We used a new-user	"Confounding	"In patients with	"Although many	The aim is to
the associations	was found to	design to capture all	factors. It is	[], [] was	adjustments have	assess the
between [] and	be the <b>safest</b>	events occurring after	possible that	associated with a	been done using	safety of a

risks of []	drug, with	starting treatment and to	patients at higher	lower risk of []	the data available	drug and they
compared []."	reduced risks	reduce the impact of	risk of [] may	than []	on the existing	use different
compared [].		confounding. []	preferentially be	(adjusted hazard	databases, there	strategies to
	[] compared	<del>-</del>		· -	· ·	_
	with []. []	Incidence rates for each	prescribed []	ratio 0.66, 95%	is a possibility of	adjust for
	and low dose	outcome were calculated	rather than [],	confidence	unmeasured	confounding,
	[] were,	based on the numbers	so all analyses	interval 0.54 to	confounding or	including
	however,	with the outcome and the	were adjusted	0.79). []Table 5	confounding by	propensity
	associated with	person years of follow-up,	for demographic	shows the	indication. []	scores,
	increased risks	and were age and sex	and clinical	number needed	Although we	provide NNT
	of all cause	standardised for each	variables, either	to treat or	used a	and discuss
	mortality	drug. To estimate the risks	because they	number needed	proportional	the
	compared with	associated with each [],	may have been	to harm to	hazard model	unmeasured
	[]."	an outcome specific Cox	used as	measure the	adjusting for all	confounding
		model containing all	indicators for	relative benefits	available	assumption.
		confounding factors was	prescribing a	or risks of [] in	confounding	
		used, with [] as a	specific [] or	comparison with	factors, we also	
		primary reference."	because they	[]."	undertook a	
			have possible		sensitivity	
			associations with		analysis using the	
			increased risk of		propensity score	
			[]. We similarly		method and	
			adjusted for		obtained very	
			comorbidities,		similar results."	
			previous events,			
			and drugs also			
			used as			
			indicators or			
			associated with			
			increased risks."			
			ilici easeu lisks.			

"To examine the	"Our study	"To evaluate the	"We first	"In multivariable	"Several factors	They provide
association	indicates that	association between []	evaluated	analyses (model	could contribute	adjusted
between [] and	adherence to a	and [], we calculated	associations with	2), [] had a	to the weak	estimates,
the <b>risk of</b>	[] is	relative risks and 95%	[] by categories	relative risk of	mediation effect	discuss
developing []."	associated with	confidence intervals using	of each low risk	3.10 (95%	of [] in the	mediation and
acveroping [].	a substantially	multivariable log-binomial	factor, adjusting	confidence	association	residual
	reduced risk of	regression models with	for []."	interval 2.69 to	between [] and	confounding
	[]. These	generalized estimating		3.57) of [],	[] risk. []	and suggest to
	findings	equations and specified an		compared with	Another	take action
	highlight the	exchangeable correlation		[]."	limitation, as in	given the
	potential	structure."		[].	any observational	findings.
	benefits of				study, is that we	
	implementing				cannot exclude	
	[]				the possibility of	
	interventions				uncontrolled	
	to curb the risk				confounding by	
	of []."				[] or residual	
					confounding. []	
					Our findings	
					highlight the	
					potentially	
					critical role of []	
					in the <b>etiology</b> of	
					[] and lend	
					support to []	
					based	
					intervention	
					strategies for	
					reducing []."	
					0. 1	

"To determine rates of [] and all cause mortality in patients with [] compared to patients with [] and without []."	"Patients with [] remain at higher risk of [] than patients without []. The risk is increased even in those in whom [] is not documented. Guidelines should be updated to advocate continued use of [] in patients with []"	"We carried out two retrospective cohort studies to determine incidence rates of [] (primary outcome) and all cause mortality (secondary outcome) in patients with [] versus randomly selected matched controls with []. We calculated crude and adjusted incidence rate ratios comparing the incidence of []"	"Poisson regression was used to calculate adjusted incidence rate ratios, adjusting for the baseline covariates []"	"The crude incidence rate ratio was 0.73 (95% confidence interval 0.65 to 0.81, P<0.001). Adjusting for potential confounders [] made little difference to the incidence rate ratio: 0.76 (95% confidence interval 0.67 to 0.85, P<0.001)"	"In light of the evidence produced by this study, it is recommended that clinical guidelines and schemes designed to incentivise appropriate management [] are updated"	Even though the use of causal language is not explicit, they compare rates of the condition in the different groups that have been matched, provide adjusted estimates and suggest to update guidelines to reflect the findings.
"To examine the association between [] at [] and []."	"[] during the period [] is safe with respect to the risk of []."	"We estimated odds ratios of [] and [] and associated Wald type two sided 95% confidence intervals by logistic regression. For [] and [], we calculated hazard ratios and associated	"[] to adjust for potential confounding due to temporal trends, we included []. [] are well established risk	"In analyses without covariate adjustment (model 1), [] was associated with an increased risk of [] (hazard ratio 1.69	"[] is not causally related to increased risks (). Instead, our results suggest other factors underlying and confounding the	The abstract suggests a causal aim when describing the intention to establish a temporal

		Wald type two sided 95% confidence intervals from Cox regression models, which allow for detailed adjustment for censoring affecting the length of follow-up of each child. Days since birth was used as the underlying time scale. Each child was followed from birth until a diagnosis of the outcome, death, or end of follow-up at 31 December 2014, whichever event occurred first. "	factors for []. [] All estimates were calculated by models with increasing complexity, beginning with models without adjustment for covariates (model 1), followed by models adjusting for all included potentially confounding covariates (model 2)."	(95% confidence interval 1.18 to 2.41)) and [] (2.14 (1.39 to 3.30); fig 2). After covariate adjustment (model 2), [] was only associated with an increased risk of [] (adjusted hazard ratio 1.66 (1.06 to 2.59); fig 2)."	associations between []. Furthermore, although our results suggest that [] are not causally associated [] could be a causal factor for other outcomes. [] although the present study did not find a causal link [], replication of the results is imperative."	relationship between the exposure and the outcome and concluding that the exposure is safe. The main text uses causal language explicitly when describing the strategies to control for confounding and concluding that a causal relationship was discarded.
"To assess the association of [] and risk factors for [] with [] at []."	"The independent association between [] and [] in [] is comparable	"We used a generalised additive mixed model (GAMM) to estimate [], with [] as fixed effect predictors and [] as random effect at the	"We considered [] as potential confounders."		"As our analyses relied on cross sectional data, these findings should be interpreted	The abstract suggests a causal aim when describing the intention to

in strongth and	intercent and [ ] class		acutiously and	astablish a
in strength and	intercept and [] slope.		cautiously and	establish a
consistency	[] We computed 95%		should not be	temporal
with those for	confidence intervals from		considered as	relationship
[]. The results	the uncertainty of the		causal estimates	between the
of this study	estimated smoothing		of the impact of	exposure and
suggest that	function. We computed		[] on []. []	the outcome
tackling all	the <b>number of years of</b>		Given that the	and
these risk	functioning lost from the		present study is	concluding
factors might	mixed model predictions"		based on	that the link is
substantially			observational	comparable to
increase life			data, our study	those for other
years spent in			informs about	established
good physical			associations but	risk factors. It
functioning."			cannot provide	is important to
			evidence of	note that In
			causality."	the abstract
				the design of
				the study is
				described as
				"Multi-cohort
				population
				based study".
				However the
				method and
				discussion
				refer to a
				"cross
				sectional"
				design that

						limits the possibility to establish causal links.
"To determine outcomes and safety of [] for [], due to [], in routine clinical practice."	"In routine clinical practice, [] for patients with [] is at least as effective and safe as in the setting of a randomised controlled trial."	"We used regression models to compare baseline characteristics and outcomes in patients [] with those in the [] intervention and control arms. The effect of [] on [] at 90 days in patients [] compared with [] was expressed as an adjusted common odds ratio, derived from multivariable ordinal logistic regression (shift analysis)."	"We adjusted for []"	"After adjustment for [], the shift towards [] was significant for patients [] compared with those [] intervention arm (adjusted common odds ratio 1.30, 95% confidence interval 1.02 to 1.67; P=0.03) and control arm (1.85, 1.64 to 2.34; P<0.01; fig 1)."	"The results of our study might have important implications for the future of [] for []. [] is at least as effective and safe as in the setting of a randomised controlled trial."	The abstract and main text point to a causal aim as the intention is to assess the safety of an exposure in relation to an outcome and the conclusion is that not only is safe but also effective.
"To investigate whether [] is associated with an increased risk of []."	"In a propensity score matched cohort, [] use was associated	"Cox proportional hazards regression, with days since start of treatment as the time scale, was used to estimate the hazard ratio	"We used two major strategies to control for confounding. To account for	"There was an increased risk of [] associated with [] (hazard ratio 1.66; 95%	"An important concern in any observational study is the possibility of	Both the abstract and main text use causal language and

	with an	for [], comparing	potential	confidence	confounding. We	causal
	increased risk	episodes of [] and []	confounding by	interval 1.12 to	used an active	methods
	of []. This	use."	indication [],	2.46). This	comparator to	including
	association		we used an	increase	limit confounding	propensity
	appeared to be		active	corresponded to	by factors	score
	largely <b>driven</b>		comparator	an absolute	associated with	matching.
	by []."		design, [] To	difference of 82	[], including	They discuss
			control for	(95% confidence	confounding by	the possibility
			potential	interval 15 to	indication, and	of residual
			confounding	181) cases of []	propensity score	confounding
			from differences	per 1 million	matching derived	mainly
			in baseline health	treatment	from a range of	because of the
			status, we used a	episodes in the	covariates.	observational
			propensity score	60 day risk	Despite this, the	nature of the
			matched design,	period."	possibility of	study but also
			taking into		residual	suggest
			account		confounding (for	possible
			demographic		example, due to	confounders
			characteristics,		[]) cannot	missed.
			medical history,		completely be	
			[]."		ruled out."	
"To examine the	"[] was	"We did a population	"Using the full	"After	"Although we	Both the
risks of [] in	associated with	based matched cohort	hospital history	adjustment for	and adjusted the	abstract and
patients with []	increased risks	study based on routinely	(inpatient and	the covariables,	analyses for a	main text
and in a general	of []. [] may	and prospectively	outpatient	[] was	wide range of	describe the
population	be an	collected data. [] We	diagnoses)	associated with	potential	exposure-
comparison	important risk	calculated the 0-1 year,	recorded in the	[] (adjusted	confounders	outcome
cohort."	factor for []."	>1-5 years, and >5-19	DNPR before the	hazard ratio 1.49,	identified a priori	relation in a
COTIOI C.	ractor for [].	71 5 years, and 75-19	DIVIN DETOTE THE	1102010 10110 1.49,	lacitilled a priori	TCIGUOTI III a

		years cumulative incidence per 1000 people for each outcome, accounting for the competing risk of death. Correspondingly, we used matching factors stratified (conditional) Cox proportional hazards regression to estimate hazard ratios, adjusting for the categorical comorbidities listed above as covariables."	index date, we obtained information on the following [] risk factors: []"	95% confidence interval 1.36 to 1.64), [] (2.26, 2.11 to 2.41), and [] (1.94, 1.68 to 2.23), as well as [] (1.59, 1.45 to 1.74) and [] (1.25, 1.16 to 1.36) (fig 2). We found no association with [] (adjusted hazard ratio 1.12, 0.96 to 1.30) or [] (1.04, 0.93 to 1.16).	on the basis of excisting literature, we cannot exclude influence of unknown or residual confounding, for example, by []" ** Typos copied as in the published version	matched cohort. They discuss the possibility of residual confounding and suggest possible confounders missed. All of these elements point to a causal aim.
"To determine if [] a critical determinant of [] is and []."	"[] does not have a clinically important association with [] or []."	"We assessed the effect of [] compared with [], using multivariable regression. Modified Park's tests were used to determine the appropriate regression models (gamma, Poisson, and logistic) for discrete [] outcomes. We also assessed the effect of []	"In all of our primary analyses we adjusted for the following key confounders:	"Table 2 shows that there was no strong evidence of a clinically important association of [] and [] with [] or []."	"We recognise that we assessed multiple associations and the isolated positive association of [] and [] may reflect a chance finding, particularly as	Both abstract and main text use causal language and explain that the aim is to identify whether the exposure is a cause of the outcome and

	on an individual's repeat		there was no	after adjusting
	[] outcomes scores. []		consistent	for potential
	Linear mixed effects		association with	confounders
	models were fitted with		[] at any other	conclude that
	time as a fixed effect and		[]. [] We	it is not, given
	a random effect of		would suggest	that they only
	subject."		the overall	identify one
			impact would be	positive
			potentially small	association
			as there was no	when multiple
			clinically	were assessed
			important	and consider it
			impact on [] at	to be by
			any age. We	chance.
			acknowledge	
			that [] may	
			have attenuated	
			to the null any	
			potential	
			detrimental	
			effect of [] on	
			[] outcomes,	
			but this would	
			further support	
			that [] does not	
			have permanent	
			consequences for	
			[]."	
			I I	

"To determine if [] is associated	"[] is  associated with	"We calculated odds ratios for each outcome []	"Based on a priori knowledge,	"In the 14 days after [], [] is	"We saw minimal differences in the	The elements that point to a
with an increased	a greater risk	within 14 days of []	we considered	associated with	odds ratios for	causal aim:
risk of [] in the	of []	comparing each []	the following	the highest odds	[]. [] analyses	confounder
general	compared with	adjusting for potential	variables as	of [] (adjusted	using	adjustment by
population."	[], but not a	confounders using logistic	potential	odds ratio 1.72,	multivariable	regression
	greater risk of	regression."	confounders of	95% confidence	regression and	models,
	death. The		the relation	interval 1.31 to	inverse	sensitivity
	relative risk		between [] and	2.24) and []	probability	analysis using
	increase is		[]: []. All	(2.27, 1.49 to	treatment	inverse
	similar across		covariates other	3.45) of all the	weighting	probability of
	population		than sex and	[] investigated.	approaches []	treatment
	groups, but the		ethnicity were	[] The odds of	were consistent.	weighting and
	higher baseline		updated over	death within 14	[] our study	discussing
	risk among		time. [] We	days of [] were	also had greater	residual
	those []		initially adjusted	similar to [] for	ability to adjust	confounding.
	translates into		for sex and age	[] (0.90, 0.76 to	for detailed	
	higher absolute		only, and then	1.07) and the	characteristics,	
	risks of [] in		fitted an adjusted	other []."	such as [],	
	these groups."		model using []."		which are likely	
					to have reduced	
					residual	
					confounding."	
"To evaluate the	"In this large	"For each comparison and	"We considered	"Table 3 shows	"Randomized	Both abstract
[] <b>safety</b> of [],	cohort study,	for all outcomes, we	the following	that after	controlled trials	and main text
in direct	[] was	calculated unadjusted and	covariates as	propensity score	are the best way	use causal
comparisons with	associated with	propensity score matched	potential	matching, for []	to assess drug	language and
	a <b>lower risk</b> of	number of events,	confounders: []	primary	efficacy [] On	they are
	l			l		

[], as used in	[] I and with a	incidence rates, and	To control for	outcome, the	the other hand,	explicit to
routine practice."	similar risk of	hazard ratios with 95%	imbalances in	number of events	strict inclusion	state that the
	[] in direct	confidence intervals."	patient	for [] and the	and exclusion	aim is to
	comparisons		characteristics	[] comparator	criteria and	evaluate
	with [] as		between cohorts,	were 91 and 124	rigorous safety	safety of the
	used in routine		we calculated	respectively (8.9	monitoring limit	exposure and
	care."		exposure	v 12.8 per 1000	the	use causal
	care.		propensity	person years;	generalizability	methods
			scores as the	hazard ratio 0.70,	of randomized	(propensity
			predicted	95% confidence	controlled trial	score
			probability of	interval 0.54 to	results. Our study	matching).
			receiving the	0.92) in cohort 1;	[] allowing	They discuss
			treatment of		better	•
				94 and 148 (7.5 v		why the design
			interest (ie, [] v	12.4; 0.61, 0.47	generalizability	was
			each	to 0.78) in cohort	to routine care	observational
			comparator)	2; and 77 and	[] provides data	and consider
			conditional upon	154 (7.3 v 14.4;	from direct	that due to
			the subjects'	0.51, 0.38 to	comparisons. []	this nature,
			baseline	0.67) in cohort	while we used	residual
			covariates using	3."	propensity score	confounding
			three separate		matching to	cannot be
			multivariable		balance more	excluded that
			logistic		than 100 baseline	may have led
			regression		characteristics	to downtown
			models. All		between the	of conclusion
			variables were		groups, residual	which is
			included and no		confounding by	phrased more
			further selection		some	in terms of
			was conducted.		unmeasured	association.

			We 1:1 matched cohorts on their propensity score using a caliper width equal to 0.2 of the standard deviation of the logit of the propensity score."		characteristic(s) cannot be ruled out. "	
INCONSISTENT						
"To evaluate the relation between [] and development of []"	"[] was associated with an increased risk of [] that was mediated by []. Systematically addressing [] may be an important public health strategy to reduce the incidence of []	"We calculated the hazard ratios for the relation of [] to the risk of MRSA using Cox proportional hazard models. [] We also calculated the absolute risk difference. [] We performed mediation analyses to examine the extent to which the effect of [] on the risk of [] was through []. Using marginal structural models we then estimated the natural	"We performed a matched cohort study [] matched on age (one year either way), sex, and study entry time (within one year either way). Such comparators were chosen to further ensure the comparability [] In the multivariable Cox	"The matched and multivariable adjusted hazard ratios for patients with [] were 1.69 (1.51 to 1.90) for [] and 1.26 (1.12 to 1.40) for []."	"Our GP practice based dataset could have missed the detection of some inpatient cases of []; however, these potential non-differential misclassifications would have biased our results towards the null, rendering our	The aim in the abstract limits to state that they are exploring the relationship of exposure and outcome. However, in the abstract conclusion and full text they describe mediation analysis,

	among patients wih []."	direct effect [] and the natural indirect effect [] while adjusting for the same confounding variables"	model we adjusted for []."		findings conservative"	identifying direct and indirect effects and use marginal structural models which are part of the causal toolkit.
"To quantify the effects of varying []"	"[] is  associated with a large increase in [] among [] patients. The data from this study suggest that [] rather than [] is more strongly associated with []"	"For adjusted analysis of time until [] we used Cox proportional hazards models."	"Adjusted models included []"	"Each additional [] increased the rate of [] by 70.7% (95% confidence interval 54.6% to 88.4%) before adjustment and increased the hazard of [] by 44.0% (40.8% to 47.2%, P<0.001) after adjusting for covariates."	"To determine the extent to which strong unobserved confounding might explain the observed association, we included this synthetic confounder in a Cox model. [] As part of a sensitivity analysis, we constructed models that removed potential	The aim uses causal language and they provided adjusted estimates. However the conclusion is phrased in terms of association. They do use sensitivity analysis to test for residual confounding and it might be that due to concern of

					confounders.	unmeasured confounding they decided to be conservative with the conclusions.
"To evaluate the long term association between []"	"Widespread utilisation of [] may be contributing to long term increased risk of []. The potential for [] should be considered when []."	"We conducted Poisson regression analyses using person years as observations."	"We included several variables as known confounders or effect modifiers in the relation between. []The final fully adjusted model adjusted for []"	"After adjustment for covariates, the rate ratio was [] indicating that during the entire period of follow- up the risk of [] was 21% higher during [] than at other times."	"The registered active [] population is generally representative of the UK population in terms of age, sex, and regional distribution"	The aim is phrased in terms of association but the conclusion uses causal language and they discuss confounder adjustment.
"To investigate the <b>association</b> of []"	"The shape of the association between [] and [] was determined by [].This finding suggests that the [] may be largely	"We used Cox proportional hazards models to estimate hazard ratios and 95% confidence intervals. We stratified the analysis by age in months and calendar year of the questionnaire cycle."	"For the main analysis, we used [] measured at baseline to minimize the effect of underlying diseases on mortality [] In multivariable	"A multivariable adjusted model showed a positive association between [] and all cause mortality, whereas [] showed a U	"Our findings remained robust in several sensitivity analyses [] we cannot entirely rule out the possibility of unmeasured or unknown	The aim is stated in terms of association but they adjust for confounders, discuss unmeasured confounding and conclude

	explained by []"		models, we adjusted for potential confounders including []"	shaped association with all cause mortality. In a mutually adjusted model including both [] and [] we consistently observed a strong positive association between [] and all cause mortality."	confounding factors that may account for the associations observed in this study."	that the outcome can be 'largely explained' by the exposure.
"To examine the associations of []"	"This association could be explained by the finding that [] These results emphasise the importance of revisiting [] or establishing specific guidelines for	"We performed Cox models with penalised splines"	"In final Cox models with penalised splines, we made adjustments for: []"	"[A]fter adjustment for confounding factors, the U shaped association with []"		The aim is phrased in terms of association but they provide adjusted estimates, discuss confounding and conclude that the exposure

	management among []"				could explain the outcome and suggest to take actions given the findings.
"To estimate long term survival, health, and educational/socia I functioning in patients with []"	"[] had no substantial effect on []"	"We calculated mortality rate ratios and incidence rate ratios as measures of relative risk."	"For each [] patient, we used the Danish Civil Registration System and the DNPR to identify all Danish residents with the same sex and date of birth as the patient who had not tested positive [] and who met the study's inclusion and exclusion criteria []. From this population, we extracted 10 people at random for each patient. People in	Patients and members of the comparison cohort were well matched with respect to [] Mortality was not higher among patients in the [] cohort"	The abstract states that they aim is to estimate survival but they use matching and conclude that the exposure has no 'substantial effect' on the outcome.

			the population comparison cohort were assigned the same date of study inclusion as [] patients to whom they were matched."			
"To compare the risk of []"	"Although residual confounding cannot be excluded, this finding deserves consideration when [] is used for []"	"We estimated the crude hazard ratio of [] using Cox proportional hazard regression, and the adjusted hazard ratio was obtained using propensity score matching"	"We identified potential confounders that were plausibly associated with both []based on clinical knowledge [] In the context of this study, the propensity score is the probability of receiving [] as opposed to [], given the baseline characteristics. Patients who received []	"The crude hazard ratio of death in the unmatched cohort was 1.51 (95% confidence interval 1.22 to 1.85) and the adjusted hazard ratio in the matched cohort was 1.50 (1.14 to 1.96)"	"Comparison of the baseline characteristics in the unmatched cohort provided little evidence of confounding [] it is unlikely that a few additional unmeasured variables can explain a 50% increase in the risk independent of all other confounder and proxies of confounders that	The abstract suggests that they aim is comparison of the risks but does not explicitly use causal language. They do adjust for confounding, using propensity score matching, and discussed unmeasured confounding which are

			were matched to patients who [] using a 1:1 nearest neighbor matching algorithm with a caliper of 0.2 of the standard deviation of the propensity score on the logit scale. Covariate balance between the two groups was assessed after matching, and we considered an absolute standardized difference less		are adjusted for in our study."	applied when aiming for causal inference.
			absolute standardized			
"To determine whether [] is associated with []"	"[] was independently associated With []"	"We fitted both a mixed effect logistic regression model (in which the outcome was defined as	"We examined the relation between [] and	"The rate of distinct criteria met per year increased by 24%	"We did a sensitivity analysis using propensity score	The aim uses causal language but the conclusion

		dichotomous [] and the Prentice, Williams, and Peterson (PWP) model"	[] adjusted for"	if a patient had been admitted to hospital (hazard ratio 1.24, 95% confidence interval 1.20 to 1.28) when controlled for the other covariates"	matching to assess whether the association between [] and [] could be due to unmeasured confounders [] Although we adjusted for a range of characteristics of patients, as with any observational study potential exists for unmeasured confounding, which may partly or fully explain the relation between []"	is phrased in terms of association. They provide adjusted estimates, use propensity score as sensitivity analysis and discuss unmeasured confounders. The only reason to present a conservative conclusion seems to be the observational nature of the study.
"To investigate associations between [] and to analyse the	"Risks of [] are inversely associated with []"	"We used multivariable Cox regression analysis to compare the rates of [] and []. "	"Confounders included in the final models were based on the literature or	"Compared with [], [] had increased hazard ratios of []"	"We believe that our findings are widely applicable and provide justification for	The aim suggests a causal aim because they evaluate the

effect of changes []"			statistical significance (P<0.10). The full model included []"		[] and continuing []"	impact of changing the exposure which makes it an intervention and they provide estimates adjusted for confounders. The conclusion is phrased in terms of association.
"To estimate the rates of []"	"In cases of [], approximately [] will become [], of which a third will have []."	"We present denominators where data for the secondary outcome are missing. We defined the population attributable fraction as (Re–Run)/Re=(RR–1)/RR, calculated using Stata. To test the robustness of our findings, we did a sensitivity analysis."	"We compared the demographic and clinical variables of []. We used the binomial Wilson score to calculate confidence intervals of single proportions and the Pearson exact method to calculate	"[] had a higher risk of [] The population attributable fraction of [] was 47% for [] and 61% for []"	"Considering these results when counselling potentially exposed [] seems reasonable"	The aim and conclusion are phrased in association terms. However, they estimate attributable fractions and suggest to act given the findings.

			confidence intervals of risk ratios and medians."			
To perform an expedited assessment of [] risk associated with exposure to []".	"The results do not imply a markedly increased short term overall risk of [] in []."	"We used Cox regression to estimate the hazard ratio with 95% confidence intervals for [] associated with [], both for ever use and for the predefined categories of cumulative use"	"Analyses were, however, performed as crude comparisons adjusted only for [] as well as adjusted for [] and the potential confounding factors."	"Overall, exposure to [] showed no association with [] compared with exposure to [] (adjusted hazard ratio 1.09, 95% confidence interval 0.85 to 1.41) and no evidence of a dose-response relation"	"This ensured that the estimates were not affected by immortal time bias []. As all comparisons were performed within users of [], the exposure to [] can reasonably be expected to be a random event, and confounding is thus expected to be limited."	The aim does not use causal language. They do provide estimates adjusted for confounding, discuss immortal time bias and conclude that the exposure does not result in an increase survival.
"To investigate the <b>risks</b> of [] in []"	"No increased risk of [] was detected in [], but increased risks of [] were found in this study. Our	"To calculate expected [], we multiplied the person years at risk by corresponding national incidence rates (by 5 year age band and individual calendar year) for the	"We obtained data relating to potential confounding factors such as []"	"There was no overall increased risk of [] (2578 observed v 2641.2 expected []; standardised incidence ratio	"Given previous inconsistent results, small study size, and lack of information on potential	The aim does not use causal language. They provide standardised estimates, discuss

	results suggest that [] risks could be due to [], rather than []."	general female population of England and Wales.  Standardised incidence ratios were calculated by the comparison of observed values with expected values."		0.98 (95% confidence interval 0.94 to 1.01); absolute excess risk -2.8 cases per 100 000 person years (95% confidence interval -7.1 to 1.8); table 2)".	confounders, we undertook a population based linkage study in []"	confounding and conclude that the risk of the outcome is due to a given exposure compared to another.
CONSISTENTLY NO	T CAUSAL					
"To determine whether [], compared [], is associated with an increased risk of []"	"In this population based cohort study, [] was associated with an increased risk of []. The association was particularly elevated among people using [] for more than five years. Additional studies, with	"We calculated crude incidence rates of [] and 95% confidence intervals, based on the Poisson distribution, for each exposure group. We used time dependent Cox proportional hazards models to estimate hazard ratios and 95% confidence intervals of [] associated with [] compared with [], using multiple imputation for variables with missing values."	"Potential confounders. All models were adjusted for the following variables measured at cohort entry: []. [] as an alternate means of controlling for confounding, we repeated the analysis by stratifying the model on tenths	"Compared with [], [] were associated with an overall 14% greater risk of [ ] (1.6 v 1.2 per 1000 person years; hazard ratio 1.14, 95% confidence interval 1.01 to 1.29)."	"We introduced a one year exposure lag period to account for a minimum latency time window and to minimize reverse causality. []The association between [] and [] is biologically plausible. [] although we were able to adjust for several	In the abstract they only describe associations but in the full text their interest points to a causal aim given the different methods applied to adjust for confounding and reverse causality. They

"To determine whether [] and [] are and [], might incidence rates of a crude incidence rate of a crude rate	of disease risk score. Finally, we repeated the analysis using a marginal structural Cox proportional hazards model using inverse probability of treatment and censoring weighting—a		important confounders, this study lacked information on other potential confounders such as [] In this large, population based study, [] was associated with an elevated risk of []	also consider elements as biologically plausibility and duration response relation. Residual confounding seems to be a concern because they
"To determine whether [] and [] are "Compared with [], [], and [], might "For each exposure category we calculated crude incidence rates of	repeated the analysis using a marginal structural Cox proportional hazards model using inverse probability of treatment and censoring		study lacked information on other potential confounders such as [] In this large, population based study, [] was associated with an elevated	biologically plausibility and duration response relation. Residual confounding seems to be a concern
"To determine whether [] and [] are "Compared with [], [], and [], might "For each exposure category we calculated crude incidence rates of	analysis using a marginal structural Cox proportional hazards model using inverse probability of treatment and censoring		information on other potential confounders such as [] In this large, population based study, [] was associated with an elevated	plausibility and duration response relation. Residual confounding seems to be a concern
"To determine whether [] and [], might "For each exposure category we calculated crude incidence rates of	marginal structural Cox proportional hazards model using inverse probability of treatment and censoring		other potential confounders such as [] In this large, population based study, [] was associated with an elevated	duration response relation. Residual confounding seems to be a concern
"To determine whether [] and [], might "For each exposure category we calculated crude incidence rates of	structural Cox proportional hazards model using inverse probability of treatment and censoring		confounders such as [] In this large, population based study, [] was associated with an elevated	response relation. Residual confounding seems to be a concern
"To determine whether [] and [], might "For each exposure category we calculated crude incidence rates of	proportional hazards model using inverse probability of treatment and censoring		such as [] In this large, population based study, [] was associated with an elevated	relation. Residual confounding seems to be a concern
whether [] and with [], [], category we calculated crude incidence rates of	hazards model using inverse probability of treatment and censoring		large, population based study, [] was associated with an elevated	Residual confounding seems to be a concern
whether [] and with [], [], category we calculated crude incidence rates of	using inverse probability of treatment and censoring		based study, [] was associated with an elevated	confounding seems to be a concern
whether [] and with [], [], category we calculated crude incidence rates of	probability of treatment and censoring		was associated with an elevated	seems to be a concern
whether [] and with [], [], category we calculated crude incidence rates of	treatment and censoring		with an elevated	concern
whether [] and with [], [], category we calculated crude incidence rates of	censoring			
whether [] and with [], [], category we calculated crude incidence rates of			risk of []	hecause they
whether [] and with [], [], category we calculated crude incidence rates of	weighting—a			because they
whether [] and with [], [], category we calculated crude incidence rates of	140 Billing a		overall, along	lacked
whether [] and with [], [], category we calculated crude incidence rates of	method designed	I	with evidence of	information on
whether [] and with [], [], category we calculated crude incidence rates of	to adjust for time	2	a duration-	relevant
whether [] and with [], [], category we calculated crude incidence rates of	dependent		response	cofounders
whether [] and with [], [], category we calculated crude incidence rates of	confounding		relation."	which could
whether [] and with [], [], category we calculated crude incidence rates of	associated with			lead to down
whether [] and with [], [], category we calculated crude incidence rates of	time varying			tone of the
whether [] and with [], [], category we calculated crude incidence rates of	exposures"			conclusions.
[] are and [], might crude incidence rates of	"The models	"Compared with	"Finally, we	The abstract
	THE HIDUEIS	[], [] was	excluded those	only refers to
	were <b>adjusted</b>	associated with a	with less than	association
<b>associated</b> with <b>be associated</b> [] with 95% confidence		associated with a	one year of	but the full
an <b>increased risk</b> with an intervals, based on the	were <b>adjusted</b> for the potential	77% increase in		text mentions
of [] in adults increased risk Poisson distribution. Tin	were <b>adjusted</b> for the potential		follow-up after	
with []." of [] in adults dependent Cox	were adjusted for the potential confounders measured at	77% increase in	follow-up after cohort entry, to	adjusting for
with []." proportional hazards	were adjusted for the potential confounders measured at	77% increase in the hazards of	· ·	adjusting for confounders

	models were used to	confounding by	interval 1.04 to	period and to	minimise
	estimate hazard ratios and	indication, we	3.01)."	minimise reverse	reverse
	95% confidence intervals	compared [].		causality. [] To	causality. They
	of [] associated with []	[] we fit a		assess possible	also describe
	and [], separately, when	marginal		duration-	its biological
	compared with []."	structural model		response	plausibility.
		to investigate the		relations, we	There is a
		impact of		investigated the	concern for
		potential time		association	residual
		dependent		between	confounding
		confounding		cumulative	due to the
		using <b>inverse</b>		duration of []	observational
		probability of		on the risk of [].	nature rather
		treatment and		An association	than missing
		censoring		between [] and	information on
		weighting."		incidence of []	particular
				is <b>biologically</b>	relevant
				plausible. [] as	confounders.
				with all	
				observational	
				studies, residual	
				confounding is	
				possible. We	
				conducted	
				several sensitivity	
				and ancillary	
				analyses	
				specifically	
				designed to	
				)	

					assess the potential impact of <b>residual</b> confounding."	
"To examine the association between [] and [] risk of []."	"[] could increase the risk of []. However, confirmation of these findings are warranted, preferably in an intervention setting"	"[] was categorised by percentiles (<10, 10-20, 20-50, 50-80, 80-90, ≥90). [] With these same categories of exposure, the association between [] and [] was examined by Cox regression. We used [] age from birth up to May 2016 as the underlying timescale censoring if death or emigration from Denmark occurred (1217 events)."	"Characteristics that might influence the risk of [] were identified a priori and included as potential confounders in our adjusted analysis. In model 1, we adjusted for: [].In model 2, additional adjustments were made for []"	"[] was significantly associated with increased risk of [] in both unadjusted and covariate adjusted analyses (table 3). Compared with [], offspring of those with [] had double the risk of [] during follow-up (hazard ratio 2.00 (95% confidence interval 1.02 to 4.00)). Risk of [] was positively associated with []: the association was	"[] the mechanism that might be responsible for this effect is not known, but could include []. [] the role of unmeasured or unidentified confounders can never be fully excluded in observational studies."	The abstract only considers associations but the full text mentions confounder adjustment and discusses potential mechanism (biological plausibility). Concern of residual confounding is due to the observational nature of the study.

				significant (Ptrend=0.016) and increased monotonically. Only minor differences were observed between the unadjusted and covariate adjusted analyses."	
"To ascertain compliance rates with []; to identify features associated with non-compliance; to rank [] by compliance; and to build a tool for live ongoing audit of compliance."	"Compliance with [] has been poor, with half of all [] non-compliant. [] commonly contain inconsistencies that might prevent even [] assessing compliance. Accessible and timely information on the compliance	"We constructed a logistic regression model with all these <b>explanatory</b> variables, as they were selected prospectively on the basis of clinical and methodological interest."	"Explanatory variables. We created variables for a range of features of each [], selected prospectively on the basis of clinical and methodological interest."	"In the adjusted multivariable analysis, [] with a [] were significantly more likely to [] (adjusted odds ratio 23.3, 95% confidence interval 19.2 to 28.2); as were [] (18.4, 15.3 to 22.1)."	 Although adjusted estimates are present, both abstract and full text limit to describe associations, rates and ranks. No causal language is used.

	status of [] and [] may help to improve reporting rates."				
"To assess how often older adults [] were [], and to identify markers of []."	"One in seven older adults [] were []. More than half of [] occurred in patients with []. More attention is needed to reduce potentially harmful [] as older adults []."	"We did multivariable mixed effect logistic regression analyses to determine associations between the outcome of [] and primary predictors of []."	"Our primary predictor variables were []. Adjusted analyses included the covariates noted above, a random effect term to account for clustering by hospital, and an interaction term to account for the relation between [] and []."	"A total of 2074 (14%) patients were []; 1293 (9%) were [] and 300 (2%) were []. Additionally, 628 (4%) patients were []. [] Patients with [] had a 25% (95% confidence interval 23% to 78%) probability of []."	 The abstract indicates that the aim is to assess the frequency of a condition and that is reflected in the main text. No causal language used.
"To describe trends in the rate and daily dose of [] used among [] from 2007 to 2016."	"[] rates were high during the study period of 2007-16, with the highest rates in [] versus [] and	"Endpoints were defined at the person quarter level. We used logistic regression to model the <b>proportion</b> of the population [] each quarter. The average []	"All analyses were stratified by beneficiary category including commercially insured, aged	"Averaged across the entire study period, 51.5% of disabled Medicare beneficiaries [] per year (n=1 128	 The abstract indicates that the aim is to describe the frequency of a condition which is

	[]. [] and average daily dose have not substantially declined from their peaks, despite increased attention to [] and awareness of their risks."	per person day by quarter was modelled by a generalized linear model with negative binomial family and log link. The dependent variable was the total [] per person in the quarter, with an exposure variable representing the number of days of insurance coverage for each person included to standardize daily []."	Medicare, and disabled Medicare (beneficiaries with Medicare coverage who were under age 65 years)"	088), compared with 14.3% (n=18 721 915) of commercial beneficiaries and 25.7% (n=3 847 676) of aged Medicare beneficiaries."		reflected in the main text. No causal language used.
"To describe []	"Mortality due	"Our primary aim was to	"We adjusted	"During the study	"[] though we	The abstract
related mortality	to [] has been	describe temporal trends	rates for age—	period, a total of	have detected	indicates that
in the United	increasing in	in death rates attributable	that is, age	460 760 deaths	worsening	the aim is to
States during	the US since	to [] and [] as the	specific mortality	were attributed	mortality since	describe the
1999-2016 by	2009. Driven by	primary or underlying	was weighted	to [] (20 661 in	2009, the precise	frequency of a
age group, sex,	deaths due to	cause of death for adults	according to the	1999 and 34 174	reasons for this	condition
race, cause of	[], people	in the USA.[] We then	age distribution	in 2016) and 136	trend and the	which is
[], and	aged 25-34	evaluated trends in death	in a standard	442 to [] (5112	geographic	reflected in
geographic 	have	rates using the National	year (2000). We	in 1999 and 11	heterogeneity in	the main text.
region."	experienced	Cancer Institute's	also sought to	073 in 2016)	our analysis	No causal
	the <b>greatest</b>	Joinpoint program. This	describe how	(table 1). Men	require further	language used.
	relative	enabled us to identify if	these trends	had a higher	study. For	
	<b>increase</b> in	there were years in the	differed based on	<b>burden</b> of age	example, we	
	mortality.	study period where the	demographic	adjusted	identify the	

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care of patients with [...]."

"To examine whether [] are associated with an increased risk of [] after []."	"Women with [], especially [], may be at higher risk of []. If these findings are replicated elsewhere, a massive amount of data exists that could aid in identifying women at higher risk of [] and that could be conveyed to them or their healthcare providers."	"The main model assessed the primary [] composite outcome, as well as the individual outcomes of [], in relation to each [] for the screened cohort, with censoring at a woman's death or arrival at the end of the study period of 31 March 2016, allowing for a maximum follow-up of 22 years. We did time to event analyses using multivariable Cox regression models, to derive a hazard ratio and 95% confidence interval for each study outcome."	"Hazard ratios were adjusted for variables chosen a priori, based on the existing literature, including: []"	"A total of 6209 women developed the primary [] composite outcome, which was typically about 1.2 to 1.3 times more likely to occur in a [], even after adjustment for other covariates"	"Potential confounders between [] and the risk of [], including [] were each accounted for in the models. Nevertheless, about 10% of [] lacked information on [], and [] and [] were entirely unknown."	The abstract indicates that the aim is to identify the association between an exposure and an outcome. They consider residual confounding due to lack of information on relevant confounders.
"To examine the association between [] and the risk of [] according to levels of []."	"Among [], increasingly worse [] was associated with a progressively increased risk of []. Even	"Using generalised linear models with a robust sandwich estimator, we estimated risk ratios for [], comparing [] according to levels of [] with []. To take into	"Analyses were adjusted for []"	"In analyses based on [] levels, the adjusted risk ratios for [] were 2.17 (95% confidence	"It is also possible that the previously demonstrated association [] has resulted in increased clinical	The abstract indicates that the aim is to identify the association between an exposure and

	I	1	1	1	1	ı
	with [] within	account possible		interval 1.37 to	surveillance for	an outcome.
	target levels	dependence from		3.42) for [],	defects among	They consider
	recommended	repeated [], we		3.17 (2.45 to	[]. [] health	residual
	by guidelines	constructed models with		4.11) for [],	registers do not	confounding
	[], the risk of	[] as a cluster variable.		2.79 (1.90 to	record data on	due to lack of
	[] was	[] were assumed to		4.12) for [], and	[] and hence we	information on
	increased more	follow a poisson		6.23 (4.32 to	could not	relevant
	than twofold.	distribution, and we		9.00) for []	account for these	confounders.
	The risk of []	estimated risk ratios using		versus []. The	factors."	
	was not	a log link function"		corresponding		
	statistically			adjusted risk		
	significantly			differences were		
	increased at			17 (95%		
	any of the []			confidence		
	levels			interval 5 to 36),		
	examined; the			32 (21 to 46), 26		
	study had			(13 to 46), and 77		
	limited			(49 to 118) cases		
	statistical			per 1000 []."		
	power for this					
	outcome and					
	was based on					
	[] only."					
"To examine the	"Regardless of	"We calculated the	"We computed	"The associated	"Our	The abstract
association	index ages at	lifetime risks for the first	lifetime <b>risk in</b>	lifetime risk of	observational	and main text
between risk	55, 65, or 75	incident [] from index	subgroups of	[] was lowest if	study design	indicate that
factor burdens—	years, an	ages 55, 65, and 75 years	participants	the risk factor	limits the ability	the study
categorized as	optimal <b>risk</b>	up to age 95 years. [] we	according to their	profile was	to establish	mainly aims at
	l	l	1	l .	l .	l

optimal, borderline, or elevated—and the lifetime risk of []."	factor profile was associated with a lifetime risk of [] of about one in five; this risk rose to more than one in three in individuals with at least one elevated risk factor."	used a modified Kaplan-Meier estimator with age as the time scale, accounting for the competing risk of death to compute the lifetime cumulative risk of [] and associated 95% confidence intervals"	risk profile at a specified index age (optimal, borderline, and elevated), for each risk factor separately and for the combination of risk factors. [] we fitted a multivariable Fine and Gray model, adjusted for competing risk of death to predict the	optimal. The lifetime risk of [] increased gradually as the risk factor profile changed from optimal to borderline and elevated at each index age."	causal pathways, and only associations between risk factor profiles and lifetime risk of [] can be concluded from our study."	identifying associations. There is a concern for residual confounding due to the observational nature rather than missing information on particular relevant confounders.
"To compare rates of [] for patients [], with patients []."	"[] was associated with lower [] rates compared with []."	"We used a Cox proportional hazards regression model, adjusting for (), to estimate hazard ratios and 95% confidence intervals for [] comparing [] with []. To summarize switchback estimates	"[] adjusting for basic demographics (age, sex, and calendar year)"	"Figure 5 shows that in the adjusted analysis, the [] rates remained consistently lower among [] than []. The magnitude of this	"[] our results indicate that [] may in part be driven by []."	Even though causal language is not used and both the abstract and main text mainly describe associations,

		across [], we conducted inverse variance weighted random effects meta-analyses"		effect was largest for [] (hazard ratio 0.52, 95% confidence interval 0.43 to 0.63) and smallest for [] (0.86, 0.77 to 0.97). The pooled hazard ratio across [] suggested that [] was associated with a 28% lower rate of [] compared with [] (0.72, 0.64 to 0.81)."		their conclusion at the end of the text suggests a causal relationship.
"To assess whether [] is associated with the incidence of [] in patients with []."	"In this first population based study, [] was associated with an increased risk of []. Although these findings need to be	"We calculated crude incidence rates of [] with 95% confidence intervals based on the Poisson distribution for the entire cohort and for each exposure group. For all analyses, we used time dependent Cox proportional hazards	"The models were adjusted for the following potential confounders measured at cohort entry: []"	"Compared with [], [] was associated with a 75% increase in risk of [] (53.4 v 34.5 per 100 000 per year; hazard ratio 1.75, 95% confidence interval 1.22 to	"[] as with all observational studies, residual confounding from unknown or unmeasured variables remains possible.  However, on the basis of the rule	The abstract mainly describes associations but in the main text they describe how their estimates were adjusted for potential

	I					
	replicated,	models to estimate hazard		2.49). The	out method, a	confounders
	physicians	ratios and 95% confidence		number needed	hypothetical	and they
	should be	intervals for []		to harm	confounder	estimate
	aware of this	associated with []		corresponded to	would need to be	numbers
	possible	compared with []. We		2291 patients	strongly	needed to
	association."	also calculated the		followed over a	associated with	harm (NNH).
		number needed to harm		two year period	both the	Also they
		for patients followed over		and 1177 over a	exposure (odds	consider
		a two year and four year		four year	ratio >4.7) and	residual
		period by using methods		period."	the outcome	confounding
		accounting for varying			(relative risk	and suggest
		patient follow-up times."			>5.0) to move	that only a
					the point	strong
					estimate towards	unmeasured
					the null."	confounder
						will remove
						the association
						observed. All
						of these, point
						to a causal
						analysis.
"To assess the	"In this large	"We used Cox	"Models were	"In model 1, [].	"Lastly, although	The abstract
prospective	prospective	proportional hazards	adjusted for []	was associated	we included a	mainly
associations	study, a 10%	models with age as the	we made	with increased	large range of	describes
between [] and	increase in the	primary timescale to	additional	risks of overall	confounding	associations
risk of [].	proportion of	evaluate the association	adjustments [].	cancer (hazard	factors in the	but in the
	[] associated	between [] and	In addition we	ratio for a 10	analyses, the	main text they
1	[]				· · / · · · /	

	significant increase of greater than10% in risks of []. Further studies are needed to better understand the relative effect of the various dimensions of [] in these associations."	models. We estimated hazard ratios and 95% confidence intervals with the lowest quarter as the reference category."	did <b>mediation</b> analyses []"	in the proportion of [] 1.12 (95% confidence interval 1.06 to 1.18), P<0.001) and [] (1.11 (1.02 to 1.22), P=0.02). "	residual confounding resulting from unmeasured factors () cannot be entirely excluded owing to the observational design of this study"	their estimates were adjusted for potential confounders and they use mediation analysis which suggest a causal aim. They also consider residual confounding due to the observational nature of the study.
"To assess the association between [] and all cause mortality in [] with []."	"Giving [] to [] with [] was associated with an increased rate of [] but a paradoxical lowered rate of all cause mortality. Careful	"We calculated the incidence of [] and all cause mortality per 100 person years of follow-up. We generated Kaplan-Meier survival curves for the outcomes of interest grouped by [] status. Cox proportion regression were reported as adjusted hazard ratios with 95%	"We used propensity score matching with demographic and clinical variables to adjust for potential confounding from imbalances in clinical characteristics	"The crude rates for [] and [] were 4.6 and 1.2 after [], and 1.5 and 0.4 in patients who [] per 100 person years, respectively. In the Cox proportion	"The study population was derived from real world evidence with the inherent limitations of diagnostic coding and case ascertainment Despite well matched groups	The abstract limits to describe associations and rates of the condition but the main text suggest a causal aim as they use propensity

year."

of 8.5% (95%

confidence

growth"

who had [...]

increased

does not use

causal

	significantly over time."			interval 7.6% to 9.3%). [] The slope of the trend line changed significantly at two points: 2004/5 (P<0.001) and 2008/9 (P=0.004) (fig 1)."		language accordingly.
"To investigate	"[] was	"[] we investigated the	"We treated []	"As shown in	"To minimise the	The abstract
the association	associated with	associations of [] with	as potential	figure 1, in both	potential	mentions
of [] with	a range of	cause specific incidence	confounders. For	men and women,	contribution of	associations
disease specific	health	and mortality over follow-	Cox proportional	[] was	reverse causality	and suggests
incidence and	outcomes and	up with Cox proportional	hazard analyses,	associated with a	to the findings,	that the aim is
mortality and	improved	hazard models. We	we ran four	higher hazard for	we did a	prediction. In
whether []	prediction of	reported the results as	models that	all cause	landmark	the main text,
enhances the	an office based	hazard ratios together	included an	mortality and	analysis	the authors
prediction ability	risk score.	with 95% confidence	increasing	incidence of and	excluding events	conclude that
of an established	Further work	intervals."	number of	mortality from	occurring within	the exposure
office based <b>risk</b>	on the use of		covariates: model	[] in model 0.	the two years	of interest
score."	[] in risk		0 (minimally	The associations	after recruitment	enhances
	scores or risk		adjusted)	were similar after	in model 4	prediction and
	screening is		included []"	adjustment for	(landmark	identification
	needed to			[] in model 1;	analysis). This	of patients
	establish its			after further	landmark	with risk of
	potential			adjustment, the	analysis was	certain
	clinical utility."			magnitude of	adjusted as in	diseases.

		associations were	model 3. []	However,
		slightly	may, therefore,	there is use of
		attenuated in	be a useful	causal
		models 2, 3, and	method of	
				language,
		4"	identifying	including
			people with []	confounder
			who are at high	adjustment
			risk of a wide	and discussing
			range of	reverse
			diseases. []	causality and
			Reverse causality	residual
			is possible in any	confounding.
			observational	They note that
			study. []	their goal is to
			Similarly,	do prediction
			residual	and that
			confounding is	reverse
			always possible	causality is not
			and the	a major
			associations	limitation but
			observed may	still adjust for
			not imply	it.
			causality.	
			However, given	
			that we are	
			largely interested	
			in <b>prediction</b> and	
			identification of	
			people at	
			<u> </u>	

				increased risk, and not seeking to make strong causal inferences, reverse causality is not a major limitation."	
"To externally validate four	"Application of the [] rules	"The sensitivity, specificity, and proportion	 "The sensitivity for identifying		Both the abstract and
commonly used	can lead to a	of patients [] (with 95%	patients with []		the full text
rules in [] for	wide variation	confidence intervals) were	ranged from		state that they
[]."	in [] among	assessed for each of the	72.5% for the []		aim to validate
	patients with	four decision rules. []	criteria to 98.8%		four decision
	[], resulting in	The Cochran's Q test was	for the [] rule		rules for a
	many	used to directly compare	(table 4;		particular
	unnecessary	the sensitivities and	appendix 3). []		condition.
	[] findings.	specificities between the	The [] criteria		They
	Until an	four decision rules [].	would have		compared the
	existing	Net proportional benefit	missed 11 of 74		tests in terms
	decision rule	has been proposed to	patients with []		of sensibility
	has been	incorporate such	(appendix 4). The		or specificity
	updated, any of	weighting in calculation of	CHIP criteria		and concluded
	the four rules	clinical usefulness of	would have		that the tests
	can be used for	decision rules. For each	missed two		are similar and
	patients	rule, we expressed the net	patients with [],		recommended
	presenting []	proportional benefit using	who both had		the use of a
	at the	the formula: (true	[]. The		particular one

	emergency department. Use of the [] rule is recommended because it leads to a substantial reduction in [] while missing few potential []."	positives/total number) – weight × (false positives/total number). "		specificity for identifying [] was lowest for the [] rule (4.4%) and highest for the [] criteria (60.9%). [] The sensitivity and specificity differed significantly between all the rules (Cochran's Q P<0.001). "	given that it can help avoid false negatives. The wording 'resulting' and 'leads to' are in fact to discuss the potential for false positives/ false negatives rather than a casual claim.
"To develop and validate a set of practical prediction tools that reliably estimate the outcome of []."	"The prediction models reliably estimate the outcome of patients who were managed in various settings for []. The predictor items are readily derived at hospital admission. The	"The association between predictor variables and [] was analysed by fitting proportional odds logistic regression models adjusting for the fixed effect of study. Prognostic strength was quantified as odds ratios with 95% confidence intervals. The relative importance of each predictor in the models was estimated	"In a published systematic review, we identified relevant predictors of outcome in patients []. Based on the results of this published review, we selected the following	"Bootstrap resampling showed negligible model optimism. The models had internally validated AUCs between 0.77 and 0.83. There was no significant lack of fit (goodness of fit	The abstract and main text state that the goal of the study is to validate a prediction tool. Consistent with the prediction aim, no causal

	web based []  prognostic  calculator []  and the related  app could be  adjunctive tools  to support  management of  patients."	with partial R2 statistic, which estimates the independent <b>contribution</b> of the <b>predictor</b> to the variance of the outcome"	predictor variables that are assessable early at hospital admission and are consistently associated with outcomes for inclusion in the prediction models: []"	P≥0.2 in all models). Cross validated performance was variable across studies []. The partial R2 values ranged between 4% and 46%, and the pooled AUC values were between 0.74 and 0.77"	language is used.
"To prospectively validate [] to triage patients with [] in routine clinical practice."	"In a population of patients referred for [], this new triaging approach accurately classified [] for most, with half the utilisation of ABPM compared with usual care. This	"To examine model performance, we constructed a logistic regression model with true [] as the dependant outcome variable and classification using [] as the independent predictor variable. From this model we estimated the area under the receiver operating characteristic (AUROC) curve statistic."		"The triaging strategy [] predicted true [] (true positives 66%, 95% confidence interval 63% to 69%; true negatives 24%, 22% to 27%) with a low error rate (false positives 8%, 6% to 10%; false negatives 2%, 1% to 3%)	 The abstract and main text describe that the aim is to validate a triage tool and assessed its performance compared to the standard of reference. As the aim is prediction, no causal language is

triaging		(table 2). The	used
strategy can		triaging strategy	accordingly.
therefore be		resulted in 49%	
recommended		(46% to 52%)	
for diagnosis or		being referred	
management of		for [] and the	
[] in patients		remainder	
where [] is		managed on the	
being		basis of their	
considered,		clinic	
particularly in		measurements."	
settings with			
limited			
resources."			

## **Supplementary Material**

Table A. Statements in each of the included observational studies published in the BMJ in 2018

Published Abstract		Published Full text							
Objective	Conclusion	Method	Confounder adjustment	Estimates provided	Authors Considerations	Comment			
CONSISTENTLY CA	CONSISTENTLY CAUSAL								
"To evaluate the impact of [] on [] in []"	"[] is associated with negative effects on []. Given the relatively low prevalence of [], population level impacts are currently modest. Nevertheless, as [] has doubled in the US over the past generation, further investigation is warranted of the impact on	"To estimate the adjusted odds ratio for each [] outcome by [] group, we created logistic regression models with [] as the reference group. [] The population attributable risk was calculated using the standard formula"	"Other subgroup analyses were done to ensure that [] association was not confounded by []"	"[] had 14% higher odds of [] compared with [] (adjusted odds ratio 1.14, 99% confidence interval 1.13 to 1.15). [] 14.5% (13.6% to 15.4%) of [] (under the assumption of a causal relation) can be attributed to []"	"The pooling of all [] during this period minimizes the risk of confounding from yearly fluctuations in [] outcomes. Finally, despite attempts to adjust [] using regression analysis and stratification, some residual confounding effects from [] could remain. [] As more than 12% of [] might have been	Both abstract and main text use causal language: they state that their aim is to assess the impact of the exposure on the outcome, adjust for confounders, provide population attributable risks and discuss residual confounding.			

"To examine the [...] risks of [...] initiation compared with initiation of other traditional [...] drugs, initiation of [...], and no initiation."

					[]. The	
					cumulative risk	
					over [] is also	
					likely to be	
					important in	
					terms of both	
					economic	
					burden and	
					overall public	
					health"	
	"[] poses a	"[W]e conducted a series	"We calculated	"[] initiators	"We performed	The use of
	[] risk	of cohort studies, each	the <b>propensity</b>	had a 50%	the following	causal
	compared with	mimicking the strict design	score for all	increased rate of	sensitivity	language
	non-use, []	criteria of a clinical trial (a	eligible	[] events	analyses, [] to	appears in
r	use, and use of	so-called emulated trial	individuals	compared with	estimate how	both abstract
	other	design), to compare rates	initiating [] at	[] non-initiators	strongly a single	and main text.
	traditional []	of [] among [] with	enrolment by	(incidence rate	unmeasured	They apply
	drugs."	rates among []. [] We	fitting a logistic	ratio 1.5, 95%	binary	causal
		estimated an	regression model	confidence	confounder	methods
		observational analogue of	including	interval 1.4 to	would need to be	including
		the intention to treat	covariates on	1.7)."	associated with	target trial
		hazard ratio, as a measure	sex, age, year,		[] to fully	emulation and
		of the incidence rate ratio,	comorbidity, and		explain our	propensity
				l .		

prevented were

[...], the importance of these data are most relevant to

	by fitting a Cox	drug treatment	findings. []	score
	proportional hazards	use. We then	Finally, an	matching and
	model, using time since	matched non-	unmeasured	discuss
	start of follow-up as the	initiators to []	confounder that	residual
	time scale and a time	initiators (1:1) by	was twice as	confounding.
	independent covariate for	propensity score	frequent among	
	treatment assignment. We	within a	[] initiators	
	pooled data from all trials	maximum	versus among	
	into one model and	matching range	non-initiators	
	included each trial as a	of 0.025 and	would still need	
	stratum in the regression	without	to increase the	
	(using values from 1 to	replacement."	risk of [] by a	
	252)."		factor of nine or	
			more to fully	
			explain the	
			results, if no	
			increased risk	
			actually existed	
			(eFigure 3). []	
			Still, the	
			emulated trial	
			design lacked	
			baseline	
			randomisation,	
			and therefore,	
			unmeasured	
			confounding	
			cannot be	
			excluded."	ļ

"To explore	"[] was	"We used Cox regression	"We considered	"Women with a	"We did	Causal
associations	associated with	with age as the underlying	[] as a priori	history of [] had	sensitivity	language is
between [] and	an <b>increased</b>	time to estimate hazard	confounders."	a 53% increase in	analyses []	present in
later[], overall	risk of [],	ratios for [] comparing		risk of []	using the array	abstract and
and by []	particularly	women with and without		overall,	approach for	main text.
subtype and	[subtype]. []	a history of [] We used		compared with	testing the effect	They apply
timing of onset."	were unlikely	competing risk methods		women with no	of an	mediation
	to <b>mediate</b> the	when analysing		history of []	unmeasured or	analysis,
	associations	associations with []		(incidence rate	incompletely	adjust for
	substantially,	subtypes. [] We		for women with a	measured	confounders,
	suggesting that	evaluated potential		history of []:	confounder. []	and discuss
	[] and []	mediation by []"		11.6 per 100 000	Sensitivity	the
	may share			person years;	analyses	unmeasured
	underlying			incidence rate for	suggested that	confounding
	mechanisms or			women with no	confounding by	assumption
	susceptibility			history of []:	[] was unlikely	and residual
	pathways.			8.33 per 100 000	to explain the	confounding.
	Asking about a			person years;	observed	
	history of []			hazard ratio 1.53,	associations for	
	could help			95% confidence	[]; in contrast,	
	physicians to			interval 1.26 to	[] could	
	identify			1.85)."	conceivably	
	women who				explain a	
	might benefit				considerable part	
	from screening				of the association	
	for early signs				between [] and	
	of disease,				[]. [] we also	
	allowing for				cannot rule out	
					the possibility of	

	early clinical intervention."				residual confounding by other unmeasured covariates"	
"To investigate	"Severe and	"We used Cox regression	"For each patient	"Table 3 shows	"Limitations of	The causal aim
whether adults	predominantly	stratified by <b>matched</b> set	with [], we	that in the	the study,	is evident in
with [] are at an	active [] are	[] with current age as the	randomly	primary analysis,	inherent to most	the abstract
increased risk of	associated with	underlying timescale to	matched up to	there was	large	because they
[] and whether	an increased	generate hazard ratios for	five patients by	evidence of	observational	intend to
the risk varies by	risk of []	the association between	age (within 15	associations	studies, include	assess how the
[] severity and	outcomes.	[] and each [] outcome	years), sex,	between [] and	the possibility for	risk of the
condition activity	Targeting []	(the unadjusted model).	general practice,	all [] outcomes,	confounding,	outcome
over time."	prevention	Subsequent multivariable	and calendar	except for [].	bias, and missing	varies when
	strategies	analyses adjusted for []	time at cohort	Associations	data. [] We	the exposure
	among these	(the <b>adjusted</b> model). The	entry. These	were strongest	have shown a	is modified
	patients should	adjusted model was	unexposed	with [] (hazard	clinically	and the
	be considered."	further adjusted for	patients were	ratio 1.25, 99%	relevant increase	conclusion is
		variables which may have	required to have	confidence	in the risk of []	to take action
		been on the causal	at least one year	interval 1.11 to	outcomes in	given the
		pathway (ie, mediators)	of follow-up in	1.41 in the	patients with	findings. The
		between [] and []	CPRD and no	adjusted model)	[].This	main text uses
		outcomes [] (the	history of []	and [] (1.19,	increased risk is	causal
		mediation model). [] The	when matched.	1.10 to 1.30),	largely confined	language,
		population attributable	[] We used a	with <b>partial</b>	to patients with	discusses
		risk of each [] outcome	directed acyclic	attenuation in	severe or more	DAGs,
		was estimated by using	graph to inform	the mediation	active [] and	mediators,
		the estimated hazard ratio	the identification	model. [] The	persists despite	collider bias

		and assuming the prevalence of [] to be 10%."	of covariates and mediators and to avoid collider bias"	greatest population attributable risks were estimated for [] (2.4%, 1.1% to 3.9%) and [] (1.9%, 1.0% to 2.9%)."	adjusting for potential mediators, including conventional risk factors for [] outcomes. Consideration should be given to developing prevention strategies to reduce the risk of [] among patients with severe or predominantly []"	and provides population attributable risks.
"To determine the effect of []	"This study did	"We used a <b>change point analysis</b> to study the	"The <b>risk factors</b> included in this	"The 90 day mortality in	"If we assume that the decrease	Causal language is
outcome	evidence that	change over time in	logistic	patients	in mortality can	present in
reporting in []	the	adjusted 90 day mortality	regression model	undergoing an	be causally	abstract and
on risk averse	introduction of	after [] and after []. We	are []. An	[] fell during the	linked to [], the	main text as
clinical practice,	[] in [] has	used a multivariable	adjusted	study period	process of []	they state that
"gaming" of	led to risk	logistic regression model	outcome was	from 952/33 638	This team	their aim is to
clinical data, and	averse clinical	for 90 day mortality, with	then produced by	(2.8%) before the	response could	determine the
90 day	practice	a slope for calendar time	indirect	introduction of	have been	effect of the
	behaviour or	and an interaction	standardisation"	[] to 552/25		exposure on

postoperative	"gaming" of	between time pre-		905 (2.1%) after	mediated	the outcome
mortality."	data. However,	introduction versus post-		(fig 4). Therefore,	through []"	and conclude
	its introduction	introduction of [], in		we carried out		that the
	coincided with	addition to all of the <b>risk</b>		change point		exposure has
	a significant	adjustment variables. This		analysis which		not led to the
	reduction in 90	modelled a change in the		showed a steeper		outcome. The
	day mortality."	slope of mortality at the		decline in 90 day		main text
		point that [] was		mortality after		explains that
		introduced but no		the introduction		confounder
		immediate change in		of [] (P=0.03).		adjustment
		mortality."		The change point		was made
				analysis also		through
				found a		standardisatio
				significant effect		n and discuss
				<b>of</b> [] when it		possible
				was modelled as		mediators for
				an immediate		this
				shift in 90 day		relationship.
				mortality		
				(P=0.01) and		
				when it was		
				modelled as both		
				an immediate		
				shift and a		
				change in slope		
				(P=0.04)."		
"To assess the	"Little evidence	"We estimated one year	"Survival	"One year	"The lack of	Causal
effectiveness of	was found of a	net survival for each []	estimates for all	survival	consistent results	language is

the [] policy	direct impact	by sex, year of diagnosis	ages combined	improved for 20	between men	present in
initiatives <b>in</b>	of [] on one	(1996 to 2013), and	were age	of the 21 []	and women, as	both abstract
improving []	year survival,	deprivation category.	standardised	examined in	well as the lack of	and main text.
and reducing []	and no	Patients with a diagnosis	with the	women and 16 of	general patterns	The aim is to
in survival in	evidence for a	between 1996 and 2013	International	the 20 []	across [] types,	evaluate the
England."	reduction in []	had the potential to be	Cancer Survival	examined in	provide <b>little</b>	effectiveness
	in cancer	followed up for at least	Standard	men. [] For	evidence for any	of a policy on a
	survival. These	one year, so we used the	weights. [] We	these [], the	strong impact of	given
	findings	classic cohort approach.	used	average annual	the [] policies	outcome, they
	emphasise that	[] We estimated net	multivariable	absolute increase	on short term []	provide
	[] in survival	survival using the	linear regression	in one year age	survival. The	standardised
	remain a major	consistent nonparametric	to investigate the	standardised net	evidence is even	net survival
	public health	estimator defined by	survival patterns	survival was	weaker for their	and suggest to
	problem for a	Pohar-Perme."	for each [] and	often greater	impact on the	take action
	healthcare		by sex"	than 1% over the	[] in []	given the
	system			whole study	survival. []	findings.
	founded on			period"	These findings	
	equity."				should be taken	
					into	
					consideration by	
					[] policy makers	
					and inform	
					future	
					initiatives."	
<u> </u>						

To investigate whether improving adherence to [] interacts with the genetic predisposition to [] in relation to long term changes in [] and []."	"These data indicate that improving adherence to [] could attenuate the genetic association with []. Moreover, the beneficial effect of improved [] on [] was particularly pronounced in people at high genetic risk for [].	"We used multivariable generalized linear models with repeated measures analyses to assess the main associations of the [] and changes in the [] with change in []"	"We used multivariable models to adjust for []"	"In general, the [] was associated with increases in [] every four years: in the two cohorts combined, each additional [] was associated with 0.02 (SE 0.01) increase in [] and 0.05 (SE 0.03) kg increase in []"	"[] unmeasured or unknown confounders may also exist. Secondly, because adherence to [] was not randomized, the association between [] and [] may not imply a causal relation. Thirdly, the results could be underestimated by potential reverse causality. [] Our study provides reproducible evidence from two prospective cohorts of US men and women that improving	Assessing if improving adherence has an effect translates to an intervention that is being assessed. They conclude that there is a beneficial effect and suggest to take action. The main text discusses unmeasured confounding assumption and reverse causality. All of the above is consistent with a causal aim.
					men and women	

					association with	
"To assess the	"[] is an	"We calculated the time	"[] adjusting for	"A statistically	"More evidence	Causal
independent and	overlooked <b>risk</b>	to event from the date of	[]."	significantly	was needed to	language is
joint associations	factor for [],	enrollment to the date of		increased risk of	clarify whether	present in
of [] and []	as important as	[] incident or [] death,		incident [] was	the inverse	abstract and
with [] risk and	five major	death due to causes other		observed for the	association was	main text.
to explore the	lifestyle factors	than [], or the end of		eight diseases	causal or related	They identify
benefit of [] in	combined. In	cohort follow-up (31		and markers.	to []. [] the	that the
reducing the []	this study, []	December 2008),		Specifically, []	dose-response	exposure
risk associated	contributed to	whichever came first. We		was inversely	relation, the	contributes to
with [] and [].	more than one	used Cox proportional		associated with	exclusion of []	the outcome,
	fifth of the risk	hazards model to estimate		risk of incident	during recent	after adjusting

	for incident [] and more than one third of the risk for [] death. [] is associated with a nearly 40% reduction in the [] risk associated with []."	hazard ratios and 95% confidence intervals"		[] in a dose- response manner"	follow-up, and further adjustment for [] minimize the likelihood of reverse causation and lend support for causality. [] Our study uncovered a substantial impact of [] jointly on [] risk, which were equally as important as five lifestyle factors combined."	for covariates. They discuss dose-response relationship and reverse causality.
"To examine the association between [] and [] in later life, and determine whether the maintenance of [] will offset age related []"	"These results show that [] is not associated with the trajectory of [] in late life, but is associated with the acquisition of ability during	"The raw scores from the [] tests were standardised to a mean of 100 and a standard deviation of 15 to produce an [] scale. Age at testing was the number of years after participants' 60th birthdays. We modelled age in this form so that	"Because our sample were all born in the same year and tested at a similar age, a confounder for age at entry was not used. We modelled cognitive	"The typical intellectual engagement models for each domain are shown in table 2 and indicated an expected significant decline in []	"In our statistical models, we introduced possible confounders available from early life and life course, including []. We also controlled for []	The causal aim is suggested when the goal is to establish temporal relationship between exposure and outcome, describing the

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	the life course. Overall, findings suggest that high performing adults engage and those that engage more being protected from relative decline."	the intercept occurred at age 60 years rather than zero years, such that the calculation for the intercept would represent a realistic adult value rather than one extrapolated 64 years earlier. [] For each model, a probability value of P<0.05 was considered significant."	performance with a linear mixed model, as a combination of []."	with age, ranging from –1.09 to –1.31 standard points per year for the [] test and –0.77 to –1.69 for the [] test. [] None of the age×TIE interaction terms were significant, indicating that [] did not influence the trajectories of age decline."	associated with repeated testing. [] significant associations remained after adjustment for age, sex, and test practice effects. [] is an independent contributor to late life [] and has a unique effect over and above the effect of other life course variables. [] It is, however, impossible for a causal effect to	exposure as a trajectory, providing standardised and adjusted estimates and considering whether it is possible to infer a causal link.
"To evaluate the associations of a [] and [] with	"In this cohort study, [] were independently	"To test the <b>association</b> of [] and [] with [] we used Cox proportional	"Cox proportional hazards models	"In Cox proportional hazards analysis,	"The present study provides further support	The abstract describes that the goal is to
incident []."	associated with incident []. These results	hazards models. The duration of follow-up was calculated as time	included adjustment for age and sex for	the <b>risk of</b> [] was higher for those with []	that common [] are implicated in the development	establish a temporal relationship

	emphasise the benefit of entire populations adhering to [], independent of [] risk."	between the baseline assessment and the first event of either [] or 1 March 2016, which was the end of follow-up for the current data release. Participants who had a [] before a [] occurred were censored at the time of the respective event."	the lifestyle score models. For the models including the genetic score we additionally adjusted for the first 10 principal components of ancestry and genotyping batch."	(hazard ratio 1.20, 95% confidence interval 1.08 to 1.34) and [] (1.35, 1.21 to 1.50) compared with those with a low genetic risk score"	of []. [] The [] was also associated with [], which suggest that the effect of the [] on risk of incident [] might at least in part be mediated by []. The effects of [] might differ according to the cause of [], although some [] factors are shared between two or more causal factors"	between the exposure and the outcome and suggest to take action given the findings. The main text describes adjusting for covariates and discusses mediation.
"To determine the longitudinal association between [] and []."	"In older adults, a higher cumulative level of [] was associated with a higher likelihood of []. These	"We used a Cox proportional hazards model to evaluate the association between time-varying [], adjusting for time-varying covariates (updated at [] measurement), and the	"We selected covariates and potential mediators based on biological interest, current or previously observed	"Figure 1 shows that after multivariable adjustment for demographic, lifestyle, cardiovascular risks, dietary	"[] we excluded participants [] who reported baseline [] (to avoid reverse causality; n=195). [] The community	The abstract describes that the goal is to establish a temporal relationship between the exposure and

	findings	likelihood []. Time at risk	associations with	habits, and other	based design	the outcome
	support	was from the first []	[], and	[], higher []	improves	and suggest to
	guidelines for	measurement until the	meaningful	levels were	generalizability,	take action
	increased	first [] event or	changes in the	associated with a	and regular	given the
	dietary	censoring [] or the latest	exposure risk	lower likelihood	physical	findings. The
	consumption of	date of adjudicated	estimate (±5%).	of unhealthy	examinations	main text
	[] in older	follow-up in June 2015."	Minimal	ageing. Overall,	ensured that	describes
	adults."		adjustments	participants in	demographics	adjusting for
			included age and	the highest group	and other risk	covariates and
			sex.	of [] had an	factors were well	discusses
			Multivariable	18% (95%	measured, which	mediation,
			adjustments	confidence	may help to	residual
			additionally	interval 3% to	minimize	confounding
			included []. We	30%; P=0.001)	confounding.	and reverse
			used the	lower risk of	[]The possibility	causality. The
			potential	[].Findings were	of <b>residual</b>	statement in
			mediators to	not appreciably	confounding by	italic is a clear
			explore what	altered after	imprecisely	causal
			additional	adjustment for	measured or	statement.
			associations	potential	unknown factors	
			could exist to	mediators (not	also cannot be	
			these potential	shown)."	excluded for an	
			pathways."		observational	
					study. [] <i>Any</i>	
					unmeasured	
					confounders	
					would have to be	
					strongly	
					associated with	

					both the exposure and the outcome, conditional on all the variables already in the model. Thus, it seems unlikely that either poorly measured or unmeasured confounders could fully account for our findings."	
"To prospectively	"Among female	"Participants contributed	"Information on	"We observed a	"From a public health	Their aim is to establish a
evaluate the joint association of	nurses, both [] were	person time from the return of the baseline	potential confounders was	positive association	standpoint,	temporal
[] and [] with	associated with	questionnaire [] until the	assessed and	between	because 71% of	relationship
risk of type 2	a higher risk of	date of diagnosis of [],	updated every	duration of []	the joint effect	exposure-
diabetes risk, and	[]. The excess	death, loss to follow-up,	other year via the	and risk of [] in	could be	outcome, they
to quantitatively	risk of [] was	or the end of the follow-	questionnaires	both cohorts.	attributed to an	discuss
decompose this	higher than the	up period (30 June 2012	throughout	Compared with	[], our findings	adjusting for
joint association	addition of risk	for the NHS and 30 June	follow-up. This	women without	underscore the	confounders,
to []"	associated with	2013 for NHS II),	information	rotating night	importance of	provide excess
	each individual	whichever came first. We	included [] In	shift work, the	maintaining	risk and
	factor. These	used <b>multivariable time</b>	multivariable	pooled	[].Our findings	suggest to
	findings	dependent Cox	analysis, we	multivariable	suggest that	take action

most cases of [] could be prevented by [], and the benefits could be greater in []."	
prevented by [], and the benefits could be greater in []."    Intervals for the associations between [] alone and in combination with []."    Intervals for the associations between [] alone and in combination with []."    Intervals for the associations between [] alone and in combination with []."    Intervals for the associations between [] alone and in combination with [] we also examined the decomposition of the joint effect: the proportion (1.22), 1.28 (1.10 effect: the proportion (1.33 to 1.62) (P for trend <0.001) [] (table 3). [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
[], and the benefits could be greater in []."    [] associations between [] alone and in combination with []."    [] We also examined the decomposition of the joint effect: the proportion attributable to []"    [] were 1.11 (95% confidence interval 1.00 to 1.22), 1.28 (1.10 to 1.49), and 1.46 (1.33 to 1.62) (P for trend < 0.001) [] (table 3). []    The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to 1.40%	
benefits could be greater in []."  alone and in combination with []."  be larger in [] "  decomposition of the joint effect: the proportion attributable to []"  []"    The attributable proportions of the joint effect were 17.1% (95% confidence interval 1.00 to 1.22), 1.28 (1.10 to 1.49), and 1.46 proportion (1.33 to 1.62) (P for trend <0.001) [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to 1.22), 1.28 (1.10 to 1.22), 1.28	
be greater in []."    decomposition of the joint   1.22), 1.28 (1.10   1.33 to 1.62) (P   1.33 to 1.62) (P   1.34 to 1.46   1.35 to 1.62) (P   1.36 to 1.36	
I]."	
effect: the proportion (1.33 to 1.62) (P attributable to []" [](table 3). [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
proportion attributable to []"  [](table 3). [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
attributable to []"  for trend <0.001) [](table 3). [] The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
[]"  [](table 3). []  The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
The attributable proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
proportions of the joint effect were 17.1% (95% confidence interval 14.0% to	
the joint effect were 17.1% (95% confidence interval 14.0% to	
were 17.1% (95% confidence interval 14.0% to	
confidence interval 14.0% to	
interval 14.0% to	
20.8%) for []	
alone, 71.2%	
(66.9% to 75.8%)	
for [] alone, and	
11.3% (7.3% to	
17.3%) for their	
interaction."	
"To assess the "In this analysis "Patients were followed "We used an "Use of [], as "The findings The goal is t	)
association of nationwide from cohort entry to active compared with should be evaluate the	
between [] and registers from treatment cessation, comparator new- [], was interpreted in the association	

seven serious	two countries,	crossover to the other	user study design	associated with	context of	with the
adverse events	use of [], as	study drug [], the	and controlled	an increased risk	limitations of	exposure to
of current	compared with	outcome event, death,	for a wide range	of [] (hazard	observational	adverse events
concern."	[], was	emigration, or the end of	of potential	ratio 2.32, 95%	studies and the	which
concern.			confounders	confidence		translates into
	associated with	the study period (31		interval 1.37 to	uncertainty of	
	an increased	December 2016). We used	(patient		the <b>effect</b>	assessing
	risk of [], but	Cox proportional hazards	characteristics	3.91) and []	estimates. []	safety. They
	not with other	regression to calculate	that might be	(2.14, 1.01 to	Therefore, the	discuss
	serious <b>adverse</b>	hazard ratios, analysing	associated with	4.52) but not	studies could	adjusting for
	events of	each outcome	both the	with [] (1.11,	suffer from	confounding,
	current	independently. The	outcome and the	0.93 to 1.33), []	compromised	resort to
	concern."	absolute risk difference	decision to	(0.69, 0.45 to	confounding	propensity
		was calculated as hazard	initiate a drug)	1.05), [] (0.89,	control, as	score
		ratio-1 multiplied by the	through a non-	0.67 to 1.19), []	indicated by the	matching and
		rate in the comparator	parsimonious	(0.99,	imbalance in []	consider
		group."	propensity score	0.71to 1.38), or	at baseline	residual
			model to	[] (1.16, 0.64 to	between users of	confounding.
			minimise the risk	2.12)."	[] versus	
			of bias, including		comparators,	
			confounding by		even after	
			indication [].		propensity score	
			We estimated		matching []	
			propensity		Finally, residual	
			scores by using		and unmeasured	
			logistic		confounding	
			regression for the		affecting the	
			probability of []		findings in our	
			conditional on		study cannot be	
			the status of 66		ruled out."	
			514143 01 30			

covariates,
defined and
selected a priori,
including
sociodemographi
c characteristics,
comorbidities,
comedications,
and healthcare
utilisation [] We
matched [] and
[] users (1:1
ratio, by country)
according to
propensity score,
by using the
nearest
neighbour
matching
algorithm (caliper
width 0.2 of the
standard
deviation of the
logit score).
Analyses were
performed in a
pooled dataset of
the two
countries."

"To determine	**In results:	"For all outcome	"We examined	"Patients []	"A confirmatory	The abstract
whether patients	"Per 100 000	comparisons we report	hospital type and	were <b>less likely</b>	time-to-event	and main text
[] have <b>fewer</b>	patients, there	unadjusted and adjusted	several	to have follow-up	analysis in a	use causal
[] and higher	were 2999	odds ratios (with 95%	characteristics of	with a physician	propensity score	language: they
rates of [] than	fewer follow-	confidence intervals).	patients and	within seven days	matched cohort	discuss risk
patients [].	up	Adjusted odds ratios were	admissions: year	(36.3% v 47.8%,	(see	attributed to
	appointments	obtained with logistic	of Charlson	adjusted odds	supplementary	the exposure,
	within 14 days,	regression models	comorbidity	ratio 0.61, 95%	appendix table 5)	provide
	26 excess	estimated using	index score,	confidence	showed	adjusted
	deaths, []	generalised estimating	socioeconomic	interval 0.60 to	consistent results	estimates
	attributable to	equations methods and	status (measured	0.62) and 14 days	(death or	using
	[]."	including all measured	using median	(59.5% v 68.7%,	readmission	propensity
	"Patients []	patient and hospital	neighbourhood	0.65, 0.64 to	hazard ratio 1.08,	score
	are less likely	characteristics."	income), length	0.66). []	95% confidence	matching and
	to have [] and		of hospital stay,	Patients	interval 1.07 to	discuss
	are at higher		arrival by	discharged	1.09). [] The	residual
	risk of []."		ambulance,	during the	differences in	confounding.
			diagnosis,	holiday period	outcomes <b>could</b>	
			discharged with	were at	not be explained	
			home support or	increased risk of	<b>by</b> observed	
			against medical	death or	hospital or	
			advice, and	readmission	patient	
			previous	within 30 days	characteristics,	
			healthcare usage	(25.9% v 24.7%,	including	
			(emergency	1.09, 1.07 to	admission	
			department	1.10). This was	diagnosis. [] the	
			visits, hospital	explained by an	possibility of	
			stays, outpatient	increased risk of	confounding due	
			visits, home care	return to the	to unmeasured	

			visits). hospital discharge, age, sex, rural residence, "	emergency department (24.3% v 23.0%, 1.09, 1.07 to 1.10), rehospitalisation (11.8% v 11.4%, 1.06, 1.04 to 1.08), and death (1.5% v 1.5%, 1.06, 1.02 to 1.10) within 30 days"	differences remains"	
"To investigate	"Use of [] is	"We calculated age	"Adjusted	"The age	"The data linkage	When
the <b>association</b>	associated with	standardised incidence	incidence rate	adjusted	study design also	assessing the
between [] and	a reduction in	rates of [] per 100 000	ratios (referred	incidence of []	enabled us to	exposure-
overall and	[] risk in	person years, using the	to here as	was highest in	adjust for several	outcome
specific types of	women of	age distribution of the	relative risks) and	women who	important	relationship,
[]."	reproductive	cohort as standard. Risk of	their surrounding	were never users	confounding	they provide
	age—an <b>effect</b>	[] among users of the	95% confidence	of [] (7.5 per	variables. We	standardised
	related to	different product groups	intervals were	100 000 person	were not able to	estimates,
	duration of	was analysed by a Poisson	calculated for	years; table 2).	adjust for some	discuss
	<b>use</b> , which	regression model in SAS	each model, with	Among ever	factors, such as	residual
	diminishes	version 9.3 (SAS Institute).	never users as	users of [],	[] Our findings,	confounding,
	after stopping	[] We calculated the	the reference	reduction in the	therefore, could	dose-response
	use. These data	population prevented	group. The	age standardised	be subject to	and provide
	suggest no	fraction (population	adjusted models	absolute rate of	residual	attributable
	protective	prevented fraction =	included the	[] was 3.2 per	confounding."	fraction.

	effect from []."	prevalence <sub>exposure</sub> (1-relative risk)) associated with ever use of [] by using the relative risk of never use versus ever use of []. The population prevented fraction is the proportion (expressed as a percentage) of the [] in the cohort that has been prevented by ever use of []."	following time varying covariates []"	100 000 person years. Overall, ever users of [] had a reduced risk of [] compared with never users (relative risk 0.66 (95% confidence interval 0.58 to 0.76)). [] use of [] prevented 21% of [] in the study population"		
"To assess whether [] is	"In participants older than 74	"To prevent survivor bias and covariate	"We explored the variables	"In participants without [], the	"To prevent residual	They use causal
associated with a	years without	measurement bias, we	associated with	hazard ratios for	confounding we	language and
reduction in []	[], [] was	selected a "new users	[] to determine	[] were 0.94	performed	causal
and mortality in	not associated	design" over "all [] users.	candidate	(95% confidence	additional	methods. To
old and very old	with a	[] Using Cox proportional	variables for the	interval 0.86 to	regression	estimate the
adults with and	reduction in	hazard regression models	propensity score	1.04) for [] and	adjustments after	effect of the
without []."	[] or in all-	adjusted by propensity	of []. From	0.98 (0.91 to	adjustment of	exposure on
	cause	score, we calculated the	SIDIAPQ we	1.05) for all cause	propensity score.	the outcome.
	mortality, even	hazard ratios of statin use	obtained data on	mortality in 75-	Variables that	They use
	when the	for the outcome events.	age, sex, []	84 year olds. []	remained	propensity
	incidence of []	Participants were	Because of non-	The one year	imbalanced after	score methods
	was	censored at the date of	random	number needed	propensity score	to adjust for

		tue meters from CIDIADO - :	tura atura a unt	4- 44 1C4	a aliakwa a wak :	fd::
	statistically	transfer from SIDIAPQ or	treatment	to treat was 164	adjustment were	confounding,
	significantly	at the end of the study	allocation, we	for [] and 306	also included in	provided a
	higher than the	period. "	used a logistic	for all cause	the models. []	NNT and
	risk thresholds		model based on	mortality."	Despite these	consider
1.	proposed for		potential		efforts, we	residual
	[]. In the		confounding		acknowledge	confounding.
	presence of		covariates to		that some	
	[], [] was		calculate the		residual	
5	statistically		propensity score		confounding	
	significantly		of []. We		might exist."	
	associated with		calculated the			
r	reductions in		propensity score			
t	the incidence		separately for			
	of [] and in		participants with			
	all-cause		and without []			
1	mortality. This		and also within			
	effect		each age group,			
	decreased after		and standardised			
	age 85 years		differences			
	and		before and after			
	disappeared in		adjustment for			
l r	nonagenarians.		propensity score.			
,	,		Variables with			
			standardised			
			differences < 0.10			
			were considered			
			to be <b>well</b>			
			balanced."			

role of [...] in the association

					between [] and increased []"	
"To assess	"[] as second	"The study cohort was	"[] exposed and	"Compared with	"Based on a post-	The aim is to
whether adding	line drugs are	formed by identifying all	reference	the use of [],	hoc analysis, the	assess the
or switching to	associated with	subjects from the base	subjects were	adding or	findings of the	effect of the
[] is associated	an increased	cohort of [] initiators	matched on	switching to []	primary analysis	intervention
with an increased	risk of []	who subsequently added	high-dimensional	was associated	on [] unlikely to	strategy of
risk of [],	compared with	or switched to a [] as	propensity score.	with an increased	be the result of	adding or
compared with	remaining on	second line treatment.	The high-	risk of [] (7.8 v	an <b>unmeasured</b>	switching to a
remaining on []	[]. Continuing	Patients who added or	dimensional	6.2 per 1000	confounder	particular
in patients with	[] when	switched to other []	propensity score	person years,	under most	drug, they
[]."	introducing []	were censored. For each	method	hazard ratio 1.26,	plausible	emulate a
	appears to be	patient adding or	empirically	95% confidence	exposure-	target trial,
	safer than	switching to a [], we	selects covariates	interval 1.01 to	confounder and	use propensity
	switching."	identified a matched	based on their	1.56), all cause	confounder-	score
		reference patient who	prevalence and	mortality (27.3 v	outcome	matching,
		also was a [] initiator but	potential for	21.5, 1.28, 1.15	associations. []	discuss
		remained on metformin,	confounding. For	to 1.44), and []	For our study, we	residual
		using a prevalent new-	each member of	(5.5 v 0.7, 7.60,	used the recently	confounding
		user design. [] we	each matched	4.64 to 12.44).	developed	and conclude
		constructed a Cox	set, we identified	There was also a	prevalent new-	that the
		proportional hazards	all available	trend towards	user design. To	strategy is
		regression model for each	information from	increased risks of	emulate the	safe.
		outcome that estimated	seven data	[] (6.7 v 5.5,	randomised	
		the hazard ratio and the	dimensions (five	1.24, 0.99 to	controlled trial,	
		95% confidence intervals	dimensions from	1.56) and [] (9.4	this design	
		for [] versus []."	the CPRD: drug	v 8.1, 1.18, 0.98	identifies (at the	
			prescriptions,	to 1.43)."	doctor visit that	

			procedures,		led to the patient	
			diagnoses,		on [] adding or	
			disease history,		being switched to	
			and		[]) a	
			administrative		comparable	
			information; two		· ·	
			dimensions form		patient with the	
					same history of	
			the HES:		[] use and of	
			diagnoses and		other	
			procedures) in		characteristics,	
			the one year		but who on that	
			period before the		visit continued	
			date of the		on []. [] owing	
			matched set. We		to its	
			then applied		observational	
			conditional		nature there is	
			logistic		the potential for	
			regression to		residual	
			estimate the		confounding."	
			propensity of			
			receiving a []			
			drug, thereby			
			considering the			
			500 most likely			
			confounders."			
"To investigate	"Overall, []	"We used a new-user	"Confounding	"In patients with	"Although many	The aim is to
the associations	was found to	design to capture all	factors. It is	[], [] was	adjustments have	assess the
between [] and	be the <b>safest</b>	events occurring after	possible that	associated with a	been done using	safety of a

risks of []	drug, with	starting treatment and to	patients at higher	lower risk of []	the data available	drug and they
compared []."	reduced risks	reduce the impact of	risk of [] may	than []	on the existing	use different
compared [].		confounding. []	preferentially be	(adjusted hazard	databases, there	strategies to
	[] compared	<del>-</del>		· -	· ·	_
	with []. []	Incidence rates for each	prescribed []	ratio 0.66, 95%	is a possibility of	adjust for
	and low dose	outcome were calculated	rather than [],	confidence	unmeasured	confounding,
	[] were,	based on the numbers	so all analyses	interval 0.54 to	confounding or	including
	however,	with the outcome and the	were adjusted	0.79). []Table 5	confounding by	propensity
	associated with	person years of follow-up,	for demographic	shows the	indication. []	scores,
	increased risks	and were age and sex	and clinical	number needed	Although we	provide NNT
	of all cause	standardised for each	variables, either	to treat or	used a	and discuss
	mortality	drug. To estimate the risks	because they	number needed	proportional	the
	compared with	associated with each [],	may have been	to harm to	hazard model	unmeasured
	[]."	an outcome specific Cox	used as	measure the	adjusting for all	confounding
		model containing all	indicators for	relative benefits	available	assumption.
		confounding factors was	prescribing a	or risks of [] in	confounding	
		used, with [] as a	specific [] or	comparison with	factors, we also	
		primary reference."	because they	[]."	undertook a	
			have possible		sensitivity	
			associations with		analysis using the	
			increased risk of		propensity score	
			[]. We similarly		method and	
			adjusted for		obtained very	
			comorbidities,		similar results."	
			previous events,			
			and drugs also			
			used as			
			indicators or			
			associated with			
			increased risks."			
			ilici easeu lisks.			

"To examine the	"Our study	"To evaluate the	"We first	"In multivariable	"Several factors	They provide
association	indicates that	association between []	evaluated	analyses (model	could contribute	adjusted
between [] and	adherence to a	and [], we calculated	associations with	2), [] had a	to the weak	estimates,
the <b>risk of</b>	[] is	relative risks and 95%	[] by categories	relative risk of	mediation effect	discuss
developing []."	associated with	confidence intervals using	of each low risk	3.10 (95%	of [] in the	mediation and
acveroping [].	a substantially	multivariable log-binomial	factor, adjusting	confidence	association	residual
	reduced risk of	regression models with	for []."	interval 2.69 to	between [] and	confounding
	[]. These	generalized estimating		3.57) of [],	[] risk. []	and suggest to
	findings	equations and specified an		compared with	Another	take action
	highlight the	exchangeable correlation		[]."	limitation, as in	given the
	potential	structure."		[].	any observational	findings.
	benefits of				study, is that we	
	implementing				cannot exclude	
	[]				the possibility of	
	interventions				uncontrolled	
	to curb the risk				confounding by	
	of []."				[] or residual	
					confounding. []	
					Our findings	
					highlight the	
					potentially	
					critical role of []	
					in the <b>etiology</b> of	
					[] and lend	
					support to []	
					based	
					intervention	
					strategies for	
					reducing []."	
					0. 1	

"To determine rates of [] and all cause mortality in patients with [] compared to patients with [] and without []."	"Patients with [] remain at higher risk of [] than patients without []. The risk is increased even in those in whom [] is not documented. Guidelines should be updated to advocate continued use of [] in patients with []"	"We carried out two retrospective cohort studies to determine incidence rates of [] (primary outcome) and all cause mortality (secondary outcome) in patients with [] versus randomly selected matched controls with []. We calculated crude and adjusted incidence rate ratios comparing the incidence of []"	"Poisson regression was used to calculate adjusted incidence rate ratios, adjusting for the baseline covariates []"	"The crude incidence rate ratio was 0.73 (95% confidence interval 0.65 to 0.81, P<0.001). Adjusting for potential confounders [] made little difference to the incidence rate ratio: 0.76 (95% confidence interval 0.67 to 0.85, P<0.001)"	"In light of the evidence produced by this study, it is recommended that clinical guidelines and schemes designed to incentivise appropriate management [] are updated"	Even though the use of causal language is not explicit, they compare rates of the condition in the different groups that have been matched, provide adjusted estimates and suggest to update guidelines to reflect the findings.
"To examine the association between [] at [] and []."	"[] during the period [] is safe with respect to the risk of []."	"We estimated odds ratios of [] and [] and associated Wald type two sided 95% confidence intervals by logistic regression. For [] and [], we calculated hazard ratios and associated	"[] to adjust for potential confounding due to temporal trends, we included []. [] are well established risk	"In analyses without covariate adjustment (model 1), [] was associated with an increased risk of [] (hazard ratio 1.69	"[] is not causally related to increased risks (). Instead, our results suggest other factors underlying and confounding the	The abstract suggests a causal aim when describing the intention to establish a temporal

		Wald type two sided 95% confidence intervals from Cox regression models, which allow for detailed adjustment for censoring affecting the length of follow-up of each child. Days since birth was used as the underlying time scale. Each child was followed from birth until a diagnosis of the outcome, death, or end of follow-up at 31 December 2014, whichever event occurred first. "	factors for []. [] All estimates were calculated by models with increasing complexity, beginning with models without adjustment for covariates (model 1), followed by models adjusting for all included potentially confounding covariates (model 2)."	(95% confidence interval 1.18 to 2.41)) and [] (2.14 (1.39 to 3.30); fig 2). After covariate adjustment (model 2), [] was only associated with an increased risk of [] (adjusted hazard ratio 1.66 (1.06 to 2.59); fig 2)."	associations between []. Furthermore, although our results suggest that [] are not causally associated [] could be a causal factor for other outcomes. [] although the present study did not find a causal link [], replication of the results is imperative."	relationship between the exposure and the outcome and concluding that the exposure is safe. The main text uses causal language explicitly when describing the strategies to control for confounding and concluding that a causal relationship was discarded.
"To assess the association of [] and risk factors for [] with [] at []."	"The independent association between [] and [] in [] is comparable	"We used a generalised additive mixed model (GAMM) to estimate [], with [] as fixed effect predictors and [] as random effect at the	"We considered [] as potential confounders."		"As our analyses relied on cross sectional data, these findings should be interpreted	The abstract suggests a causal aim when describing the intention to

in strongth and	intercent and [ ] class		acutiously and	actablish a
in strength and	intercept and [] slope.		cautiously and	establish a
consistency	[] We computed 95%		should not be	temporal
with those for	confidence intervals from		considered as	relationship
[]. The results	the uncertainty of the		causal estimates	between the
of this study	estimated smoothing		of the impact of	exposure and
suggest that	function. We computed		[] on []. []	the outcome
tackling all	the <b>number of years of</b>		Given that the	and
these risk	functioning lost from the		present study is	concluding
factors might	mixed model predictions"		based on	that the link is
substantially			observational	comparable to
increase life			data, our study	those for other
years spent in			informs about	established
good physical			associations but	risk factors. It
functioning."			cannot provide	is important to
			evidence of	note that In
			causality."	the abstract
				the design of
				the study is
				described as
				"Multi-cohort
				population
				based study".
				However the
				method and
				discussion
				refer to a
				"cross
				sectional"
				design that

						limits the possibility to establish causal links.
"To determine outcomes and safety of [] for [], due to [], in routine clinical practice."	"In routine clinical practice, [] for patients with [] is at least as effective and safe as in the setting of a randomised controlled trial."	"We used regression models to compare baseline characteristics and outcomes in patients [] with those in the [] intervention and control arms. The effect of [] on [] at 90 days in patients [] compared with [] was expressed as an adjusted common odds ratio, derived from multivariable ordinal logistic regression (shift analysis)."	"We adjusted for []"	"After adjustment for [], the shift towards [] was significant for patients [] compared with those [] intervention arm (adjusted common odds ratio 1.30, 95% confidence interval 1.02 to 1.67; P=0.03) and control arm (1.85, 1.64 to 2.34; P<0.01; fig 1)."	"The results of our study might have important implications for the future of [] for []. [] is at least as effective and safe as in the setting of a randomised controlled trial."	The abstract and main text point to a causal aim as the intention is to assess the safety of an exposure in relation to an outcome and the conclusion is that not only is safe but also effective.
"To investigate whether [] is associated with an increased risk of []."	"In a propensity score matched cohort, [] use was associated	"Cox proportional hazards regression, with days since start of treatment as the time scale, was used to estimate the hazard ratio	"We used two major strategies to control for confounding. To account for	"There was an increased risk of [] associated with [] (hazard ratio 1.66; 95%	"An important concern in any observational study is the possibility of	Both the abstract and main text use causal language and

	with an	for [], comparing	potential	confidence	confounding. We	causal
	increased risk	episodes of [] and []	confounding by	interval 1.12 to	used an active	methods
	of []. This	use."	indication [],	2.46). This	comparator to	including
	association		we used an	increase	limit confounding	propensity
	appeared to be		active	corresponded to	by factors	score
	largely <b>driven</b>		comparator	an absolute	associated with	matching.
	by []."		design, [] To	difference of 82	[], including	They discuss
			control for	(95% confidence	confounding by	the possibility
			potential	interval 15 to	indication, and	of residual
			confounding	181) cases of []	propensity score	confounding
			from differences	per 1 million	matching derived	mainly
			in baseline health	treatment	from a range of	because of the
			status, we used a	episodes in the	covariates.	observational
			propensity score	60 day risk	Despite this, the	nature of the
			matched design,	period."	possibility of	study but also
			taking into		residual	suggest
			account		confounding (for	possible
			demographic		example, due to	confounders
			characteristics,		[]) cannot	missed.
			medical history,		completely be	
			[]."		ruled out."	
"To examine the	"[] was	"We did a population	"Using the full	"After	"Although we	Both the
risks of [] in	associated with	based matched cohort	hospital history	adjustment for	and adjusted the	abstract and
patients with []	increased risks	study based on routinely	(inpatient and	the covariables,	analyses for a	main text
and in a general	of []. [] may	and prospectively	outpatient	[] was	wide range of	describe the
population	be an	collected data. [] We	diagnoses)	associated with	potential	exposure-
comparison	important risk	calculated the 0-1 year,	recorded in the	[] (adjusted	confounders	outcome
cohort."	factor for []."	>1-5 years, and >5-19	DNPR before the	hazard ratio 1.49,	identified a priori	relation in a

		years cumulative incidence per 1000 people for each outcome, accounting for the competing risk of death. Correspondingly, we used matching factors stratified (conditional) Cox proportional hazards regression to estimate hazard ratios, adjusting for the categorical comorbidities listed above as covariables."	index date, we obtained information on the following [] risk factors: []"	95% confidence interval 1.36 to 1.64), [] (2.26, 2.11 to 2.41), and [] (1.94, 1.68 to 2.23), as well as [] (1.59, 1.45 to 1.74) and [] (1.25, 1.16 to 1.36) (fig 2). We found no association with [] (adjusted hazard ratio 1.12, 0.96 to 1.30) or [] (1.04, 0.93 to 1.16).	on the basis of excisting literature, we cannot exclude influence of unknown or residual confounding, for example, by []" ** Typos copied as in the published version	matched cohort. They discuss the possibility of residual confounding and suggest possible confounders missed. All of these elements point to a causal aim.
"To determine if [] a critical determinant of [] is and []."	"[] does not have a clinically important association with [] or []."	"We assessed the effect of [] compared with [], using multivariable regression. Modified Park's tests were used to determine the appropriate regression models (gamma, Poisson, and logistic) for discrete [] outcomes. We also assessed the effect of []	"In all of our primary analyses we adjusted for the following key confounders:	"Table 2 shows that there was no strong evidence of a clinically important association of [] and [] with [] or []."	"We recognise that we assessed multiple associations and the isolated positive association of [] and [] may reflect a chance finding, particularly as	Both abstract and main text use causal language and explain that the aim is to identify whether the exposure is a cause of the outcome and

	on an individual's repeat		there was no	after adjusting
	[] outcomes scores. []		consistent	for potential
	Linear mixed effects		association with	confounders
	models were fitted with		[] at any other	conclude that
	time as a fixed effect and		[]. [] We	it is not, given
	a random effect of		would suggest	that they only
	subject."		the overall	identify one
			impact would be	positive
			potentially small	association
			as there was no	when multiple
			clinically	were assessed
			important	and consider it
			impact on [] at	to be by
			any age. We	chance.
			acknowledge	
			that [] may	
			have attenuated	
			to the null any	
			potential	
			detrimental	
			effect of [] on	
			[] outcomes,	
			but this would	
			further support	
			that [] does not	
			have permanent	
			consequences for	
			[]."	
			I I	

"To determine if [] is associated	"[] is  associated with	"We calculated odds ratios for each outcome []	"Based on a priori knowledge,	"In the 14 days after [], [] is	"We saw minimal differences in the	The elements that point to a
with an increased	a greater risk	within 14 days of []	we considered	associated with	odds ratios for	causal aim:
risk of [] in the	of []	comparing each []	the following	the highest odds	[]. [] analyses	confounder
general	compared with	adjusting for potential	variables as	of [] (adjusted	using	adjustment by
population."	[], but not a	confounders using logistic	potential	odds ratio 1.72,	multivariable	regression
	greater risk of	regression."	confounders of	95% confidence	regression and	models,
	death. The		the relation	interval 1.31 to	inverse	sensitivity
	relative risk		between [] and	2.24) and []	probability	analysis using
	increase is		[]: []. All	(2.27, 1.49 to	treatment	inverse
	similar across		covariates other	3.45) of all the	weighting	probability of
	population		than sex and	[] investigated.	approaches []	treatment
	groups, but the		ethnicity were	[] The odds of	were consistent.	weighting and
	higher baseline		updated over	death within 14	[] our study	discussing
	risk among		time. [] We	days of [] were	also had greater	residual
	those []		initially adjusted	similar to [] for	ability to adjust	confounding.
	translates into		for sex and age	[] (0.90, 0.76 to	for detailed	
	higher absolute		only, and then	1.07) and the	characteristics,	
	risks of [] in		fitted an adjusted	other []."	such as [],	
	these groups."		model using []."		which are likely	
					to have reduced	
					residual	
					confounding."	
"To evaluate the	"In this large	"For each comparison and	"We considered	"Table 3 shows	"Randomized	Both abstract
[] <b>safety</b> of [],	cohort study,	for all outcomes, we	the following	that after	controlled trials	and main text
in direct	[] was	calculated unadjusted and	covariates as	propensity score	are the best way	use causal
comparisons with	associated with	propensity score matched	potential	matching, for []	to assess drug	language and
	a <b>lower risk</b> of	number of events,	confounders: []	primary	efficacy [] On	they are
	l			l		

[], as used in	[] I and with a	incidence rates, and	To control for	outcome, the	the other hand,	explicit to
routine practice."	similar risk of	hazard ratios with 95%	imbalances in	number of events	strict inclusion	state that the
	[] in direct	confidence intervals."	patient	for [] and the	and exclusion	aim is to
	comparisons		characteristics	[] comparator	criteria and	evaluate
	with [] as		between cohorts,	were 91 and 124	rigorous safety	safety of the
	used in routine		we calculated	respectively (8.9	monitoring limit	exposure and
	care."		exposure	v 12.8 per 1000	the	use causal
	care.		propensity	person years;	generalizability	methods
			scores as the	hazard ratio 0.70,	of randomized	(propensity
			predicted	95% confidence	controlled trial	score
			probability of	interval 0.54 to	results. Our study	matching).
			receiving the	0.92) in cohort 1;	[] allowing	They discuss
			treatment of		better	•
				94 and 148 (7.5 v		why the design
			interest (ie, [] v	12.4; 0.61, 0.47	generalizability	was
			each	to 0.78) in cohort	to routine care	observational
			comparator)	2; and 77 and	[] provides data	and consider
			conditional upon	154 (7.3 v 14.4;	from direct	that due to
			the subjects'	0.51, 0.38 to	comparisons. []	this nature,
			baseline	0.67) in cohort	while we used	residual
			covariates using	3."	propensity score	confounding
			three separate		matching to	cannot be
			multivariable		balance more	excluded that
			logistic		than 100 baseline	may have led
			regression		characteristics	to downtown
			models. All		between the	of conclusion
			variables were		groups, residual	which is
			included and no		confounding by	phrased more
			further selection		some	in terms of
			was conducted.		unmeasured	association.

			We 1:1 matched cohorts on their propensity score using a caliper width equal to 0.2 of the standard deviation of the logit of the propensity score."		characteristic(s) cannot be ruled out. "	
INCONSISTENT						
"To evaluate the relation between [] and development of []"	"[] was associated with an increased risk of [] that was mediated by []. Systematically addressing [] may be an important public health strategy to reduce the incidence of []	"We calculated the hazard ratios for the relation of [] to the risk of MRSA using Cox proportional hazard models. [] We also calculated the absolute risk difference. [] We performed mediation analyses to examine the extent to which the effect of [] on the risk of [] was through []. Using marginal structural models we then estimated the natural	"We performed a matched cohort study [] matched on age (one year either way), sex, and study entry time (within one year either way). Such comparators were chosen to further ensure the comparability [] In the multivariable Cox	"The matched and multivariable adjusted hazard ratios for patients with [] were 1.69 (1.51 to 1.90) for [] and 1.26 (1.12 to 1.40) for []."	"Our GP practice based dataset could have missed the detection of some inpatient cases of []; however, these potential non-differential misclassifications would have biased our results towards the null, rendering our	The aim in the abstract limits to state that they are exploring the relationship of exposure and outcome. However, in the abstract conclusion and full text they describe mediation analysis,

	among patients wih []."	direct effect [] and the natural indirect effect [] while adjusting for the same confounding variables"	model we adjusted for []."		findings conservative"	identifying direct and indirect effects and use marginal structural models which are part of the causal toolkit.
"To quantify the effects of varying []"	"[] is  associated with a large increase in [] among [] patients. The data from this study suggest that [] rather than [] is more strongly associated with []"	"For adjusted analysis of time until [] we used Cox proportional hazards models."	"Adjusted models included []"	"Each additional [] increased the rate of [] by 70.7% (95% confidence interval 54.6% to 88.4%) before adjustment and increased the hazard of [] by 44.0% (40.8% to 47.2%, P<0.001) after adjusting for covariates."	"To determine the extent to which strong unobserved confounding might explain the observed association, we included this synthetic confounder in a Cox model. [] As part of a sensitivity analysis, we constructed models that removed potential	The aim uses causal language and they provided adjusted estimates. However the conclusion is phrased in terms of association. They do use sensitivity analysis to test for residual confounding and it might be that due to concern of

					confounders.	unmeasured confounding they decided to be conservative with the conclusions.
"To evaluate the long term association between []"	"Widespread utilisation of [] may be contributing to long term increased risk of []. The potential for [] should be considered when []."	"We conducted Poisson regression analyses using person years as observations."	"We included several variables as known confounders or effect modifiers in the relation between. []The final fully adjusted model adjusted for []"	"After adjustment for covariates, the rate ratio was [] indicating that during the entire period of follow- up the risk of [] was 21% higher during [] than at other times."	"The registered active [] population is generally representative of the UK population in terms of age, sex, and regional distribution"	The aim is phrased in terms of association but the conclusion uses causal language and they discuss confounder adjustment.
"To investigate the <b>association</b> of []"	"The shape of the association between [] and [] was determined by [].This finding suggests that the [] may be largely	"We used Cox proportional hazards models to estimate hazard ratios and 95% confidence intervals. We stratified the analysis by age in months and calendar year of the questionnaire cycle."	"For the main analysis, we used [] measured at baseline to minimize the effect of underlying diseases on mortality [] In multivariable	"A multivariable adjusted model showed a positive association between [] and all cause mortality, whereas [] showed a U	"Our findings remained robust in several sensitivity analyses [] we cannot entirely rule out the possibility of unmeasured or unknown	The aim is stated in terms of association but they adjust for confounders, discuss unmeasured confounding and conclude

	explained by []"		models, we adjusted for potential confounders including []"	shaped association with all cause mortality. In a mutually adjusted model including both [] and [] we consistently observed a strong positive association between [] and all cause mortality."	confounding factors that may account for the associations observed in this study."	that the outcome can be 'largely explained' by the exposure.
"To examine the associations of []"	"This association could be explained by the finding that [] These results emphasise the importance of revisiting [] or establishing specific guidelines for	"We performed Cox models with penalised splines"	"In final Cox models with penalised splines, we made adjustments for: []"	"[A]fter adjustment for confounding factors, the U shaped association with []"		The aim is phrased in terms of association but they provide adjusted estimates, discuss confounding and conclude that the exposure

	management among []"				could explain the outcome and suggest to take actions given the findings.
"To estimate long term survival, health, and educational/socia I functioning in patients with []"	"[] had no substantial effect on []"	"We calculated mortality rate ratios and incidence rate ratios as measures of relative risk."	"For each [] patient, we used the Danish Civil Registration System and the DNPR to identify all Danish residents with the same sex and date of birth as the patient who had not tested positive [] and who met the study's inclusion and exclusion criteria []. From this population, we extracted 10 people at random for each patient. People in	Patients and members of the comparison cohort were well matched with respect to [] Mortality was not higher among patients in the [] cohort"	The abstract states that they aim is to estimate survival but they use matching and conclude that the exposure has no 'substantial effect' on the outcome.

			the population comparison cohort were assigned the same date of study inclusion as [] patients to whom they were matched."			
"To compare the risk of []"	"Although residual confounding cannot be excluded, this finding deserves consideration when [] is used for []"	"We estimated the crude hazard ratio of [] using Cox proportional hazard regression, and the adjusted hazard ratio was obtained using propensity score matching"	"We identified potential confounders that were plausibly associated with both []based on clinical knowledge [] In the context of this study, the propensity score is the probability of receiving [] as opposed to [], given the baseline characteristics. Patients who received []	"The crude hazard ratio of death in the unmatched cohort was 1.51 (95% confidence interval 1.22 to 1.85) and the adjusted hazard ratio in the matched cohort was 1.50 (1.14 to 1.96)"	"Comparison of the baseline characteristics in the unmatched cohort provided little evidence of confounding [] it is unlikely that a few additional unmeasured variables can explain a 50% increase in the risk independent of all other confounder and proxies of confounders that	The abstract suggests that they aim is comparison of the risks but does not explicitly use causal language. They do adjust for confounding, using propensity score matching, and discussed unmeasured confounding which are

			were matched to patients who [] using a 1:1 nearest neighbor matching algorithm with a caliper of 0.2 of the standard deviation of the propensity score on the logit scale. Covariate balance between the two groups was assessed after matching, and we considered an absolute standardized difference less		are adjusted for in our study."	applied when aiming for causal inference.
			absolute standardized			
"To determine whether [] is associated with []"	"[] was independently associated With []"	"We fitted both a mixed effect logistic regression model (in which the outcome was defined as	"We examined the relation between [] and	"The rate of distinct criteria met per year increased by 24%	"We did a sensitivity analysis using propensity score	The aim uses causal language but the conclusion

		dichotomous [] and the Prentice, Williams, and Peterson (PWP) model"	[] adjusted for"	if a patient had been admitted to hospital (hazard ratio 1.24, 95% confidence interval 1.20 to 1.28) when controlled for the other covariates"	matching to assess whether the association between [] and [] could be due to unmeasured confounders [] Although we adjusted for a range of characteristics of patients, as with any observational study potential exists for unmeasured confounding, which may partly or fully explain the relation between []"	is phrased in terms of association. They provide adjusted estimates, use propensity score as sensitivity analysis and discuss unmeasured confounders. The only reason to present a conservative conclusion seems to be the observational nature of the study.
"To investigate associations between [] and to analyse the	"Risks of [] are inversely associated with []"	"We used multivariable Cox regression analysis to compare the rates of [] and []. "	"Confounders included in the final models were based on the literature or	"Compared with [], [] had increased hazard ratios of []"	"We believe that our findings are widely applicable and provide justification for	The aim suggests a causal aim because they evaluate the

effect of changes []"			statistical significance (P<0.10). The full model included []"		[] and continuing []"	impact of changing the exposure which makes it an intervention and they provide estimates adjusted for confounders. The conclusion is phrased in terms of association.
"To estimate the rates of []"	"In cases of [], approximately [] will become [], of which a third will have []."	"We present denominators where data for the secondary outcome are missing. We defined the population attributable fraction as (Re–Run)/Re=(RR–1)/RR, calculated using Stata. To test the robustness of our findings, we did a sensitivity analysis."	"We compared the demographic and clinical variables of []. We used the binomial Wilson score to calculate confidence intervals of single proportions and the Pearson exact method to calculate	"[] had a higher risk of [] The population attributable fraction of [] was 47% for [] and 61% for []"	"Considering these results when counselling potentially exposed [] seems reasonable"	The aim and conclusion are phrased in association terms. However, they estimate attributable fractions and suggest to act given the findings.

			confidence intervals of risk ratios and medians."			
To perform an expedited assessment of [] risk associated with exposure to []".	"The results do not imply a markedly increased short term overall risk of [] in []."	"We used Cox regression to estimate the hazard ratio with 95% confidence intervals for [] associated with [], both for ever use and for the predefined categories of cumulative use"	"Analyses were, however, performed as crude comparisons adjusted only for [] as well as adjusted for [] and the potential confounding factors."	"Overall, exposure to [] showed no association with [] compared with exposure to [] (adjusted hazard ratio 1.09, 95% confidence interval 0.85 to 1.41) and no evidence of a dose-response relation"	"This ensured that the estimates were not affected by immortal time bias []. As all comparisons were performed within users of [], the exposure to [] can reasonably be expected to be a random event, and confounding is thus expected to be limited."	The aim does not use causal language. They do provide estimates adjusted for confounding, discuss immortal time bias and conclude that the exposure does not result in an increase survival.
"To investigate the <b>risks</b> of [] in []"	"No increased risk of [] was detected in [], but increased risks of [] were found in this study. Our	"To calculate expected [], we multiplied the person years at risk by corresponding national incidence rates (by 5 year age band and individual calendar year) for the	"We obtained data relating to potential confounding factors such as []"	"There was no overall increased risk of [] (2578 observed v 2641.2 expected []; standardised incidence ratio	"Given previous inconsistent results, small study size, and lack of information on potential	The aim does not use causal language. They provide standardised estimates, discuss

	results suggest that [] risks could be due to [], rather than []."	general female population of England and Wales.  Standardised incidence ratios were calculated by the comparison of observed values with expected values."		0.98 (95% confidence interval 0.94 to 1.01); absolute excess risk -2.8 cases per 100 000 person years (95% confidence interval -7.1 to 1.8); table 2)".	confounders, we undertook a population based linkage study in []"	confounding and conclude that the risk of the outcome is due to a given exposure compared to another.
CONSISTENTLY NO	T CAUSAL					
"To determine whether [], compared [], is associated with an increased risk of []"	"In this population based cohort study, [] was associated with an increased risk of []. The association was particularly elevated among people using [] for more than five years. Additional studies, with	"We calculated crude incidence rates of [] and 95% confidence intervals, based on the Poisson distribution, for each exposure group. We used time dependent Cox proportional hazards models to estimate hazard ratios and 95% confidence intervals of [] associated with [] compared with [], using multiple imputation for variables with missing values."	"Potential confounders. All models were adjusted for the following variables measured at cohort entry: []. [] as an alternate means of controlling for confounding, we repeated the analysis by stratifying the model on tenths	"Compared with [], [] were associated with an overall 14% greater risk of [ ] (1.6 v 1.2 per 1000 person years; hazard ratio 1.14, 95% confidence interval 1.01 to 1.29)."	"We introduced a one year exposure lag period to account for a minimum latency time window and to minimize reverse causality. []The association between [] and [] is biologically plausible. [] although we were able to adjust for several	In the abstract they only describe associations but in the full text their interest points to a causal aim given the different methods applied to adjust for confounding and reverse causality. They

"To determine whether [] and [] are and [], might incidence rates of a crude incidence rate of a crude rate	of disease risk score. Finally, we repeated the analysis using a marginal structural Cox proportional hazards model using inverse probability of treatment and censoring weighting—a		important confounders, this study lacked information on other potential confounders such as [] In this large, population based study, [] was associated with an elevated risk of []	also consider elements as biologically plausibility and duration response relation. Residual confounding seems to be a concern because they
"To determine whether [] and [] are "Compared with [], [], and [], might "For each exposure category we calculated crude incidence rates of	repeated the analysis using a marginal structural Cox proportional hazards model using inverse probability of treatment and censoring		study lacked information on other potential confounders such as [] In this large, population based study, [] was associated with an elevated	biologically plausibility and duration response relation. Residual confounding seems to be a concern
"To determine whether [] and [] are "Compared with [], [], and [], might "For each exposure category we calculated crude incidence rates of	analysis using a marginal structural Cox proportional hazards model using inverse probability of treatment and censoring		information on other potential confounders such as [] In this large, population based study, [] was associated with an elevated	plausibility and duration response relation. Residual confounding seems to be a concern
"To determine whether [] and [], might "For each exposure category we calculated crude incidence rates of	marginal structural Cox proportional hazards model using inverse probability of treatment and censoring		other potential confounders such as [] In this large, population based study, [] was associated with an elevated	duration response relation. Residual confounding seems to be a concern
"To determine whether [] and [], might "For each exposure category we calculated crude incidence rates of	structural Cox proportional hazards model using inverse probability of treatment and censoring		confounders such as [] In this large, population based study, [] was associated with an elevated	response relation. Residual confounding seems to be a concern
"To determine whether [] and [], might "For each exposure category we calculated crude incidence rates of	proportional hazards model using inverse probability of treatment and censoring		such as [] In this large, population based study, [] was associated with an elevated	relation. Residual confounding seems to be a concern
whether [] and with [], [], category we calculated crude incidence rates of	hazards model using inverse probability of treatment and censoring		large, population based study, [] was associated with an elevated	Residual confounding seems to be a concern
whether [] and with [], [], category we calculated crude incidence rates of	using inverse probability of treatment and censoring		based study, [] was associated with an elevated	confounding seems to be a concern
whether [] and with [], [], category we calculated crude incidence rates of	probability of treatment and censoring		was associated with an elevated	seems to be a concern
whether [] and with [], [], category we calculated crude incidence rates of	treatment and censoring		with an elevated	concern
whether [] and with [], [], category we calculated crude incidence rates of	censoring			
whether [] and with [], [], category we calculated crude incidence rates of			risk of []	hecause they
whether [] and with [], [], category we calculated crude incidence rates of	weighting—a			because they
whether [] and with [], [], category we calculated crude incidence rates of	140 Billing a		overall, along	lacked
whether [] and with [], [], category we calculated crude incidence rates of	method designed	I	with evidence of	information on
whether [] and with [], [], category we calculated crude incidence rates of	to adjust for time	2	a duration-	relevant
whether [] and with [], [], category we calculated crude incidence rates of	dependent		response	cofounders
whether [] and with [], [], category we calculated crude incidence rates of	confounding		relation."	which could
whether [] and with [], [], category we calculated crude incidence rates of	associated with			lead to down
whether [] and with [], [], category we calculated crude incidence rates of	time varying			tone of the
whether [] and with [], [], category we calculated crude incidence rates of	exposures"			conclusions.
[] are and [], might crude incidence rates of	"The models	"Compared with	"Finally, we	The abstract
	THE HIDUEIS	[], [] was	excluded those	only refers to
	were <b>adjusted</b>	associated with a	with less than	association
associated with be associated [] with 95% confidence		associated with a	one year of	but the full
an <b>increased risk</b> with an intervals, based on the	were <b>adjusted</b> for the potential	77% increase in		text mentions
of [] in adults increased risk Poisson distribution. Tin	were <b>adjusted</b> for the potential		follow-up after	
with []." of [] in adults dependent Cox	were adjusted for the potential confounders measured at	77% increase in	follow-up after cohort entry, to	adjusting for
with []." proportional hazards	were adjusted for the potential confounders measured at	77% increase in the hazards of	· ·	adjusting for confounders

	models were used to	confounding by	interval 1.04 to	period and to	minimise
	estimate hazard ratios and	indication, we	3.01)."	minimise reverse	reverse
	95% confidence intervals	compared [].		causality. [] To	causality. They
	of [] associated with []	[] we fit a		assess possible	also describe
	and [], separately, when	marginal		duration-	its biological
	compared with []."	structural model		response	plausibility.
		to investigate the		relations, we	There is a
		impact of		investigated the	concern for
		potential time		association	residual
		dependent		between	confounding
		confounding		cumulative	due to the
		using <b>inverse</b>		duration of []	observational
		probability of		on the risk of [].	nature rather
		treatment and		An association	than missing
		censoring		between [] and	information on
		weighting."		incidence of []	particular
				is <b>biologically</b>	relevant
				plausible. [] as	confounders.
				with all	
				observational	
				studies, residual	
				confounding is	
				possible. We	
				conducted	
				several sensitivity	
				and ancillary	
				analyses	
				specifically	
				designed to	
				)	

					assess the potential impact of <b>residual</b> confounding."	
"To examine the association between [] and [] risk of []."	"[] could increase the risk of []. However, confirmation of these findings are warranted, preferably in an intervention setting"	"[] was categorised by percentiles (<10, 10-20, 20-50, 50-80, 80-90, ≥90). [] With these same categories of exposure, the association between [] and [] was examined by Cox regression. We used [] age from birth up to May 2016 as the underlying timescale censoring if death or emigration from Denmark occurred (1217 events)."	"Characteristics that might influence the risk of [] were identified a priori and included as potential confounders in our adjusted analysis. In model 1, we adjusted for: [].In model 2, additional adjustments were made for []"	"[] was significantly associated with increased risk of [] in both unadjusted and covariate adjusted analyses (table 3). Compared with [], offspring of those with [] had double the risk of [] during follow-up (hazard ratio 2.00 (95% confidence interval 1.02 to 4.00)). Risk of [] was positively associated with []: the association was	"[] the mechanism that might be responsible for this effect is not known, but could include []. [] the role of unmeasured or unidentified confounders can never be fully excluded in observational studies."	The abstract only considers associations but the full text mentions confounder adjustment and discusses potential mechanism (biological plausibility). Concern of residual confounding is due to the observational nature of the study.

				significant (Ptrend=0.016) and increased monotonically. Only minor differences were observed between the unadjusted and covariate adjusted analyses."	
"To ascertain compliance rates with []; to identify features associated with non-compliance; to rank [] by compliance; and to build a tool for live ongoing audit of compliance."	"Compliance with [] has been poor, with half of all [] non-compliant. [] commonly contain inconsistencies that might prevent even [] assessing compliance. Accessible and timely information on the compliance	"We constructed a logistic regression model with all these <b>explanatory</b> variables, as they were selected prospectively on the basis of clinical and methodological interest."	"Explanatory variables. We created variables for a range of features of each [], selected prospectively on the basis of clinical and methodological interest."	"In the adjusted multivariable analysis, [] with a [] were significantly more likely to [] (adjusted odds ratio 23.3, 95% confidence interval 19.2 to 28.2); as were [] (18.4, 15.3 to 22.1)."	 Although adjusted estimates are present, both abstract and full text limit to describe associations, rates and ranks. No causal language is used.

	status of [] and [] may help to improve reporting rates."				
"To assess how often older adults [] were [], and to identify markers of []."	"One in seven older adults [] were []. More than half of [] occurred in patients with []. More attention is needed to reduce potentially harmful [] as older adults []."	"We did multivariable mixed effect logistic regression analyses to determine associations between the outcome of [] and primary predictors of []."	"Our primary predictor variables were []. Adjusted analyses included the covariates noted above, a random effect term to account for clustering by hospital, and an interaction term to account for the relation between [] and []."	"A total of 2074 (14%) patients were []; 1293 (9%) were [] and 300 (2%) were []. Additionally, 628 (4%) patients were []. [] Patients with [] had a 25% (95% confidence interval 23% to 78%) probability of []."	 The abstract indicates that the aim is to assess the frequency of a condition and that is reflected in the main text. No causal language used.
"To describe trends in the rate and daily dose of [] used among [] from 2007 to 2016."	"[] rates were high during the study period of 2007-16, with the highest rates in [] versus [] and	"Endpoints were defined at the person quarter level. We used logistic regression to model the <b>proportion</b> of the population [] each quarter. The average []	"All analyses were stratified by beneficiary category including commercially insured, aged	"Averaged across the entire study period, 51.5% of disabled Medicare beneficiaries [] per year (n=1 128	 The abstract indicates that the aim is to describe the frequency of a condition which is

	[]. [] and average daily dose have not substantially declined from their peaks, despite increased attention to [] and awareness of their risks."	per person day by quarter was modelled by a generalized linear model with negative binomial family and log link. The dependent variable was the total [] per person in the quarter, with an exposure variable representing the number of days of insurance coverage for each person included to standardize daily []."	Medicare, and disabled Medicare (beneficiaries with Medicare coverage who were under age 65 years)"	088), compared with 14.3% (n=18 721 915) of commercial beneficiaries and 25.7% (n=3 847 676) of aged Medicare beneficiaries."		reflected in the main text. No causal language used.
"To describe []	"Mortality due	"Our primary aim was to	"We adjusted	"During the study	"[] though we	The abstract
related mortality	to [] has been	describe temporal trends	rates for age—	period, a total of	have detected	indicates that
in the United	increasing in	in death rates attributable	that is, age	460 760 deaths	worsening	the aim is to
States during	the US since	to [] and [] as the	specific mortality	were attributed	mortality since	describe the
1999-2016 by	2009. Driven by	primary or underlying	was weighted	to [] (20 661 in	2009, the precise	frequency of a
age group, sex,	deaths due to	cause of death for adults	according to the	1999 and 34 174	reasons for this	condition
race, cause of	[], people	in the USA.[] We then	age distribution	in 2016) and 136	trend and the	which is
[], and	aged 25-34	evaluated trends in death	in a standard	442 to [] (5112	geographic	reflected in
geographic 	have	rates using the National	year (2000). We	in 1999 and 11	heterogeneity in	the main text.
region."	experienced	Cancer Institute's	also sought to	073 in 2016)	our analysis	No causal
	the <b>greatest</b>	Joinpoint program. This	describe how	(table 1). Men	require further	language used.
	relative	enabled us to identify if	these trends	had a higher	study. For	
	<b>increase</b> in	there were years in the	differed based on	<b>burden</b> of age	example, we	
	mortality.	study period where the	demographic	adjusted	identify the	

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care of patients with [...]."

"To examine whether [] are associated with an increased risk of [] after []."	"Women with [], especially [], may be at higher risk of []. If these findings are replicated elsewhere, a massive amount of data exists that could aid in identifying women at higher risk of [] and that could be conveyed to them or their healthcare providers."	"The main model assessed the primary [] composite outcome, as well as the individual outcomes of [], in relation to each [] for the screened cohort, with censoring at a woman's death or arrival at the end of the study period of 31 March 2016, allowing for a maximum follow-up of 22 years. We did time to event analyses using multivariable Cox regression models, to derive a hazard ratio and 95% confidence interval for each study outcome."	"Hazard ratios were adjusted for variables chosen a priori, based on the existing literature, including: []"	"A total of 6209 women developed the primary [] composite outcome, which was typically about 1.2 to 1.3 times more likely to occur in a [], even after adjustment for other covariates"	"Potential confounders between [] and the risk of [], including [] were each accounted for in the models. Nevertheless, about 10% of [] lacked information on [], and [] and [] were entirely unknown."	The abstract indicates that the aim is to identify the association between an exposure and an outcome. They consider residual confounding due to lack of information on relevant confounders.
"To examine the association between [] and the risk of [] according to levels of []."	"Among [], increasingly worse [] was associated with a progressively increased risk of []. Even	"Using generalised linear models with a robust sandwich estimator, we estimated risk ratios for [], comparing [] according to levels of [] with []. To take into	"Analyses were adjusted for []"	"In analyses based on [] levels, the adjusted risk ratios for [] were 2.17 (95% confidence	"It is also possible that the previously demonstrated association [] has resulted in increased clinical	The abstract indicates that the aim is to identify the association between an exposure and

	with [] within target levels	account possible dependence from		interval 1.37 to 3.42) for [],	surveillance for defects among	an outcome. They consider
	recommended	repeated [], we		3.17 (2.45 to	[]. [] health	residual
	by guidelines	constructed models with		4.11) for [],	registers do not	confounding
	[], the risk of	[] as a cluster variable.		2.79 (1.90 to	record data on	due to lack of
	[] was	[] were assumed to		4.12) for [], and	[] and hence we	information on
	increased more	follow a poisson		6.23 (4.32 to	could not	relevant
	than twofold.	distribution, and we		9.00) for []	account for these	confounders.
	The risk of []	estimated risk ratios using		versus []. The	factors."	
	was not	a log link function"		corresponding		
	statistically			adjusted risk		
	significantly			differences were		
	increased at			17 (95%		
	any of the []			confidence		
	levels			interval 5 to 36),		
	examined; the			32 (21 to 46), 26		
	study had			(13 to 46), and 77		
	limited			(49 to 118) cases		
	statistical			per 1000 []."		
	power for this					
	outcome and					
	was based on					
	[] only."					
"To examine the	"Regardless of	"We calculated the	"We computed	"The associated	"Our	The abstract
association	index ages at	lifetime risks for the first	lifetime <b>risk in</b>	lifetime risk of	observational	and main text
between risk	55, 65, or 75	incident [] from index	subgroups of	[] was lowest if	study design	indicate that
factor burdens—	years, an	ages 55, 65, and 75 years	participants	the risk factor	limits the ability	the study
categorized as	optimal <b>risk</b>	up to age 95 years. [] we	according to their	profile was	to establish	mainly aims at

optimal, borderline, or elevated—and the lifetime risk of []."	factor profile was associated with a lifetime risk of [] of about one in five; this risk rose to more than one in three in individuals with at least one elevated risk factor."	used a modified Kaplan-Meier estimator with age as the time scale, accounting for the competing risk of death to compute the lifetime cumulative risk of [] and associated 95% confidence intervals"	risk profile at a specified index age (optimal, borderline, and elevated), for each risk factor separately and for the combination of risk factors. [] we fitted a multivariable Fine and Gray model, adjusted for competing risk of death to predict the	optimal. The lifetime risk of [] increased gradually as the risk factor profile changed from optimal to borderline and elevated at each index age."	causal pathways, and only associations between risk factor profiles and lifetime risk of [] can be concluded from our study."	identifying associations. There is a concern for residual confounding due to the observational nature rather than missing information on particular relevant confounders.
"To compare rates of [] for patients [], with patients []."	"[] was associated with lower [] rates compared with []."	"We used a Cox proportional hazards regression model, adjusting for (), to estimate hazard ratios and 95% confidence intervals for [] comparing [] with []. To summarize switchback estimates	"[] adjusting for basic demographics (age, sex, and calendar year)"	"Figure 5 shows that in the adjusted analysis, the [] rates remained consistently lower among [] than []. The magnitude of this	"[] our results indicate that [] may in part be driven by []."	Even though causal language is not used and both the abstract and main text mainly describe associations,

		across [], we conducted inverse variance weighted random effects meta-analyses"		effect was largest for [] (hazard ratio 0.52, 95% confidence interval 0.43 to 0.63) and smallest for [] (0.86, 0.77 to 0.97). The pooled hazard ratio across [] suggested that [] was associated with a 28% lower rate of [] compared with [] (0.72, 0.64 to 0.81)."		their conclusion at the end of the text suggests a causal relationship.
"To assess whether [] is associated with the incidence of [] in patients with []."	"In this first population based study, [] was associated with an increased risk of []. Although these findings need to be	"We calculated crude incidence rates of [] with 95% confidence intervals based on the Poisson distribution for the entire cohort and for each exposure group. For all analyses, we used time dependent Cox proportional hazards	"The models were adjusted for the following potential confounders measured at cohort entry: []"	"Compared with [], [] was associated with a 75% increase in risk of [] (53.4 v 34.5 per 100 000 per year; hazard ratio 1.75, 95% confidence interval 1.22 to	"[] as with all observational studies, residual confounding from unknown or unmeasured variables remains possible.  However, on the basis of the rule	The abstract mainly describes associations but in the main text they describe how their estimates were adjusted for potential

	replicated,	models to estimate hazard		2.49). The	out method, a	confounders
	physicians	ratios and 95% confidence		number needed	hypothetical	and they
	should be	intervals for []		to harm	confounder	estimate
	aware of this	associated with []		corresponded to	would need to be	numbers
	possible	compared with []. We		2291 patients	strongly	needed to
	association."	also calculated the		followed over a	associated with	harm (NNH).
		number needed to harm		two year period	both the	Also they
		for patients followed over		and 1177 over a	exposure (odds	consider
		a two year and four year		four year	ratio >4.7) and	residual
		period by using methods		period."	the outcome	confounding
		accounting for varying			(relative risk	and suggest
		patient follow-up times."			>5.0) to move	that only a
					the point	strong
					estimate towards	unmeasured
					the null."	confounder
						will remove
						the association
						observed. All
						of these, point
						to a causal
						analysis.
"To assess the	"In this large	"We used Cox	"Models were	"In model 1, [].	"Lastly, although	The abstract
prospective	prospective	proportional hazards	adjusted for []	was associated	we included a	mainly
associations	study, a 10%	models with age as the	we made	with increased	large range of	describes
between [] and	increase in the	primary timescale to	additional	risks of overall	confounding	associations
risk of [].	proportion of	evaluate the association	adjustments [].	cancer (hazard	factors in the	but in the
	[] associated	between [] and	In addition we	ratio for a 10	analyses, the	main text they
1	[]				· · / · · · /	

	significant increase of greater than10% in risks of []. Further studies are needed to better understand the relative effect of the various dimensions of [] in these associations."	models. We estimated hazard ratios and 95% confidence intervals with the lowest quarter as the reference category."	did <b>mediation</b> analyses []"	in the proportion of [] 1.12 (95% confidence interval 1.06 to 1.18), P<0.001) and [] (1.11 (1.02 to 1.22), P=0.02). "	residual confounding resulting from unmeasured factors () cannot be entirely excluded owing to the observational design of this study"	their estimates were adjusted for potential confounders and they use mediation analysis which suggest a causal aim. They also consider residual confounding due to the observational nature of the study.
"To assess the association between [] and all cause mortality in [] with []."	"Giving [] to [] with [] was associated with an increased rate of [] but a paradoxical lowered rate of all cause mortality. Careful	"We calculated the incidence of [] and all cause mortality per 100 person years of follow-up. We generated Kaplan-Meier survival curves for the outcomes of interest grouped by [] status. Cox proportion regression were reported as adjusted hazard ratios with 95%	"We used propensity score matching with demographic and clinical variables to adjust for potential confounding from imbalances in clinical characteristics	"The crude rates for [] and [] were 4.6 and 1.2 after [], and 1.5 and 0.4 in patients who [] per 100 person years, respectively. In the Cox proportion	"The study population was derived from real world evidence with the inherent limitations of diagnostic coding and case ascertainment Despite well matched groups	The abstract limits to describe associations and rates of the condition but the main text suggest a causal aim as they use propensity

year."

of 8.5% (95%

confidence

growth"

who had [...]

increased

does not use

causal

	significantly over time."			interval 7.6% to 9.3%). [] The slope of the trend line changed significantly at two points: 2004/5 (P<0.001) and 2008/9 (P=0.004) (fig 1)."		language accordingly.
"To investigate	"[] was	"[] we investigated the	"We treated []	"As shown in	"To minimise the	The abstract
the association	associated with	associations of [] with	as potential	figure 1, in both	potential	mentions
of [] with	a range of	cause specific incidence	confounders. For	men and women,	contribution of	associations
disease specific	health	and mortality over follow-	Cox proportional	[] was	reverse causality	and suggests
incidence and	outcomes and	up with Cox proportional	hazard analyses,	associated with a	to the findings,	that the aim is
mortality and	improved	hazard models. We	we ran four	higher hazard for	we did a	prediction. In
whether []	prediction of	reported the results as	models that	all cause	landmark	the main text,
enhances the	an office based	hazard ratios together	included an	mortality and	analysis	the authors
prediction ability	risk score.	with 95% confidence	increasing	incidence of and	excluding events	conclude that
of an established	Further work	intervals."	number of	mortality from	occurring within	the exposure
office based <b>risk</b>	on the use of		covariates: model	[] in model 0.	the two years	of interest
score."	[] in risk		0 (minimally	The associations	after recruitment	enhances
	scores or risk		adjusted)	were similar after	in model 4	prediction and
	screening is		included []"	adjustment for	(landmark	identification
	needed to			[] in model 1;	analysis). This	of patients
	establish its			after further	landmark	with risk of
	potential			adjustment, the	analysis was	certain
	clinical utility."			magnitude of	adjusted as in	diseases.

		associations were	model 3. []	However,
		slightly	may, therefore,	there is use of
		attenuated in	be a useful	causal
		models 2, 3, and	method of	
				language,
		4"	identifying	including
			people with []	confounder
			who are at high	adjustment
			risk of a wide	and discussing
			range of	reverse
			diseases. []	causality and
			Reverse causality	residual
			is possible in any	confounding.
			observational	They note that
			study. []	their goal is to
			Similarly,	do prediction
			residual	and that
			confounding is	reverse
			always possible	causality is not
			and the	a major
			associations	limitation but
			observed may	still adjust for
			not imply	it.
			causality.	
			However, given	
			that we are	
			largely interested	
			in <b>prediction</b> and	
			identification of	
			people at	
			<u> </u>	

				increased risk, and not seeking to make strong causal inferences, reverse causality is not a major limitation."	
"To externally validate four	"Application of the [] rules	"The sensitivity, specificity, and proportion	 "The sensitivity for identifying		Both the abstract and
commonly used	can lead to a	of patients [] (with 95%	patients with []		the full text
rules in [] for	wide variation	confidence intervals) were	ranged from		state that they
[]."	in [] among	assessed for each of the	72.5% for the []		aim to validate
	patients with	four decision rules. []	criteria to 98.8%		four decision
	[], resulting in	The Cochran's Q test was	for the [] rule		rules for a
	many	used to directly compare	(table 4;		particular
	unnecessary	the sensitivities and	appendix 3). []		condition.
	[] findings.	specificities between the	The [] criteria		They
	Until an	four decision rules [].	would have		compared the
	existing	Net proportional benefit	missed 11 of 74		tests in terms
	decision rule	has been proposed to	patients with []		of sensibility
	has been	incorporate such	(appendix 4). The		or specificity
	updated, any of	weighting in calculation of	CHIP criteria		and concluded
	the four rules	clinical usefulness of	would have		that the tests
	can be used for	decision rules. For each	missed two		are similar and
	patients	rule, we expressed the net	patients with [],		recommended
	presenting []	proportional benefit using	who both had		the use of a
	at the	the formula: (true	[]. The		particular one

	emergency department. Use of the [] rule is recommended because it leads to a substantial reduction in [] while missing few potential []."	positives/total number) – weight × (false positives/total number). "		specificity for identifying [] was lowest for the [] rule (4.4%) and highest for the [] criteria (60.9%). [] The sensitivity and specificity differed significantly between all the rules (Cochran's Q P<0.001). "	given that it can help avoid false negatives. The wording 'resulting' and 'leads to' are in fact to discuss the potential for false positives/ false negatives rather than a casual claim.
"To develop and validate a set of practical prediction tools that reliably estimate the outcome of []."	"The prediction models reliably estimate the outcome of patients who were managed in various settings for []. The predictor items are readily derived at hospital admission. The	"The association between predictor variables and [] was analysed by fitting proportional odds logistic regression models adjusting for the fixed effect of study. Prognostic strength was quantified as odds ratios with 95% confidence intervals. The relative importance of each predictor in the models was estimated	"In a published systematic review, we identified relevant predictors of outcome in patients []. Based on the results of this published review, we selected the following	"Bootstrap resampling showed negligible model optimism. The models had internally validated AUCs between 0.77 and 0.83. There was no significant lack of fit (goodness of fit	The abstract and main text state that the goal of the study is to validate a prediction tool. Consistent with the prediction aim, no causal

	web based []  prognostic  calculator []  and the related  app could be  adjunctive tools  to support  management of  patients."	with partial R2 statistic, which estimates the independent <b>contribution</b> of the <b>predictor</b> to the variance of the outcome"	predictor variables that are assessable early at hospital admission and are consistently associated with outcomes for inclusion in the prediction models: []"	P≥0.2 in all models). Cross validated performance was variable across studies []. The partial R2 values ranged between 4% and 46%, and the pooled AUC values were between 0.74 and 0.77"	language is used.
"To prospectively validate [] to triage patients with [] in routine clinical practice."	"In a population of patients referred for [], this new triaging approach accurately classified [] for most, with half the utilisation of ABPM compared with usual care. This	"To examine model performance, we constructed a logistic regression model with true [] as the dependant outcome variable and classification using [] as the independent predictor variable. From this model we estimated the area under the receiver operating characteristic (AUROC) curve statistic."		"The triaging strategy [] predicted true [] (true positives 66%, 95% confidence interval 63% to 69%; true negatives 24%, 22% to 27%) with a low error rate (false positives 8%, 6% to 10%; false negatives 2%, 1% to 3%)	 The abstract and main text describe that the aim is to validate a triage tool and assessed its performance compared to the standard of reference. As the aim is prediction, no causal language is

triaging		(table 2). The	used
strategy can		triaging strategy	accordingly.
therefore be		resulted in 49%	
recommended		(46% to 52%)	
for diagnosis or		being referred	
management of		for [] and the	
[] in patients		remainder	
where [] is		managed on the	
being		basis of their	
considered,		clinic	
particularly in		measurements."	
settings with			
limited			
resources."			
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