Reviewer’s report

Title: Total versus long-term prescribing of high risk medications in older people using 2012 Beers Criteria: results from three cross-sectional samples of general practice records for 2003/4, 2007/8 AND 2011/12

Version: 1  
Date: 25 May 2015

Reviewer: Marie Bradley

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Total versus long-term prescribing of high risk medications in older people using 2012 Beers Criteria: results from three cross-sectional samples of general practice records for 2003/4, 2007/8 AND 2011/12

This paper seeks to estimate the use of high risk medications at a number of time points in the UK CPRD using a modified Beers 2012 criteria. Whilst this is an important issue, which seems to have been investigated thoroughly, in a high quality medical record database, in the UK, the paper is poorly written and needs major revisions before it could be considered for publication. I have included an extensive list of potential amendments.

Overall, the methodology is very hard to follow and understand it needs to be more concise and simplified for the reader. There are too many additional files for the reader. The authors should be able to explain their work in the allotted space in the manuscript with limited use of additional files. Perhaps consider splitting the findings over two separate manuscripts id this is not possible

Title: total vs longterm? The word Total is confusing and should be changed perhaps ever vs longer. Total is very misleading- total would reflect a total amount over a period of time not just a one of prescription

Abstract

Abstract: line 5: “in the older UK population” – please change to a subset of the UK population ( whilst CPRD is representative of the UK population it is incorrect to assume UK population when using cprd)

Must mention statistical analysis briefly in methods section of abstract

Introduction

Polypharmacy is usually defined as 4 or 5 or more repeat medications. The average number of prescribed items per person per year in England may not be an accurate refelection of polypharmacy as it may account for acute medications that are not given on a repeat or long term basis

“UK cross-sectional research(19, 20) has identified that increasing drug burden is consistently associated with greater exposure to potentially inappropriate prescribing; - define drug burden or consider rephrasing
Methods

“The study protocol was scientifically and ethically reviewed and approved by the Independent Scientific Advisory Committee (12_017A3) for the UK Medicines and Healthcare products Regulatory Agency (MHRA)”-CPRD has blanket ethical approval for observational studies- ISAC does not approve on ethical grounds only scientific content please rephrase. Also this statement should go at the end of the methods section.

How did you define HRM??- you used the BEERs criteria and stated “Our definition of HRM is conceptually similar with the Beers “potentially inappropriate medications” (PIMs)” then you use the Beers criteria for appropriateness- this is very confusing. You need to clearly specify the differences between HRM and PIM- Beers has been designed as an explicit process measure for estimating PIMs.

The authors used a “modified” Beers criteria as they added in some of their own UK based criteria and omitted some US drugs please consistently state this when referring to Beers

Line 70 please refer to practices as general practices for audiences outside of the UK

The authors need to concisely explain how they selected their study population from CPRD. This is not clear whatsoever.

Please explain why centerians were matched to younger 65+

Line 71- which older protocol? This is confusing

Of the 50,313 patients in the original sample – what is the original sample.??

There appears to be Much emphasis on the older old in the methods- those over 100. I feel it is not adequately explained or focused upon in the introduction. Please clarify

“Patients who contributed data to the Clinical Practice Research Datalink (CPRD)(21) GOLD version (data sampled: July 2012)” over how long? Were patients selected from the practice UTS date until July 2012?? Again very unclear how study population was selected

“noting that each subject contributed only to one of the three year groups”- what does this mean?? that patients included in 2003/2004 were not included in 2011/2012- this is unclear please clarify

“whose practices had consented for patient postcodes to be linked to socio-economic data.”- what proportion of practices did this in CPRD??

“For each year, for each person we calculated the total number of drugs and HRM prescribed (i.e. at least once that year) to derive a ‘total’ medication count- it may be easier to state we identified those ever exposed to a HRM in each year and the number of drugs prescribed.

“We focused on the 34 drugs or drug classes defined as ‘drugs to avoid in older
adults’ —……….The results were discussed and consensus reached: 47 drugs that are not available as UK-licensed prescription-only products were removed and the final list of 92 drugs”” – this is very confusing it is stated that the focus will be on the 34 drugs only list but then some how there are 92 drugs- I assume they mean 34 criteria. Please state so-also a list of all criteria applied needs to be in the results section in form of a table or figure please.

“seven drugs (all benzodiazepines) added as scoping work identified them within the dataset” – please discuss scoping work in the database- what exactly were you looking for and why did you decide to include these?- I am not sure it is appropriate to do scoping work prior to conducting this study!!

Why did the authors choose this multi-morbidity index over the modified charlson index that has been used in previous CPRD studies??

“Model 1: year sampled, age, gender; Model 2: plus medication count; and Model 3: plus multimorbidity and socio-economic status”

Was there an overall model- combined version including all explanatory variables that might influence the outcome variable. The explanation of the various logistic regression models is confusing- perhaps a statistician should review and give amore concise description.

“Combining data from all three samples, we undertook multivariable logistic regression analyses”- did this include same patients from different years?? Again methods are very unclear

Line 155- please cite the stata software appropriately

Results

Table 1- how do the proportion of people prescribed 0 drugs at least once a year and over all quarters change- if they were prescribed 0 drugs then how could that change over quarters??

Why are HRM results not documented in table 1

Please state in all tables what the logistic regression models are adjusted for.

Line 181 Accounting for confounders – which confounders?

How did the authors apply the 2012 Beers NSAID criteria? It states that regular NSAID use is inappropriate but how did they define regular

Discussion

“We present the first UK primary care data on the prevalence, correlates and appropriateness of high risk medication prescribing in older people using the updated 2012 Beers Criteria” – a study assessing potentially inappropriate prescribing according to the STOPP criteria in CPRD was published recently ref “BMC Geriatr. 2014 Jun 12;14:72. doi: 10.1186/1471-2318-14-72.

Potentially inappropriate prescribing among older people in the United Kingdom.

Bradley MC1, Motterlini N, Padmanabhan S, Cahir C, Williams T, Fahey T, Hughes CM.”
Your criteria were adapted for use in the UK and so it is not appropriate to
directly compare these to the US- I seriously doubt that HRM risk is higher in the
UK than the US. The fragmented nature of the US health care system and the
lack of comprehensive medical record databases such as CPRD in the US would
make any such assessment very difficult. Please revise this statement.

Line 217 please omit the word statistical
The reason why an association was observed between oldest old and increased
risk of regular but not total HRM is most likely related to numbers. (small
numbers of patients exposed long term and so more likely to find significant
associations when they don’t exist)

Line 226 please consider changing the term worrying to concerning
Consistent with previous reports, we found being female, and taking increasing
numbers of concomitant medications are strongly associated with the risk of
PIMs exposure- this is the first time you mentioned PIM?????????????. Again a firm
explanation of PIM vs HRM needed early on in the paper.

Line 242- please acknowledge that you are referring to data contained in CPRD
“Prescribing data, the focus of this study, is deemed accurate as the issuing of
scripts is computerised(30)”

CPRD prescription data has been validated by review of original medical records
and shows high levels of accuracy. This is nothing to do with prescriptions being
issued electronically- many practices in the UK still issue some handwritten
scripts and certainly many still did so in the 2000s

HRM is likely underestimated as you applied a modified and shortened beers list-
please acknowledge this.

A mention that targeting the most prevalent HRMS- NSAIDs and benzodiazepines
in the discussion is important.

“265 HRMs rates for older people in UK general practice remain largely
unchanged since 2003/4 against”- CPRD represents about 8%-9% of the UK
population. Practices included in CPRD meet pre-defined standards and are
deemed high quality in terms of data collection and recording- these practices
may also be superior in terms of managing medicines and so you cannot say that
your findings reflect what is occurring in “general practice” in the UK as a whole-
you may actually be underestimating the problem by sampling from some of the
“better” practices. Please change to CPRD rather than UK general practice

The authors discuss targeted interventions to tackle the problems of HRM use-
please suggest from the literature which possible interventions they would
consider appropriate? Especially for the ten drugs deemed most problematic.

"We also assessed the clinical conditions most frequently associated with HRM
use and the appropriateness of HRM use according to Beers recommendations
in 2011/12 patient records”- very little mention of this in discussion and
conclusion
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

No competing interests to declare