Reviewer’s report

Title: Current and future perspectives on the management of polypharmacy

Version: 0 Date: 29 Jul 2016

Reviewer: Peter Bower

Reviewer's report:

The authors point out that taking many appropriate medications may well be good for health, and that it may be more about monitoring and avoiding poor quality prescribing when multiple medications are used. I felt that they could have explored the issue of the difficulties of determining the added value of additional medications in the context of polypharmacy, as the evidence base here is poorly developed. I felt the definitions in the Box rather 'begged the question' as it was not clear how these judgments would be made. The limitations of these simple categories might be highlighted and explored. There may be a role for large scale analysis of routine data to improve the evidence base in this regard.

In the section on risks, it would be helpful to explore effects on clinical outcomes, costs and mortality. The restriction to risky prescribing seemed a bit limited, as it is not clear how these impact on critical outcomes (despite being an important quality measure).

The statement that 'The risks from polypharmacy are higher in vulnerable groups, including those with existing comorbidities such as diabetes and rheumatological disease, multimorbidity and older patients' could be rephrased, as describing multimorbidity as an existing comorbidity is not very clear.

A more critical approach to some of the findings may be useful. Although 'pragmatic', what is the evidence that reference 8 is a good basis for judgements? What is the nature of the 'risk scores' that they describe - is this likely to be features of patients, or the medications that they are taking?

Is care.data a useful analogue here, despite some broad relevance? Presumably they are talking about using data to plan clinical care for individual patients, not harvesting? I was unconvinced that this was of high relevance, and thought consideration of other likely problems (data quality, the overall validity of risk indices, the limited variables included which may miss critical variables of interest) would be of greater importance.

They state that 'all prescribers need to carefully consider the potentials costs as well as the benefits of treatment before starting a drug' - but how does a clinician do this, if there is little evidence on the risk/benefit ratio for a new medication in the context of existing polypharmacy? What is the role of patient preference versus clinical judgement, versus costs? What decision making tools are likely of most relevance?
Can they provide more detail about what AI would add value? It was not immediately obvious to me what that would involve?

They discuss 'medicines reconciliation' as key, but state nothing about the evidence in this area. Is this cost effective? What is the size and quality of the evidence base?

I did not understand the relevance of the 4P section in the current context, and felt the links needed to be much improved.

In the section on patients, is there scope for consideration of issues of 'treatment burden' as identified by May et al? What about the role of 'minimally disruptive medicine' and deprescribing, especially in the context of older, frail patients with limited life expectancy? I think some discussion of these debates would be useful, to complement the focus on technical fixes.

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