Reviewer's report

Title: Reduction of antibiotic prescriptions for acute respiratory tract infections in primary care: a systematic review

Version: 1 Date: 16 Jan 2018

Reviewer: Kathryn Suh

Reviewer's report:

This paper addresses an important implementation question of how to reduce the overuse of antibiotic medication in those 13 and older. The authors have conducted a rigorous, although not exhaustive search of the literature and summarized findings from 13 randomized controlled trials, most but not all are group randomized. The paper should be of interest to Implementation Science readers, even readers like me who have a limited medical background. I would, however, suggest the authors add a few explanatory sentences about some of the terms that are used, e.g., POCT, which is mentioned on line 282 but does not describe the primary relevance that CRT- one of two POC tests described in the paper -- and hence infection can be tested and used in consultation in a single office visit. The potential use of POCT during a single office visit has general relevance to implementation. Other approaches, such as those using a clinical decision support system (CDSS), delayed prescribing, and communication skills training are relevant to other settings besides treatment for respiratory tract infections.

One of the major challenges in improving the specificity of delivery of Abx prescriptions is that, although we know that the prescription rate currently is too high, we don't know what the optimum rate should be in practices. Indeed, the title of the paper is somewhat of a misnomer, as "optimization" of antibiotic treatment is not just dependent on reducing the percentage with RTI who are given antibiotics. There have been broad recommendations, such as Pew's 2016 report for the US that 30% of outpatient prescriptions were unnecessary and a 15% overall reduction in prescriptions would presumably meet the US plan of action to reduce this inappropriate use by half. The authors use an absolute 10% reduction in rates as their major criterion of success. However, the huge variation in base rates, where the lowest value is 24% and the highest is over 89% makes this an unsatisfactory single criterion for defining the number of trials that show a successful reduction. For example, under this criterion, the McGinn study, which found a 9% reduction from a 38% control condition would be considered a failure. Can the authors make a better justification for using such a difference in rates? Is there not a bound where reduction the rate would be too high?

The paper could do with some reorganization and adding some lead sentences to inform the reader what different parts of the paper are about. For example, the section starting in line 213 seems to summarize some of the individual level trial findings on the 3 trials that involve CDSS. In my reading it is unclear why just these 3 trials are discussed at this point, particularly before discussing what the interventions are around line 233. Aren't the two sentences starting on line
310 reversed? If not I don't understand the point. Line 315 is this decayed effect after 6 weeks pertain to the Altiner trial (only)? Regarding a secondary endpoint, the authors' state (line 204) that the intervention groups' reduction in inappropriate prescriptions as 60% versus 27% in the control. The text is unclear to me whether this is based on a single trial, or a subset of the 17. I found it difficult to understand the descriptions of effects from multifaceted interventions, especially around line 397. "Two RCTs combined all three categories" - what categories are these?

There is a description in the text regarding interventions, but the control condition descriptions are embedded in the tables; is there any explanation of why one of the control sites was able to reduce their rates 13% over time? That's as large as the overall intervention effect at T1.

As to the methodology used to compare differences, the authors only used comparisons that came from the original studies, clustered into different types of interventions and countries. This makes it hard to absorb the material, and I found only one summary paragraph on page 513 to be an actual summary of the findings. I recognize that there are a limited number of trials and comparisons that are being made, but the authors could well have used meta-regression to check whether there are some predictive indicators that could be extracted from these studies.

There are sections that examine the distinguished effects of single element and multifaced interventions. While the ranges of intervention differences are given, there is no overall point and confidence interval for these overall effects. This makes it impossible to compare the two sets of interventions.

Line 149: Define times T1 and T2. I presume T2 is over one year based on line 192 but it is not clear.

I wasn't able to find footnotes to the figures in the version that I received, included the downloaded figures. These footnotes are essential to understanding the differences in all the colored diamonds and circles, please check that they are available.
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