## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Patient information leaflets to reduce antibiotic use and reconsultation rates in general practice: a systematic review |
| **AUTHORS** | de Bont, Eefje; Alink, M.; Falkenberg, F.; Dinant, Geert-Jan; Cals, Jochen |

## VERSION 1 - REVIEW

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| **REVIEWER** | Moore, Michael<br>University of Southampton<br><br>I am a co-author on several of the cited publications |
| **REVIEW RETURNED** | 27-Feb-2015 |

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| **GENERAL COMMENTS** | This is a clear and well written article and contributes to the AMR literature by systematically reviewing the evidence for information leaflets in the consultation. I was surprised the authors chose not to opt for meta analysis of the main outcomes. I suspect this would have made the results more compelling. Although there was heterogeneity the authors could have presented planned subgroup analysis. For example<br>-Respiratory tract infection<br>-Leaflets without delayed prescription as a co-intervention<br>-Interactive leaflets<br>-Non interactive use of leaflets.<br>This may shed further light on the circumstances when leaflets are more useful and whether the interaction in leaflet use leads to a greater effect.<br><br>I found the first sentence in introduction in the abstract slightly confusing<br>'Prescribing antibiotics is influenced by patients' expectations and knowledge'<br>Should it be that patients knowledge and expectations may influence the prescription of antibiotics.<br>This may look similar but by starting with 'prescribing' it is seems to suggest the patients themselves prescribe.<br>I noted reference 25 refers to the Action plan in year 2000.<br>there are several more recent references<br>The chief medical officers annual report<br>https://www.gov.uk/government/publications/chief-medical-officer-annual-report-volume-2<br>The WHO report<br>http://www.who.int/drugresistance/documents/surveillancereport/en/<br>The latest UK action plan http://antibiotic-action.com/wp-content/uploads/2011/07/DH-UK-antimicrobial-resistance-strategy-and-action-plan.pdf |

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| **REVIEWER** | An De Sutter, MD PhD Asscociate Professor<br>Department of Familiy Medicine and Primary Health Care, Ghent University, Belgium |
| **REVIEW RETURNED** | 13-Mar-2015 |

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| **GENERAL COMMENTS** | This is a correctly performed systematic literature review on a relevant topic. The discussion could place the results more thoroughly in the context of the effectiveness of patient leaflets in general: what makes this "indication" different from the other situations in which leaflets have been tested? And are the results different or similar? Why? etc<br>Secondly, although I fully agree that strategies to decrease antibiotic use are badly necessary, sometimes treatment with antibiotics is necessary. It should at least be discussed that any strategy to reduce antibiotic prescribing and reconsultation should also check for inappropriate "non-use" as well an inappropriate use. |

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| **REVIEWER** | Hannah Thornton<br>Centre for Academic Primary Care<br>NIHR School for Primary Care Research<br>School of Social and Community Medicine<br>University of Bristol<br>UK |
| **REVIEW RETURNED** | 13-Mar-2015 |

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| **GENERAL COMMENTS** | Thank you for asking me to review this systematic review, which is in my opinion well-executed and well-written. I have a few very minor comments:<br>Abstract line 47: State if reconsultation is for the same illness episode or for subsequent illnesses<br>Page 7 (of PDF) line 14: The term "folder brochure" is unusual; do you mean "folder", "brochure"?<br>Page 10 lines 23 and 25: You refer to one Macfarlane paper but it seems to be referenced in this sentence as both 20 and 21 - which is it?<br>Page 10 lines 27 and 31: Might be clearer if instead of saying 'one study' and 'a study' you use the author names as you have elsewhere<br>Page 10 line 41 and page 12 line 13: State that reconsultation is for the same illness episode<br>Page 13 line 43: 'reasonably well to good' should perhaps read 'reasonably good to good'?<br>Page 13 line 44: Should this say 'high risk in blinding' not 'of blinding'?<br>Page 13 line 52: I didn't really understand what you are suggesting here; could you clarify? |

## VERSION 1 – AUTHOR RESPONSE

Reviewer 1

1. This is a clear and well written article and contributes to the AMR literature by systematically reviewing the evidence for information leaflets in the consultation. I was surprised the authors chose not to opt for meta analysis of the main outcomes. I suspect this would have made the results more compelling. Although there was heterogeneity the authors could have presented planned subgroup analysis. For example
-Respiratory tract infection
-Leaflets without delayed prescription as a co-intervention
-Interactive leaflets
-Non interactive use of leaflets.
This may shed further light on the circumstances when leaflets are more useful and whether the interaction in leaflet use leads to a greater effect.

Response: We thank the reviewer for his compliments and agree with him that a meta-analysis would have helped us to shed further light on the circumstances when leaflets are more useful. For this exact reason we did in fact plan a meta-analysis as is stated in the methods section and a subgroup analysis. However, when performing the systematic review we found that there was a great variety in study population samples (adults, children or both) and in the primary and secondary outcome measurements, which were measured both objectively and subjectively. We specifically choose not to perform a heterogeneity analysis because of this heterogeneity in methodologies and study populations. Because we believe that, in this case, methodological heterogeneity is superior to statistical heterogeneity. However, relative risks and applied confidence intervals were calculated for our outcomes of interest to compare and interpret outcome data and described qualitatively, as were the suggested subgroups (RTI, co-interventions and interactive vs. non-interactive use) suggested by reviewer 1 which are described in the results section, table 3 and the discussion.

2. I found the first sentence in introduction in the abstract slightly confusing 'Prescribing antibiotics is influenced by patients' expectations and knowledge' Should it be that patients knowledge and expectations may influence the prescription of antibiotics. This may look similar but by starting with 'prescribing' it is seems to suggest the patients themselves prescribe.

Response and revision: We agree with the reviewer and changed the first sentence of the abstract in the way that is suggested.

3. I noted reference 25 refers to the Action plan in year 2000. there are several more recent references:
The chief medical officers annual report https://www.gov.uk/government/publications/chief-medical-officer-annual-report-volume-2
The WHO report http://www.who.int/drugresistance/documents/surveillancereport/en/
The latest UK action plan http://antibiotic-action.com/wp-content/uploads/2011/07/DH-UK-antimicrobial-resistance-strategy-and-action-plan.pdf

Response: We would like to thank the reviewer for drawing our attention and completely agree that we should refer to the most recent action plan.

Revision: We changes reference 25 to the most recent action plan.

Reviewer 2

4. This is a correctly performed systematic literature review on a relevant topic. The discussion could place the results more thoroughly in the context of the effectiveness of patient leaflets in general: what makes this "indication" different from the other situations in which leaflets have been tested? And are the results different or similar? Why? Etc

Response: We agree with the reviewer that this could place the results more thoroughly in context and therefore added this to the discussion.

Revision: We added a short paragraph to the discussion comparing the effectiveness and use of patient information leaflets in general to acute infections.

5. Secondly, although I fully agree that strategies to decrease antibiotic use are badly necessary, sometimes treatment with antibiotics is necessary. It should at least be discussed that any strategy to reduce antibiotic prescribing and reconsultation should also check for inappropriate "non-use" as well an inappropriate use.

Response: We thank the reviewer for drawing to our attention that we might not have stated this clear enough and added this to the discussion.

Revision: We added a paragraph to the implications for practice section of the discussion (page 14).

Reviewer 3

6. Thank you for asking me to review this systematic review, which is in my opinion well-executed and well-written. I have a few very minor comments:
Abstract line 47: State if reconsultation is for the same illness episode or for subsequent illnesses

Response and revision: We would like to thank the reviewer for her compliments and we added this to line 47 of the abstract.

7. Page 7 (of PDF) line 14: The term "folder brochure" is unusual; do you mean "folder", "brochure"?

Response and revision: We thank the reviewer for pointing this out and changed this because we did indeed mean "folder", "brochure".

8. Page 10 lines 23 and 25: You refer to one Macfarlane paper but it seems to be referenced in this sentence as both 20 and 21 - which is it?

Response and revision: We double checked reference 20 and 21 and changed it to 21 which is the correct paper.

9. Page 10 lines 27 and 31: Might be clearer if instead of saying 'one study' and 'a study' you use the author names as you have elsewhere.

Revision: We changed ‘one study’ to the authors names as suggested.

10. Page 10 line 41 and page 12 line 13: State that reconsultation is for the same illness episode.

Revision: As suggested by the reviewer we stated that reconsultation is for the same illness episode or similar illnesses were relevant.

11. Page 13 line 43: 'reasonably well to good' should perhaps read 'reasonably good to good'?

Revision: We changed this to 'reasonably good to good' as suggested by the reviewer.

12. Page 13 line 44: Should this say 'high risk in blinding' not 'of blinding'?

Revision: We changes this to 'high risk in blinding as suggested by the reviewer.

13. Page 13 line 52: I didn't really understand what you are suggesting here; could you clarify?

Response: We aimed to explain that although cluster randomisation has possible limitations, the main advantage for studies examining the effect of information leaflets is that it avoids contamination bias. Meaning that if patients are randomised on an individual level the GP could potentially have to use the leaflet in one patient and then provide his next patient with care as usual. This causes a risk that he will also use part of the intervention (or in this case information that is provided) in the control patients who therefore receive part of the intervention instead of care as usual.