

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Do NHS GP surgeries employing GPs additionally trained in Integrative or Complementary Medicine have lower antibiotic prescribing rates? Retrospective cross-sectional analysis of national primary care prescribing data in England in 2016.
AUTHORS	van der Werf, Esther; Duncan, Lorna; Von Flotow, Paschen; Baars, Erik

VERSION 1 – REVIEW

REVIEWER	Marjukka Mäkelä National Institute for Health and Welfare Finland
REVIEW RETURNED	09-Nov-2017

GENERAL COMMENTS	<p>Major comments:</p> <p>The topic is interesting, national data sources have been used imaginatively and the methods used to elicit the differences have been chosen carefully. Although the sample of CAM/IM practices is small, a significant difference was found. An interesting additional piece of information for people outside the UK would be to describe briefly what the national guidelines (references 1 and 11) actually say on antibiotic prescribing in general, for UTI and RTI.</p> <p>The authors seem to have a tendency to support the application of CAM/IM in primary care. It would be fair to remind readers of the fact that most complementary and alternative medicine practices are, by definition, not based on evidence, and some have harmful side effects. Reducing the use of antibiotic prescriptions by symptom management with CAM therapies may predispose patients to interventions that may have harmful effects.</p> <p>Minor comments:</p> <p>The authors could state more clearly if their main outcome was overall use of antibiotics and the two disease groups were an additional analysis.</p> <p>On page 4, lines 51-52, the statement “GPs as a professional group are expected to react homogeneously to external demands, basing their prescription on objective measures and (local) guidelines” is not quite correct. Not only GPs but all doctors are known NOT to react homogeneously; the principle of evidence-based medicine is to apply best available evidence (which hopefully is presented in guidelines) to patient’s individual situation, within the framework of funding and administrative guidance. The text in the previous paragraph presents well “the complex array of factors (that) influence antibiotic prescribing”.</p>
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	<p>p.6 l.55: There seems to be something missing in “Location – the registers enabled us to search for practitioners either a country...”</p> <p>In Table 3 and text on p.9, a statistically significant difference in the percentage of patients with cancer is reported while the median percentage is 2.4 (1.7-3.0) for conventional GP surgeries and 2.5 (2.2-2.9) for IM/CAM surgeries. It seems this could be a misreading, as the values are nearly identical. Table 4 should state the period of observation.</p> <p>There are some typos that need to be corrected, e.g. In the Abstract, the acronym STAR-PU is written twice without the dash. p. 13 tranferability of lifestyle skills</p>
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REVIEWER	Gloria Cordoba University of Copenhagen, Denmark
REVIEW RETURNED	23-Nov-2017

GENERAL COMMENTS	<p>This observational study aimed to compare antibiotic prescription rates between conventional General Practice surgeries and GP surgeries employing GPs additionally trained in integrative medicine or complementary and alternative medicine (IM GP surgeries) working within the NHS England. They found that there is a lower prescription rate in IM GP surgeries overall and for respiratory tract infections than in conventional GP surgeries. No difference was found for the prescription rate in patients with suspected UTI.</p> <p>The topic of the study is interesting. Nonetheless, it needs some improvement specifically in the introduction and discussion part to frame the importance of their findings on the debate about the role of GPs characteristics in the variation in prescription of antibiotics.</p> <p>Major revision:</p> <ul style="list-style-type: none"> • In the conclusion of the abstract, you do not answer to your research question. Your first sentence should be: whether there is a difference between the two type of practices. Afterwards, mention the two most important limitations for the interpretation and the relevance of the findings. Furthermore, in the abstract as well as in the discussion part you should write about the role of GPs and practice characteristics for explaining variation in prescription of antibiotics. • Line 11 page 4: reference 2 is not about reduction in antibiotic use leading to reduction in antibiotic resistance. • Line 28 page 4: reference 9 is not about the number of UTI in their lifetime. • Between line 36 and 52 part of the text is very similar to the introduction text from the article: Cordoba G, et al. Prescribing style and variation in antibiotic prescriptions for sore throat: cross-sectional study across six countries. BMC Fam Pract. 2015;16:7. When one google some the sentences this article pops-up and you use the same references in the same order. Two things should be done:
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	<ul style="list-style-type: none"> • First, as the article was a source of inspiration to write your article , it should be cited. • Secondly, your article and Cordoba et al. article deal with possible determinants of variation in prescription of antibiotics at GP level so your introduction and discussion part should be expanded regarding this topic. You need to expand what is known about determinants in variation in the introduction and in the discussion part to explain why you chose education in integrative medicine as an explanatory variable and the shortcomings of confounding bias. • Lines 51-60 page 9 and 1-6 page 10. The numbers differ between the text and table 4. Furthermore, interpretation like 21% less likely... it is not necessary, as you have just presented the numbers. • Lines 15-29 page 23. The following two paragraph can stand without this one to make your point about the limitations for interpreting the results due to the small number of IM practices. This paragraph may fit better in the last part of the discussion to point out some secondary findings of your research. <p>Minor revision:</p> <ul style="list-style-type: none"> • Line 34 page 2: you should delete the sentence “despite the very small proportion of NHS IM GPs”. In the results you should just show how many conventional and IM surgeries were included in the study. • Line 13-18 page 12: I am not sure whether one can cite with specific numbers unpublished data. • Line 13 page 10 from however.... This sentence should be removed. Although still it has to be discussed in the limitations of the study. • Lines 8-13 page 11 should be the first part of your discussion section “summary of main findings” afterwards you can start explaining the limitation “like the few number of IM GPs”.
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REVIEWER	Laura Shallcross UCL, London
REVIEW RETURNED	30-Nov-2017

GENERAL COMMENTS	<p>The authors provide a clear description of their analysis and the rationale for the study. However, there are so many limitations to this analysis that it is difficult to draw any conclusions. The work is of interest, but the only conclusion that can really be drawn is that more research is required to establish whether IM therapies can reduce inappropriate antibiotic use.</p> <p>The authors need to be much more explicit about the limitations of their study including:</p> <ol style="list-style-type: none"> 1. Ecological data per practice is presented but there is no information on the proportion of IM GP’s per practice. In a large practice with only 1 IM GP, that GPs prescribing behaviour is unlikely to have much impact on prescribing at practice level. 2. People accessing IM GPs are likely to be systematically different to patient who do not access IM GPs. For example the reason why they are accessing an IM GP could be because they do not want an antibiotic.
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	<p>This is touched on in the discussion but needs to be highlighted more clearly</p> <p>3. What is the geographical spread of these practices? Rural/urban?</p> <p>4. People may be independently accessing IM GPs in the private sector and then seeking antibiotics from non-IM GPs in the NHS</p> <p>5. Use of prescribing data to infer the type of infection is prone to errors e.g. amoxicillin may be prescribed for uti</p> <p>6. Lack of data on consultation rate is a significant limitation for the reasons the authors state, but this has a major impact on the conclusions that can be drawn from this analysis</p> <p>7. Is this the best approach to identify IM-GPs?</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Marjukka Mäkelä

Institution and Country: National Institute for Health and Welfare, Finland

Please state any competing interests: None declared

Please leave your comments for the authors below:

Major comments:

1. The topic is interesting, national data sources have been used imaginatively and the methods used to elicit the differences have been chosen carefully. Although the sample of CAM/IM practices is small, a significant difference was found. An interesting additional piece of information for people outside the UK would be to describe briefly what the national guidelines (references 1 and 11) actually say on antibiotic prescribing in general, for UTI and RTI.

Answer 1: we have added the following information on usual care in UK for RTI and UTI in the introduction section:

RTI (p.4, lines 12-16): NICE guidelines on respiratory tract infection⁵ (RTI) management advise that a no antibiotic prescribing strategy or a delayed antibiotic prescribing strategy should be considered for patients with the following conditions: acute otitis media, acute sore throat/acute pharyngitis/acute tonsillitis, common cold, acute rhinosinusitis and acute cough/acute bronchitis.

UTI (p.4, lines 24-29): For example, the NICE guideline on uncomplicated UTIs in women advise to offer symptom relief and an antibiotic to all women with a suspected urinary tract infection. It states that for a woman with mild symptoms who has normal immunity, normal renal function, and a normal renal tract, treatment can be delayed if the patient wishes to see if symptoms will resolve without treatment. For all other women treatment needs to start without delay.¹³

2. The authors seem to have a tendency to support the application of CAM/IM in primary care. It would be fair to remind readers of the fact that most complementary and alternative medicine practices are, by definition, not based on evidence, and some have harmful side effects. Reducing the use of antibiotic prescriptions by symptom management with CAM therapies may predispose patients to interventions that may have harmful effects.

Answer 2: we have changed the sentences accordingly to the reviewer's suggestions by adding added the words 'proven effective and safe' to the following sentence in the discussion section (p.12, line 17): "As such, symptom management with paracetamol, ibuprofen or the use of CAM therapies proven to be effective and safe for RTIs may safely reduce antibiotic prescribing among patients with a low risk for pneumonia".

Minor comments:

1. The authors could state more clearly if their main outcome was overall use of antibiotics and the two disease groups were an additional analysis.

Answer: we have added the word 'additionally' to the analysis of the 2 disease groups (p. 8, line 24): 'We additionally evaluated associations between IM GPs and antibiotics commonly used for respiratory tract infection (RTI) (amoxicillin, amoxicillin and enzyme inhibitor, ampicillin, clarithromycin, doxycycline, erythromycin, and phenoxymethylpenicillin) and for urinary tract infection (UTI) (cephalexin, cefixime, ciprofloxacin, nitrofurantoin, pivmecillinam, and trimethoprim)'.

2. On page 4, lines 51-52, the statement "GPs as a professional group are expected to react homogenously to external demands, basing their prescription on objective measures and (local) guidelines" is not quite correct. Not only GPs but all doctors are known NOT to react homogenously; the principle of evidence-based medicine is to apply best available evidence (which hopefully is presented in guidelines) to patient's individual situation, within the framework of funding and administrative guidance. The text in the previous paragraph presents well "the complex array of factors (that) influence antibiotic prescribing".

Answer: we agree with the reviewer that the current statement might lead to misunderstanding, therefore have changed the sentences accordingly. We have deleted: "GPs as a professional group are expected to react homogenously to external demands, basing their prescription on objective measures and (local) guidelines" and replaced with (p.5, lines 4-6): "GPs as a professional group are expected, following the principles of evidence based medicine, to apply best available evidence to patient's individual situation, within the framework of national and local funding and administrative guidance."

3. p.6 l.55: There seems to be something missing in "Location – the registers enabled us to search for practitioners either a country..."

Answer: we have rephrased the sentence (p.6. lines 23-35): "Location – the registers enabled us to search for practitioners either on a nationwide (England/ UK) basis or by county (in the latter case, all English counties were checked, including recent boundary changes)."

4. In Table 3 and text on p.9, a statistically significant difference in the percentage of patients with cancer is reported while the median percentage is 2.4 (1.7-3.0) for conventional GP surgeries and 2.5 (2.2-2.9) for IM/CAM surgeries. It seems this could be a misreading, as the values are nearly identical.

Answer: we have re-checked the outcome of our analysis and the difference is statistically significant. The median and 25th and 75th percentile are indeed rather similar. However, when using a random effects model for proportions, the difference is significant ($p=0.0109$). No changes have been made according to this comment.

5. Table 4 should state the period of observation.

Answer: we have added the setting and period of observation to the title of the table: "Table 4. Median antibiotic prescription rates and Relative Risk (RR) of prescribing antibiotics in primary care England over 2016."

6. There are some typos that need to be corrected, e.g.

In the Abstract, the acronym STAR-PU is written twice without the dash.

p. 13 transferability of lifestyle skills

Answer: we have re-checked the paper on typos and made the requested changes to the abstract (p.2, lines 19 and 38) and discussion section abstract (p.13, line 16) as suggested by the reviewer.

Reviewer: 2

Reviewer Name: Gloria Cordoba

Institution and Country: University of Copenhagen, Denmark

Please state any competing interests: None declared

Please leave your comments for the authors below

This observational study aimed to compare antibiotic prescription rates between conventional General Practice surgeries and GP surgeries employing GPs additionally trained in integrative medicine or complementary and alternative medicine (IM GP surgeries) working within the NHS England. They found that there is a lower prescription rate in IM GP surgeries overall and for respiratory tract infections than in conventional GP surgeries. No difference was found for the prescription rate in patients with suspected UTI.

The topic of the study is interesting. Nonetheless, it needs some improvement specifically in the introduction and discussion part to frame the importance of their findings on the debate about the role of GPs characteristics in the variation in prescription of antibiotics.

Major revision:

1. In the conclusion of the abstract, you do not answer to your research question. Your first sentence should be: whether there is a difference between the two type of practices. Afterwards, mention the two most important limitations for the interpretation and the relevance of the findings. Furthermore, in the abstract as well as in the discussion part you should write about the role of GPs and practice characteristics for explaining variation in prescription of antibiotics.

Answer: we have changed the first part of the conclusion of the abstract accordingly (p.2, lines 30-32):
““NHS England GP surgeries employing GPs additionally trained in Integrative or Complementary Medicine have lower antibiotic prescribing rates. Accessibility of IM/CAM within NHS England primary care is limited. Main study limitation is the lack of consultation-data.”

2. behaviour of patients self-selecting to consult a IM GP or conventional surgery, and its effect on antibiotic prescription. Additional treatment strategies for common primary care infections used by the IM GPs should be explored to see if they could be used to assist in the fight against AMR.”

Answer: our analyses are on practice level and we have used the available information on practice level to explain variation in prescription of antibiotics. The NHS digital data we have used include no data on GP and GP practice characteristics, else then list size and population characteristics which have been included in our analysis and described in the result section. We have additionally provided information on deprivation score on practice level (p.7 and 8 and table 3).

• We have now added an extra limitation to the discussion section in which we acknowledge the fact that GP characteristics on individual level might play a role in explaining the variation in antibiotic prescribing as well (p. 11 Lines: 25, 28-32): “Our analyses are on GP practice level and include information on GP practice characteristics, like list size and population. Data on GP characteristics on individual level are not part of NHS digital data and are therefore not included in our analysis. However, these GP characteristics might partly explain variation in antibiotic prescribing as well. 40-42”

• The references 40-42 have been added as well.

3. Line 11 page 4: reference 2 is not about reduction in antibiotic use leading to reduction in antibiotic resistance.

Answer: we agree with the reviewer and we have changed the reference into the reference to the original study of Butler et al (p.4, line:7).

4. Line 28 page 4: reference 9 is not about the number of UTI in their lifetime.

Answer: According to the reviewer's comment we have added the right reference about the number of UTI in their lifetime (p.4, line:22).

5. Between line 36 and 52 part of the text is very similar to the introduction text from the article: Cordoba G, et al. Prescribing style and variation in antibiotic prescriptions for sore throat: cross-sectional study across six countries. BMC Fam Pract. 2015;16:7. When one google some the sentences this article pops-up and you use the same references in the same order. Two things should be done:

- First, as the article was a source of inspiration to write your article , it should be cited.

Answer: we have added the reference Cordoba G, et al. Prescribing style and variation in antibiotic prescriptions for sore throat: cross-sectional study across six countries. BMC Fam Pract. 2015;16:7 (p.4, line:35).

- Secondly, your article and Cordoba et al. article deal with possible determinants of variation in prescription of antibiotics at GP level so your introduction and discussion part should be expanded regarding this topic. You need to expand what is known about determinants in variation in the introduction and in the discussion part to explain why you chose education in integrative medicine as an explanatory variable and the shortcomings of confounding bias.

Answer: Based on the reviewer's comments we have changed and expanded the introduction section with the following sentences (p.5, line:4-8): "GPs as a professional group are expected, following the principles of evidence based medicine, to apply best available evidence to patient's individual situation, within the framework of national and local funding and administrative guidance. Prescription style (measured as the prevalence of prescriptions per GP) is found to be an important factor in the variation in antibiotic prescribing behaviour.18"

- Reference 18 has been added as well.

6. Lines 51-60 page 9 and 1-6 page 10. The numbers differ between the text and table 4.

Answer: we thank the reviewer for noticing these differences and we have changed the figures accordingly. The following changes have been made to the 1) abstract (p.2, lines:24-28): "Despite the very small proportion of NHS IM GPs in England (n=9), negative binomial regression models showed that statistically significantly fewer total antibiotics (RR: 0.78, 95% CI:0.64 – 0.97) and RTI antibiotics (RR 0.74, 95% CI: 0.59 – 0.94) were prescribed at IM GP surgeries compared with conventional NHS GP surgeries. In contrast, the number of antibiotics prescribed for UTI were similar between both practices (RR: 0.91, 95% CI: 0.72 – 1.17)."

2) result section (p.9/10, line:38-1): Our analysis show that IM GP surgeries were associated with lower prescriptions of 'any antibiotic' (RR: 0.78, 95% CI:0.64 – 0.97) and with lower prescriptions of 'RTI specific antibiotic' (RR: 0.74, 95% C.I: 0.59 – 0.94).

7. Furthermore, interpretation like 21% less likely... it is not necessary, as you have just presented the numbers.

Answer: we feel the interpretation might be useful to some readers and therefore we have not deleted this text. Percentages has been changed (see comment above) (p.9/10, lines: 38-2): "Patients consulting an IM GP surgery were 22% less likely to get 'any antibiotic' prescription compared to those who consulted a conventional GP surgery. Receiving a RTI specific antibiotic prescription was

26% less likely among those who consulted an IM GP surgery compared with those who consulted a conventional GP surgery.”

8. Lines 15-29 page 23. The following two paragraphs can stand without this one to make your point about the limitations for interpreting the results due to the small number of IM practices. This paragraph may fit better in the last part of the discussion to point out some secondary findings of your research.

Answer: the reviewer might refer here to page 11 instead of page 23. We have re-ordered the discussion section according the comments of reviewer 2 and reviewer 3. We have moved lines 15-29 after the section on limitations (p.12, lines:22-31).

Minor revision:

9. Line 34 page 2: you should delete the sentence “despite the very small proportion of NHS IM GPs”. In the results you should just show how many conventional and IM surgeries were included in the study.

Answer: we have changed the text accordingly (p.2, lines:30-32): “NHS England GP surgeries employing GPs additionally trained in Integrative or Complementary Medicine have lower antibiotic prescribing rates. Accessibility of IM/CAM within NHS England primary care is limited. Main study limitation is the lack of consultation-data.”

Answer 2: we have added this information more clear to the results (p.9, lines:20-21): “In total 7283 NHS England General Practices (Nconventional=7217/ NimGPs= 9) were included in the analyses.”

10. Line 13-18 page 12: I am not sure whether one can cite with specific numbers unpublished data.

Answer: we have contacted the editorial office. They have agreed this is allowed and advised to add the words “unpublished data” (p.12, line:6): “...prescribed less antimicrobials: -13% (2012), -10% (2013) and -7% (2014) (unpublished data).”

11. Line 13 page 10 from however.... This sentence should be removed. Although still it has to be discussed in the limitations of the study.

12. Lines 8-13 page 11 should be the first part of your discussion section “summary of main findings” afterwards you can start explaining the limitation “like the few number of IM GPs”.

Answer: We have re-ordered the discussion section according the comments of reviewer 2 and reviewer 3. We have moved lines 15-29 after the section on limitations (p.12, lines:22-31). We have changed the second paragraph into (p.12, line:9-14): “This is the first study that retrospectively prescribed antibiotic prescribing in primary care in England with a specific focus on the possible association between the knowledge/use of CAM/IM by GPs and antibiotic prescribing. However, the small proportion of NHS IM GPs in England asks for careful interpretation of the results. Accounting for one other variable (e.g. deprivation or diabetes) did not change our results, but, due to the low number of cases it was not possible to similarly account for more variables.

Reviewer: 3

Reviewer Name: Laura Shallcross

Institution and Country: UCL, London

Please state any competing interests: None declared

Please leave your comments for the authors below

The authors provide a clear description of their analysis and the rationale for the study. However, there are so many limitations to this analysis that it is difficult to draw any conclusions. The work is of interest, but the only conclusion that can really be drawn is that more research is required to establish whether IM therapies can reduce inappropriate antibiotic use.

The authors need to be much more explicit about the limitations of their study including:

1. Ecological data per practice is presented but there is no information on the proportion of IM GP's per practice. In a large practice with only 1 IM GP, that GPs prescribing behaviour is unlikely to have much impact on prescribing at practice level.

Answer: we feel that this information has already been provided in the result section (p.9, lines:3-5) and in table 2: "850 CAM practitioner records were checked against the various CAM registers (Table 1) to identify 21 GPs who are conventionally trained as a GP and also trained in CAM at 19 NHS GP surgeries in England (Table 2)."

We have added the following information (p.9, lines:15-16): "9 NHS IM GP surgeries (urban (N=6), semi-urban (N=2) and semi-rural (N=1)) were included in the analysis."

We feel that the rest of this comment has been answered in the following paragraph (p.12 and 13, lines:37-3): "The impact which any one IM GP could have in terms of antibiotic prescribing may vary hugely between practices partly depending on their status at the practice - as a partner or a salaried employee for example, or as a full-time or part-time worker. In the presented analysis we did not include NHS GP practices that are offering NHS IM/CAM provision by a 'non-GP NHS CAM practitioner' or private IM/CAM practitioner. However, having even one CAM contact within a surgery might give the possibility for others to experience CAM perspectives either formally or informally from them, and for long-held attitudes to be perhaps modified."

2. People accessing IM GPs are likely to be systematically different to patient who do not access IM GPs. For example the reason why they are accessing an IM GP could be because they do not want an antibiotic. This is touched on in the discussion but needs to be highlighted more clearly.

Answer: we agree with the reviewer that the question why patients do want to access an IM GP is an interesting question, but it is not part of our study aim and cannot be answered using our data.

Therefore, we feel that this needs to be addressed in the future like we have stated in the discussion section (p.13, lines:15-17): "However, as patients who self-select to consult IM GPs might be less likely to demand antibiotics, differences in lifestyle and the 'transferability of lifestyle skills' need to be taken into account as well in future study design."

3. What is the geographical spread of these practices? Rural/urban?

Answer: we have added this information to the results section (p.9, lines:15-16): "9 NHS IM GP surgeries (urban (N=6), semi-urban (N=2) and semi-rural (N=1)) were included in the analysis."

4. People may be independently accessing IM GPs in the private sector and then seeking antibiotics from non-IM GPs in the NHS

Answer: we agree with the reviewer that this might be an option and we have added this thought to our discussion section (p.13, lines:3-5): "Additionally, it would be of interest to explore if patients may be independently accessing IM GPs in the private sector and then seeking antibiotics from non-IM GPs in the NHS."

5. Use of prescribing data to infer the type of infection is prone to errors e.g. amoxicillin may be prescribed for uti

Answer: we agree with the reviewer that this is a general limitation of using prescribing data. We have added this remark to our discussion section (p.12, line:8-11): "Although it should be borne in mind that the use of prescribing data to infer the type of infection may be prone to errors, our finding reflects current UK GP clinical guidance."

6. Lack of data on consultation rate is a significant limitation for the reasons the authors state, but this has a major impact on the conclusions that can be drawn from this analysis

Answer: we agree with the reviewer. Therefore, we have added this limitation to the conclusion in the abstract (p.2, line:32): and it is extensively discussed as a main limitation in the discussion section (p.11, lines:16-22).

7. Is this the best approach to identify IM-GPs?

Answer: we are convinced we have used a thorough method to identify NHS IM GPs. Currently there is no existing register which registers IM GPs working in a NHS setting in England.

VERSION 2 – REVIEW

REVIEWER	Marjukka Mäkelä Institute for Health and Welfare Finland
REVIEW RETURNED	12-Dec-2017

GENERAL COMMENTS	The authors have considered the comments and made appropriate revisions or replies. Major comment: The number of IM /CAM practices should be mentioned in the abstract to help readers understand the challenges in the comparison. Minor comment: On p.11, line 9, authors write “This is the first study of retrospectively prescribed antibiotic prescribing in primary care in England...”. The sentence is unclear and should be revised, as this is apparently the first retrospective study comparing antibiotic prescribing practices between IM GP surgeries and conventional GP surgeries in England.
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REVIEWER	Gloria Cordoba University of Copenhagen, Denmark
REVIEW RETURNED	14-Dec-2017

GENERAL COMMENTS	The authors have answered all my comments
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REVIEWER	Laura Shallcross UCL, UK
REVIEW RETURNED	14-Dec-2017

GENERAL COMMENTS	I am happy that the authors have addressed the concerns previously raised. However there is still no explanation about the proportion of IM trained GP's per practice. The authors present practice level data on antibiotic prescribing but it is unclear whether practices that have been included have only IM GP's i.e. all the GPs are IM trained or if the IM GP represents a proportion of all GP's in the practice, in which case their influence on practice level prescribing could be minimal. In my view this is not addressed in either Table 1 or Table 2 or in lines 3-5 on page 9 and it would be helpful for more information on this point to be included please.
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Marjukka Mäkelä

Institution and Country: Institute for Health and Welfare, Finland

Please state any competing interests: None declared

Please leave your comments for the authors below

The authors have considered the comments and made appropriate revisions or replies.

Answer: we thank the reviewer for her valuable comments on the original manuscript.

Major comment: The number of IM /CAM practices should be mentioned in the abstract to help readers understand the challenges in the comparison.

Answer: we have added the number of NHS IM GP surgeries to the abstract (P.2, lines 23-24): "IM GPs (N=9) were comparable to conventional GPs in terms of list sizes, demographics, deprivation scores and comorbidity prevalence.

Minor comment: On p.11, line 9, authors write "This is the first study of retrospectively prescribed antibiotic prescribing in primary care in England..." . The sentence is unclear and should be revised, as this is apparently the first retrospective study comparing antibiotic prescribing practices between IM GP surgeries and conventional GP surgeries in England.

Answer: we have changed the sentence accordingly (P.11, lines: 9-10): "This is the first (retrospective) study comparing antibiotic prescribing rates between IM GP surgeries and conventional GP surgeries in England."

Reviewer: 2

Reviewer Name: Gloria Cordoba

Institution and Country: University of Copenhagen, Denmark

Please state any competing interests: None declared

Please leave your comments for the authors below

Comment: The authors have answered all my comments

Answer: we thank the reviewer for her valuable comments on the original manuscript.

Reviewer: 3

Reviewer Name: Laura Shallcross

Institution and Country: UCL, UK

Please state any competing interests: None declared

Please leave your comments for the authors below

I am happy that the authors have addressed the concerns previously raised. However there is still no explanation about the proportion of IM trained GP's per practice.

Answer: we thank the reviewer for her valuable comments on the original manuscript.

Comment: The authors present practice level data on antibiotic prescribing but it is unclear whether practices that have been included have only IM GP's i.e. all the GPs are IM trained or if the IM GP represents a proportion of all GP's in the practice, in which case their influence on practice level

prescribing could be minimal. In my view this is not addressed in either Table 1 or Table 2 or in lines 3-5 on page 9 and it would be helpful for more information on this point to be included please.

Answer: Due to the differences in the number of (IM) GP partners/salaried (IM) GPs and full time (IM) GP and part time (IM) GP FTE in the practices, meaningful and comparable proportions cannot be calculated. To explain, additional information has been added in the result- and discussion section of the manuscript (P.9, lines 17-21): "Each practice included has at least one IM GP, as GP partner or salaried. The number of IM GPs per practice varies from a minimum of 1 IM GP in a practice with 12 GPs of whom 6 part-time, to a maximum of 3 IM GPs (of whom 2 full time GP practice partners) in a practice with 7 GPs (2 fulltime GPs and 5 part time GPs)."

(P.12-13, lines 38-3): "In our study each of the NHS IM GP practices included at least 1 IM GP. However, as the number of (IM) GP partners and salaried (IM) GPs (full time and part time) in these practices varies, proportions of the number of IM GPs per included NHS IM GP surgery are difficult to determine and in addition, will not provide meaningful information as they do not take into account the power balance of the different GPs within these practices."