PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Primary Care Physicians' Attitudes and Perceptions toward Antibiotic Resistance and Outpatient Antibiotic Stewardship in the United States: A Qualitative Study
AUTHORS	Zetts, Rachel; Stoesz, Andrea; Garcia, Andrea; Doctor, Jason; Gerber, Jeffrey S.; Linder, Jeffrey; Hyun, David

VERSION 1 - REVIEW

REVIEWER	Maria Teresa Herdeiro University of Aveiro, Portugal.
REVIEW RETURNED	01-Nov-2019

GENERAL COMMENTS	Dear authors This is an interesting study about an important and current subject. The article is well structured and written as well. Major comments: 1.The research ethics (e.g. ethics approval) are not mentioned in the paper, as the authorization from national commission of data protection. 2.it is very important to discuss these results, with results from other countries to improve the discussion and to update the references. Minor comments 3. in second paragraph of introduction, put the references as (6,8,9) 4. please update the bibliography.

REVIEWER	Chenxi Liu School of Medicine and Health Management, Tongji Medical School of Huazhong University of Science and Technology China
REVIEW RETURNED	05-Nov-2019

GENERAL COMMENTS	This is an easy-to-read and well-structured study on physicians' attitudes and perceptions of antibiotic resistance and antibiotic stewardship. Minor revision: In the results, providing personal characteristics (age, gender and etc.) of recruited physicians would help readers to better understand that current results were based on what kinds of physicians, Particularly that a few physicians were involved.

REVIEWER	Emma Kirby UNSW Sydney, Australia
REVIEW RETURNED	12-Dec-2019

GENERAL COMMENTS	This paper reports on a study of U.S.-based primary care physicians' attitudes towards resistance, prescribing and stewardship of antibiotics. In doing so it adds to the rapidly growing corpus of research on AMS, AMR and physician attitudes, within broader attempts to curb inappropriate use and thus reduce the threat of resistance. The results describe the views and attitudes of physicians through a series of focus groups. I enjoyed reviewing the paper, and hope that the comments that follow are constructive, and improve the contribution of the manuscript. The introduction/background is brief. The third paragraph of Discussion (p14) could be moved to the background section to give a better sense of what is already known on the topic. In addition, a brief overview of the context of PCPs in the US relative to other high income countries would complement and contextualise the findings of existing work on the topic. P5: "Research has shown clear differences in overall outpatient antibiotic prescribing rates by geographic region". It would be useful, for international readers, to briefly outline or indicate some of these differences (and possible reasons why). Methods: Both deductive and inductive content analysis methods were used – more explanation of the steps for both, if these processes were done discretely or in combination (and so on) is needed. Methods: a reporting checklist should be included (e.g. SRQR) P9: clarify use of language in relation to methodological/epistemological approach/representation. Saying 'participant's believed' needs to be amended; we cannot know if they believed, rather that this is what they said, or said they believed etc. Same re: "the pressure participants experience" – this is picky I know, but it should be 'the pressure participants talked about experiencing' The distinction between themes and responses in the results needs to be articulated a bit more clearly. There are quite a lot of themes; was there a hierarchy/tree? (more on methods will also help this). Are the themes covered overarching? Ie did these run across the questions/exercises, and in what ways etc? It would also be useful to refer to the tables and the data within them more explicitly, as the indicative quotations do add richness to the descriptions. Re: methods. More discussion/explanation of why focus groups were chosen is needed (particularly vis a vis one-on-one interviews). One of the benefits of focus groups is the working together/discursive aspect, but discussion between participants is not shown in the data. It would be great for the reader to see (in the data especially) areas of agreement, disagreement, clarification and so on 'between' participants. This would also give more insight as to whether all the participants had the same or similar views across the

	exercises and respective themes. (for example, when saying 'participants highlighted XXX', was this all participants, a majority, a minority etc? And did participants highlight certain issues because they were asked to, or did these emerge within discussion? (this refers back to my above point re: more explanation of deductive/inducutive analysis too). The first two paragraphs of the discussion section would be better placed in the results section. Discussion: several themes/findings are similar to those in studies of hospital physicians – more commentary/discussion on these parallels across settings (and the implications therein) would be useful. Particularly in thinking about how to improve induvial practices when responsibility for the problem of resistance is often thought to lie with others (ie hospital physicians think the problem lies in the community, PCPs think the problem is one for hospitals, not to mention the responsibility/problem of veterinary practice, agriculture and so on to AMR…) The implications for practice need to be outlined and discussed in more depth. More on the strengths of the study are needed (which is not to say that there are not strengths, but rather, that these could be pointed out more explicitly throughout).

REVIEWER	Eli Feiring University of Oslo, Norway
REVIEW RETURNED	16-Dec-2019

GENERAL COMMENTS	Thank you for this interesting paper. General comments: 1. The literature on AMR-stewardship in hospitals might further inform the paper's discussion about barriers to stewardship implementation in PC (see for example, Skodvin et al Antimicr resistance and infection control 2015, Feiring et al BMC Health Serv Research 2017 , Bjørkman et al Qual Safety HC 2010, Hulcher et al Lancet Infec Dis 2010). 2. The authors should make use of: Mc Cullough AR et al: Not in my backyard: a systematic review of clinicians' knowledge and beliefs about antibiotic resistance. J Antimicrob Chemother 2015; 70 Methods: P6, line 39/40: Did the study participants provide informed written consent, if not, why? P7, line 45: Why did you video-record the groups – did this provide additional data, how did you analyze that data? P7, line 49: How exactly did you use deductive methods? P7, line 51: Which literature are you referring to? P8, line 7: The authors should say something about saturation. Results: P8, line 33: Did some of the potential participants decline the invitation? Why? Discussion: P15, line 50: Conclusion: "…more work is needed to elevate the

	issue of …" This point should have been discussed more systematically in the Discussion. P16, line 5: Conclusion: What can be done "….when designing interventions …"more specifically? This point should have been discussed more systematically in the Discussion.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1
Reviewer Name: Maria Teresa Herdeiro
Institution and Country: University of Aveiro, Portugal.
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below Dear authors This is an interesting study about an important and current subject.
The article is well structured and written as well.

Major comments:
1.The research ethics (e.g. ethics approval) are not mentioned in the paper, as the authorization from national commission of data protection.
RESPONSE: The research ethics question is addressed through the IRB exempt determination. We have added clarifying language to the text to address this concern.

2.it is very important to discuss these results, with results from other countries to improve the discussion and to update the references.
RESPONSE: We have added additional references to studies from other countries in both the introduction and discussion sections – highlighting consistent findings between countries. Added references include:
van der Zande et al. General practitioners' accounts of negotiating antibiotic prescribing decisions with patients: a qualitative study on what influences antibiotic prescribing in low, medium, and high prescribing practices.
O'Doherty et al. Over prescribing of antibiotics for acute respiratory tract infections; a qualitative study to explore Irish general practitioners' perspectives.
Fletcher-Lartey et al. Why do general practitioners prescribe antibiotics for upper respiratory tract infections to meet patient expectations: a mixed methods study.
Rose et al. A qualitative literature review exploring the drivers influencing antibiotic over-prescribing by GPs in primary care and recommendations to reduce unnecessary prescribing.
Sunde et al. General practitioners' attitudes toward municipal initiatives to improve antibiotic prescribing – a mixed-methods study.
McCullough et al. Not in my backyard: a systematic review of clinicians' knowledge and beliefs about antibiotic resistance.
Björkman et al. Perceptions among Swedish hospital physicians on prescribing of antibiotics and antibiotic resistance.
Krockow et al. Balancing the risks to individual and society: a systematic review and synthesis of qualitative research on antibiotic prescribing behaviour in hospitals.
Feiring et al. Antimicrobial stewardship: a qualitative study of the development of national guidelines for antibiotic use in hospitals.
Skodvin et al. An antimicrobial stewardship program initiative: a qualitative study on prescribing practices among hospital doctors.

Minor comments
3. in second paragraph of introduction, put the references as (6,8,9)
RESPONSE: We have made the necessary adjustments to the citation style.

4. please update the bibliography.
RESPONSE: We have updated to include additional studies and references.

Reviewer: 2
Reviewer Name: Chenxi Liu
Institution and Country: School of Medicine and Health Management, Tongji Medical School of Huazhong University of Science and Technology, China Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below This is an easy-to-read and well-structured study on physicians' attitudes and perceptions of antibiotic resistance and antibiotic stewardship.

Minor revision:
In the results, providing personal characteristics (age, gender and etc.) of recruited physicians would help readers to better understand that current results were based on what kinds of physicians, Particularly that a few physicians were involved.
RESPONSE: We did not collect demographic data on our participants. We've added a statement to that effect to the results section.

Reviewer: 3
Reviewer Name: Emma Kirby
Institution and Country: UNSW Sydney, Australia Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below This paper reports on a study of U.S.-based primary care physicians' attitudes towards resistance, prescribing and stewardship of antibiotics. In doing so it adds to the rapidly growing corpus of research on AMS, AMR and physician attitudes, within broader attempts to curb inappropriate use and thus reduce the threat of resistance. The results describe the views and attitudes of physicians through a series of focus groups. I enjoyed reviewing the paper, and hope that the comments that follow are constructive, and improve the contribution of the manuscript.

The introduction/background is brief. The third paragraph of Discussion (p14) could be moved to the background section to give a better sense of what is already known on the topic. In addition, a brief overview of the context of PCPs in the US relative to other high income countries would complement and contextualise the findings of existing work on the topic.
RESPONSE: Thank you for your comment. We have moved the summary of past research from the discussion section to the background section as recommended. We also expanded on a few areas of commonality from previous research on this topic area. Finally, we included a new paragraph providing additional information about the context of primary care in the U.S. compared to other high-income countries.

P5: "Research has shown clear differences in overall outpatient antibiotic prescribing rates by geographic region". It would be useful, for international readers, to briefly outline or indicate some of these differences (and possible reasons why).
RESPONSE: We have added clarifying language to the text to highlight that the difference we are referring to is overall prescribing rates. We also provide an example of the magnitude of difference by comparing the state with the highest prescribing rate to the state with the lowest.

Methods: Both deductive and inductive content analysis methods were used – more explanation of the steps for both, if these processes were done discretely or in combination (and so on) is needed.
RESPONSE: We have added additional information to the methods section to clarify the analytic steps taken by the study authors to analyze the focus group transcripts. We used a deductive analytic approach to identify an initial list of themes (via review of published literature and data familiarity) and apply this list of themes to the transcripts. We then used an inductive approach to identify new themes upon further review of the transcripts.

Methods: a reporting checklist should be included (e.g. SRQR)
RESPONSE: This has been completed.

P9: clarify use of language in relation to methodological/epistemological approach/representation. Saying 'participant's believed' needs to be amended; we cannot know if they believed, rather that this is what they said, or said they believed etc. Same re: "the pressure participants experience" – this is picky I know, but it should be 'the pressure participants talked about experiencing'
RESPONSE: Thank you for highlighting this. We've worked to address this throughout the results section to be more clear in our presentation of the data.

The distinction between themes and responses in the results needs to be articulated a bit more clearly. There are quite a lot of themes; was there a hierarchy/tree? (more on methods will also help this). Are the themes covered overarching? Ie did these run across the questions/exercises, and in what ways etc?
RESPONSE: We've added additional clarification to the text and reformatted to make the themes and groupings clearer for the reader. We had four overarching areas of discussion, with consistent themes identified in each. In particular, the patient demand theme reemerged throughout the focus groups discussions. We've added additional text describing this to that section of the manuscript.

It would also be useful to refer to the tables and the data within them more explicitly, as the indicative quotations do add richness to the descriptions.
RESPONSE: We have reformatted to highlight the relevant table with quotations for each of the four thematic areas. We have not added quotations to the text in order to minimize the word count but hope this will be addressed when formatted for publication, with the tables more in line with the relevant text summaries.

Re: methods. More discussion/explanation of why focus groups were chosen is needed (particularly vis a vis one-on-one interviews). One of the benefits of focus groups is the working together/discursive aspect, but discussion between participants is not shown in the data. It would be great for the reader to see (in the data especially) areas of agreement, disagreement, clarification and so on 'between' participants. This would also give more insight as to whether all the participants had the same or similar views across the exercises and respective themes. (for example, when saying 'participants highlighted XXX', was this all participants, a majority, a minority etc? And did participants highlight certain issues because they were asked to, or did these emerge within discussion? (this refers back to my above point re: more explanation of deductive/inducutive analysis too).
RESPONSE: Thank you for this comment. We used a focus group approach for this study to allow the moderator to draw out areas of agreement and disagreement. We've added language to that effect in the manuscript and have worked to draw out the areas of agreement and disagreement in the description of study results. In regard to how issues were brought up in the discussion, some emerged due to specific questions included in the moderator guide and exercises, and some were more organic. We've highlighted this a bit more in the methods section when describing the moderator guide.

The first two paragraphs of the discussion section would be better placed in the results section.

RESPONSE: We intended the first two paragraphs of the discussion section to re-summarize the results at a high-level that could serve as a basis for discussing similarities and differences to previously published research, delving into how this adds to the existing literature, and highlighting the significance of our study. For the purposes of maintaining the narrative flow for the discussion section, we have opted to keep these summarizations in the discussion section. We have edited to better merge these summaries with how these findings compare to previous research, and to address other reviewer comments.

Discussion: several themes/findings are similar to those in studies of hospital physicians – more commentary/discussion on these parallels across settings (and the implications therein) would be useful. Particularly in thinking about how to improve induvial practices when responsibility for the problem of resistance is often thought to lie with others (ie hospital physicians think the problem lies in the community, PCPs think the problem is one for hospitals, not to mention the responsibility/problem of veterinary practice, agriculture and so on to AMR…)
RESPONSE: Thank you for this recommendation. We have added in references to how some of our findings compare to those from studies in inpatient settings in the discussion section of the manuscript. Additional references include:
Björkman et al. Perceptions among Swedish hospital physicians on prescribing of antibiotics and antibiotic resistance.
Krockow et al. Balancing the risks to individual and society: a systematic review and synthesis of qualitative research on antibiotic prescribing behaviour in hospitals.
Feiring et al. Antimicrobial stewardship: a qualitative study of the development of national guidelines for antibiotic use in hospitals.
Skodvin et al. An antimicrobial stewardship program initiative: a qualitative study on prescribing practices among hospital doctors.

The implications for practice need to be outlined and discussed in more depth. More on the strengths of the study are needed (which is not to say that there are not strengths, but rather, that these could be pointed out more explicitly throughout).
RESPONSE: We have expanded on how healthcare stakeholders should use this information to identify barriers to stewardship implementation and work to overcome these barriers. We've also included additional language around strengths of this study – both new insight (particularly around how these findings relate to the implementation of the CDC's core elements of outpatient stewardship) and study design.

Reviewer: 4
Reviewer Name: Eli Feiring
Institution and Country: University of Oslo, Norway Please state any competing interests or state 'None declared': Noe declared

Please leave your comments for the authors below Thank you for this interesting paper.

General comments:
1. The literature on AMR-stewardship in hospitals might further inform the paper's discussion about barriers to stewardship implementation in PC (see for example, Skodvin et al Antimicr resistance and infection control 2015, Feiring et al BMC Health Serv Research 2017 , Bjørkman et al Qual Safety HC 2010, Hulcher et al Lancet Infec Dis 2010).
REPSONSE: Thank you for this recommendation. We have added in references to how some of our findings compare to those from studies in inpatient settings in the discussion section of the manuscript – including three of the above references:
Björkman et al. Perceptions among Swedish hospital physicians on prescribing of antibiotics and antibiotic resistance.

Feiring et al. Antimicrobial stewardship: a qualitative study of the development of national guidelines for antibiotic use in hospitals.
Skodvin et al. An antimicrobial stewardship program initiative: a qualitative study on prescribing practices among hospital doctors.

2. The authors should make use of: Mc Cullough AR et al: Not in my backyard: a systematic review of clinicians' knowledge and beliefs about antibiotic resistance. J Antimicrob Chemother 2015; 70
RESPONSE: Thank you for this recommendation. We have added reference to this study in the introduction section in order to provide additional context around what is already known on this topic.

Methods:
P6, line 39/40: Did the study participants provide informed written consent, if not, why?
RESPONSE: We added clarification that the study participants all signed informed consent forms.

P7, line 45: Why did you video-record the groups – did this provide additional data, how did you analyze that data?
RESPONSE: Video recordings were provided by the focus group facilities used to conduct each focus group. We added clarification that only the audio-recordings were used to transcribe the focus groups, and the transcriptions were used to identify themes.

P7, line 49: How exactly did you use deductive methods?
RESPONSE: We added additional clarification to the methods section on the specific steps taken by study authors to identify themes. We used a deductive analytic approach to identify an initial list of themes (via review of published literature and data familiarity) and apply this list of themes to the transcripts.

P7, line 51: Which literature are you referring to?
RESPONSE: We have added in the appropriate citations (11-18, 34, 35) to highlight the literature referenced. Two of these were new references for the manuscript:
de Bont et al. Childhood fever: a qualitative study on GPs' experiences during out-of-hours care.
Teixeira Rodrigues et al. Understanding physician antibiotic prescribing behaviour: a systematic review of qualitative studies.

P8, line 7: The authors should say something about saturation.
RESPONSE: We added in an explanation that coding was considered complete once thematic saturation was reached.

Results:
P8, line 33: Did some of the potential participants decline the invitation? Why?
RESPONSE: Some participants did decline the invitation, but the reasons for doing so were not collected. We did add language to the results section that the 52 participants represent those who both accepted the invitation and participated.

Discussion:
P15, line 50: Conclusion: "…more work is needed to elevate the issue of …" This point should have been discussed more systematically in the Discussion.
RESPONSE: Thank you for your recommendation. We have added additional information regarding this earlier in the Discussion section.

P16, line 5: Conclusion: What can be done "….when designing interventions …"more specifically? This point should have been discussed more systematically in the Discussion.

RESPONSE: Thank you for your recommendation. We have added additional information regarding this earlier in the Discussion section.

VERSION 2 – REVIEW

REVIEWER	Maria Teresa herderio iBiMED, Medical Science Department, Aveiro University, Portugal
REVIEW RETURNED	04-Feb-2020

GENERAL COMMENTS	Dear authors This is an interesting study about an important and actual subject. The article is well structured and written. Minor comments: The introduction must be improved with a better comparation with other European studies. The discuss must be improved with a better comparation with other European studies and please describe in more detailed the limitations of the study.

REVIEWER	Eli Feiring University of Oslo, Norway
REVIEW RETURNED	29-Jan-2020

GENERAL COMMENTS	Thank you for the revised paper. I have no further comments.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 4
Reviewer Name: Eli Feiring
Institution and Country: University of Oslo, Norway
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
Thank you for the revised paper. I have no further comments.
RESPONSE: We appreciate your additional review of this manuscript.

Reviewer: 1
Reviewer Name: Maria Teresa Herderio
Institution and Country: iBiMED, Medical Science Department, Aveiro University, Portugal
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
Dear authors
This is an interesting study about an important and actual subject.
The article is well structured and written.

Minor comments:
The introduction must be improved with a better comparation with other European studies.
RESPONSE: Thank you for this comment. We've revised the introduction and added studies to better draw out the similarities previous European qualitative research has shown around drivers of inappropriate antibiotic prescribing.

The discuss must be improved with a better comparation with other European studies and please describe in more detailed the limitations of the study.
RESPONSE: Thank you for these recommendations. We have added in additional studies and comparisons that present findings from previous qualitative research from European and other countries that highlight the impact of stewardship and quality improvement interventions. We also expanded the limitations section to acknowledge limitations in geographic generalizability.