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

TITLE (PROVISIONAL)	Understanding the delayed prescribing of antibiotics for respiratory tract infection in primary care: A qualitative analysis.
AUTHORS	Ryves, Rachel; Eyles, Caroline; Moore, Michael; McDermott, Lisa; Little, Paul; Leydon, Gerry

VERSION 1 - REVIEW

REVIEWER	Chris Butler University of Oxford UK I have had grants in common with some of the authors, published together and worked within the same field.
REVIEW RETURNED	24-Mar-2016

GENERAL COMMENTS	Many thanks for asking me to review this highly relevant, well conducted, and well reported study. Delayed prescribing is an important area for the topical and pressing field of antimicrobial stewardship and better understanding its use and maximising its potential will be of great interest to a wide rage of stakeholders. I have only one or two comments to make which may help gild the lily ever so slightly. Only one is substance and that relates to probably inadvertent assertions about effects that changes to clinical practice (suggested by the findings of this qualitative research) would have. • Abstract Results: Suggest indicate what the headline findings were within the topic “GP Factors”, “Patient -practitioner” factors: add something concrete such as lack of agreed prescribing strategy. GP experience was found to be important: I would suggest saying this rather than simply saying that GP factors were relevant. • Based on the data presented in the results, we can’t say that greater emphasis in the way in which GPs communicate with patients about RTIs would be beneficial…” • Maximum variation sampling is well justified and appropriate • Participant recruitment is well explained with a very clear and useful useful diagram • The term ‘GP factors’ is a bit unclear to my ear: do the authors mean GP demographic features and characteristics? • Results: Data are well presented and interpretations well well supported by the data • In the Conclusion again, the authors assert that greater emphasis on the way GPs communicate would be beneficial. It might well be the case, but a trial would be needed to demonstrate that.

REVIEWER	Carl Llor

	Primary Healthcare Centre Via Roma. University Institute in Primary Care Research Jordi Gol, Barcelona. I report a grant from the Jordi Gol i Gurina Foundation for a research stage at the University of Cardiff in 2013, as well as research grants from the European Commission (Sixth and Seventh Programme Frameworks), Catalan Society of Family Medicine, and Instituto de Salud Carlos III.
REVIEW RETURNED	26-Mar-2016

GENERAL COMMENTS	The paper is well done and is written very clearly. This is a nice study about the views and understanding of GPs about the delayed antibiotic prescribing strategies addressed to reduce the inappropriate use of antibiotics. This qualitative-based study is, however, not innovative, since other UK researchers have already published a qualitative study on the same topic in 2011 (Managing self-limiting respiratory tract infections: a qualitative study of the usefulness of the delayed prescribing strategy). Some of the themes and sub-themes are in fact quite similar and, in my opinion, you study should make a stronger argument about how the present paper improves the old one, since this comparison between the two papers is not mentioned in the Introduction section. In fact, you should mention Peters's study in this section and better explain why the present study was necessary. Although this is a qualitative-based study, the GPs response rate was low. This finding should be discussed more in depth when you discuss the results. You point out the pros and cons of delayed prescribing of antibiotics very clearly but I wonder what these results would have been if more GPs had participated. You paid 50 pounds for the phone interview and despite this, only 32 out of the 156 practices took part in the interviews. Qualitative analysis is a good way to elicit the positive and negative sides of a topic, but I think you might have recruited more favourable GPs in this study and therefore other negative aspects of the delayed prescribing of antibiotics may have been missed. You should better explain this point. Linked to the previous query, and despite being a study based on a qualitative analysis, readers would like to know how many GPs of those you interviewed actually used delayed prescribing on a regular basis. It is not clear to me if you read the different delayed antibiotic prescribing strategies when you asked them to select the preferred strategy used in their consultations as most of them were more prone to issue the prescription in consultation and advise patients to collect it. You should better explain this part in the text. Why did you consider the 'offer re-consultation if symptoms worsen' as a type of delayed prescribing of antibiotics? In fact, this strategy is not involved in the definition you considered. When a GP asks a patient to reconsult if his/her symptoms worsen he/she is supposed to have another clinical examination and the management will be based on the second history taken plus examination. Please explain. One of the key messages of this study is the low feedback received by GPs when they used the delayed antibiotic prescribing. However, there is no explanation of the strategies used by the GPs

	themselves to overcome this problem, such as calling patients several days after the visit to know if they cashed in the prescription, or they talked to the patients about this issue in other consultations, etc. Did you get any information about this in the interviews?

REVIEWER	Nick Francis Cardiff University UK I collaborate with Paul Little and Mike Moore, but do not consider this to be a conflict of interest. I have no other potential conflicts of interest.
REVIEW RETURNED	05-May-2016

GENERAL COMMENTS	This qualitative study makes a useful addition to our understanding of antimicrobial stewardship challenges, and particularly the use of delayed prescribing, in primary care. I feel that the paper could be enhanced by addressing the following points: Introduction Asking a patient to arrange a clinical review if their condition worsens (page 4, line 23 and page 9, line 47) is not really 'delayed prescribing', as has been previously described in the literature. Page 4, line 31 is a little misleading. The evidence (including the evidence cited) suggests that delayed prescribing is associated with antibiotic consumption that is a little bit higher than not prescribing initially. Methods There were problems with recruitment. Did this result in participants that are unlike most GPs? It is not clear to me whether you identified the prescribing level of the practice or the CCG? Ideally, you want the prescribing level of the participating clinician, but failing that surely the practice prescribing level is the next best thing. Within a CCG there will be higher and lower prescribing practices (and clinicians), even if the CCG is a higher prescribing CCG overall. The study was conducted by a team that have conducted lots of trials of delayed prescribing. It would be nice to know if the participating practices had experience of using delayed prescribing as part of a trial? Discussion The discussion is a bit repetitive (of the results). It could be improved by tightening it up. Page 18, line 50 mentions the RCGP TARGET Toolkit, but this is not mentioned in the results. It would help if this was added in parentheses after the sentence on page 14, lines 31-32). The sentence on page 18, lines 21-24 could be taken to suggest that delayed prescriptions that are used are 'necessary' or 'beneficial'. There is little evidence to suggest that longer duration of symptoms is associated with greater response to antibiotics, in fact the evidence suggests the contrary. It is helpful to give people an accurate idea of how long their symptoms are likely to last, but perhaps it is not important to give them a 'timeline' for collecting a delayed prescription. Suggest revising page 18, line 52 so that it is more relevant to a wider audience and not just those in England.

	One of the main things that I got from reading this paper was that if I implement the practice described by GP 17 on page 10 then I will at least get some feedback on how often these prescriptions are collected. You might want to incorporate something along these lines (i.e. GPs might want to consider experimenting with different approaches …) into the discussion? Minor More accurate to say reduces unnecessary consumption, rather than prescribing (page 4, line 16).

REVIEWER	Sigurd Høye Department of General Practice, University of Oslo, Norway
REVIEW RETURNED	09-May-2016

GENERAL COMMENTS	Thank you for the opportunity to review this interesting manuscript. It is of great importance to understand why and how delayed prescribing is being used in primary care, and how the strategy best can be performed. The study is performed in the method's "country of origin", which I consider a strength. I have some major comments and some minor comments that I hope can contribute to making this manuscript even better. Major comments: My main worry is that it seems to be taken for granted that delayed prescribing is an effective tool for GPs to reduce antibiotics consumption. There is an overwhelming evidence from RCTs that this is the case, however, everyday practice is something different from RCTs, and when it comes to delayed prescribing, this is a crucial point. In connection to this, I miss information on the researchers – what are your opinions on delayed prescribing? (Item 7-8 in COREQ checklist http://intqhc.oxfordjournals.org/content/19/6/349.long) What did you expect to find? This is particularily important, since your conclusion is quite the opposite of the conclusion Peters et al came to. Also – it seems that you postulate a "correct use" of delayed prescribing. What defines how DP "should be used" (P2L20)? In the interview topic guide, you ask the respondents "If you don't use delayed prescribing, could you tell my why this is" – but you do not ask them why they use it (if they use it). In order to understand delayed prescriping, I would say that such a question would be necessary. However, it seems that you have some material on this (P10L51). I would have preferred some more information on the repondents use of DP – how often, in what situations, to which patients. In the discussion, some points/conclusions are made without letting the reader know how you came to these conclusions (mentioned in detail under Minor points). The manuscript is quite extensive – more than 7000 words (including the quotes). In my opinion, qualitative manuscripts do not need to be more extensive than quantitative manuscripts, given a thorough analysis. In my opinion (again), the scientific value increases if the analysis and the results presentation focuses on what is new, unexpected and relevant, leaving the obvious out of the manuscript. It seems that you have succeeded in this to a great

	extent, but there is room for improvement: To me, reporting of theme 1 seems to be unnecessary in this manuscript. I would recommend using a checklist for qualitative research (BMJ Open suggests COREQ: http://intqhc.oxfordjournals.org/content/19/6/349.long) Minor comments: P2L21: “These included GP factors, the role of the patient-practitioner relationship during the consultation, and a lack of an agreed prescribing strategy within and between practices.» You specify the last of these three factors, but not the two first factors. For the reader, it would be nice – even in the abstract – to get to know how GP factors and patient-practitioner relationship are influential. P2L30: I am afraid that the conclusion does not guide clinicians, researchers and policy makers in what do to next. How to accomplish “greater uniformity” and “greater emphasis”? P3L23: “Individual prescribing data was not available and this may have been beneficial to ensure maximum variance of the sample interviewed.” To me, the sentence seems to say that the lack of data was beneficial. I guess you mean the opposite. P4L26: “The use of delayed prescribing can limit the collection of prescriptions by patients to just 40% (9, 10).” The number (40%) and the references seem to have been chosen a bit arbitrarly. I suggest using the Cochrane review. P4L31: “delayed prescribing may be as effective as no prescribing in reducing antibiotic use for RTI,” I find this a bit exaggerated. P4L42: «Reports suggest that the delayed prescribing technique is not widely or consistently used by GPs (2). I have searched the document (ref 2), but I did not find data on this. P4L44: «Moreover, some GPs have been reported to be critical of the delayed prescribing approach when faced with uncertainty or a lack of clarity concerning the pathophysiology of a condition (14).» I can not find anything on this in ref 14. P6L32: I do not understand why all the 664 GPs in the eligible areas were invited. Even though the participants «varied according to key parameters», an acceptance rate of 6-7% should be discussed more in detail. P9L38: I find that table 3 is unnecessary. The sample is not representative, and the numbers give no valuable information. P16L39: «One notable finding was that GPs recruited from high-prescribing

	practices gave responses expected from GPs with low individual prescribing rates.» This needs some more explanation. Which responses? And what did you expect? Also: I would like to see a definition on high- and low-prescribing. How large is the difference? And does delayed prescribing count as a prescribing in this high-low dicotomy? In Francis' GRACE- paper, both Southampton and Cardiff had a low no-prescribing rate, but the delayed prescribing rate in Southamptom was 10 times that in Cardiff: http://www.ncbi.nlm.nih.gov/pubmed/22947585 P15L52: «the findings reflect those of another qualitative study investigating delayed prescribing strategies in primary care» I do not fully agree – the respondents in this study seems to be more positive towards DP, compared to the respondents in Peters' study. It might be that you did not succeed in recruiting GPs who were negative towards the method. P17L6: «Antibiotic prescriptions would be post-dated with a considerably short delay compared to research suggesting delays of up to 14 days for some RTIs (22).» I can not find anything on this in the results section. P18L18: «Our findings further suggest that GPs are more positive towards delayed antibiotic prescribing strategies through clearer understanding of the process.» I do not fully understand this. Which results are referred to here? P18L19: «Moreover, the current study suggested that GPs were not taking into account the variation in the natural history of RTI» Same as above.

REVIEWER	Dr Sarah Peters University of Manchester I have published a similar study, and mention this in my review.
REVIEW RETURNED	10-May-2016

GENERAL COMMENTS	The topic of ways to increase management of RTIs without recourse to antibiotics is an extremely important. Delayed prescribing is within NICE guidelines, yet the evidence base that it is a useful alternative to 'no-prescribing policy' is lacking. Understanding how GPs perceive and use this approach and why they adopt it in contrast to immediate prescribing, or not prescribing is a valuable step in informing how to support prescribers better manage these consultations. It is good to see a qualitative approach taken to this question and this seems a reasonably well-conducted study. However I do have some concerns about the reporting of the methods, the completeness of the analysis and discussion of findings. 1. The details of the methods need explaining further. Firstly around the sampling (what variables were sampled on for the purposive sampling) and sample size. An n of 50 was suggested, which seems very large and beyond what would be expected for a study of rich

	data. More justification is needed of this. The abstract says the n was 32, but Figure 2 suggests it was 46. Secondly, more detail is needed about the steps taken to increase trustworthiness of the final analysis, including use of wider research team (and their backgrounds) in establishing the coding framework and its application. It currently looks like it was done entirely by one person, which wouldn't be usual or good practice in qualitative methods. How was thematic saturation achieved and how did you know? Mention saturation is in the limitations section. I do not think that 'face validity' is a meaningful construct in qualitative research and it would be more appropriate to discuss trustworthiness of analysis. Although recruitment was low, how might this have influenced the data, e.g. respondents may be more familiar/use DP so data around the challenges of using it may have been limited. Taking a purposive approach to sampling does, to some extent address this issue. Furthermore, interestingly, Figure 2 suggests recruitment was better in high-prescribing practice which would counter this hypothesis. This could be discussed further. 2. The findings are very long and at times descriptive rather than analytical. Sometimes the phrasing suggests a theme is simply a section of the topic guide (e.g. line 55, GPs were invited to reflect on factors that acted as facilitators or barriers… theme being 'factors that influence use of DP). Several sections report what a single GP said, and then another GP. Together this suggests that it would be possible to achieve further synthesis and more analysis was needed. With this number of interviews I would imagine the data were very rich, and I was disappointed the authors haven't taken the analysis further and been more interpretive. I was hoping that more nuanced findings might have emerged. For example, the idea that a DP is a 'contradictory message' (line 46) and 'Muddies the water' (line 41) was raised but not explored in relation to other areas that seem to influence the interaction, e.g. maintaining patient relationship. None of this comes out in the abstract, article summary and is lost in the dense description of the data. 3. The introduction section suggests the evidence base for DP as an approach is clear, in terms of reassuring patients and validating their concerns around respiratory tract infections. I do not believe the evidence about this is as clear as is intimated. Delayed prescribing potentially provides patients with a confused message (they aren't effective for a viral infection, but here is one just in case), and the patients views on this phenomenon are lacking from the literature. I conducted a very similar study to the one reported here (mentioned in the Discussion, ref 21) and was hoping that this study would have taken that work on further. There is certainly scope for more work in this field, but the authors need to make it clear what is novel here, and how the data and analysis extends current knowledge.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 Comments

"Only one is substance and that relates to probably inadvertent assertions about effects that changes to clinical practice (suggested by the findings of this qualitative research) would have."
RESPONSE
Thank you for this comment. We are uncertain of the point being made and would appreciate it if the reviewer could expand/point to the particular parts of the manuscript in question.

"Abstract Results: Suggest indicate what the headline findings were within the topic “GP Factors”, “Patient -practitioner” factors: add something concrete such as lack of agreed prescribing strategy. GP experience was found to be important: I would suggest saying this rather than simply saying that GP factors were relevant."
RESPONSE
Thank you for your comments on this – we have changed the results section to highlight some headline findings (Page 2, lines 21-26).

"Based on the data presented in the results, we can’t say that greater emphasis in the way in which GPs communicate with patients about RTIs would be beneficial…”
RESPONSE
We have changed the statement in the abstract to read: “Finally, GPs may need further guidance on how to answer the concerns of patients without interpreting these questions as a demand for antibiotics, as well as educating the patient about antimicrobial resistance and supporting a good patient-practitioner relationship.” (Page 2, Line 35-40). We feel this reflects the key message of the study.

"Maximum variation sampling is well justified and appropriate"
RESPONSE
Thank you.

"Participant recruitment is well explained with a very clear and useful diagram"
RESPONSE
Thank you.

"The term ‘GP factors’ is a bit unclear to my ear: do the authors mean GP demographic features and characteristics?"
RESPONSE
We have changed the sub-theme heading to “Influences on GP decision making” for clarity.

"Results: Data are well presented and interpretations well supported by the data"
RESPONSE
Thank you.

"In the Conclusion again, the authors assert that greater emphasis on the way GPs communicate would be beneficial. It might well be the case, but a trial would be needed to demonstrate that."
RESPONSE
We have changed the conclusion to say that emphasis on the way GPs communicate “may” be beneficial, and suggested a trial in this in the further research section (Page 20, Line 37).

Reviewer 2 Comments:

"This qualitative-based study is, however, not innovative, since other UK researchers have already published a qualitative study on the same topic in 2011 (Managing self-limiting respiratory tract infections: a qualitative study of the usefulness of the delayed prescribing strategy). Some of the themes and sub-themes are in fact quite similar and, in my opinion, you study should make a stronger argument about how the present paper improves the old one, since this comparison between the two papers is not mentioned in the Introduction section. In fact, you should mention Peters’s study in this section and better explain why the present study was necessary."
RESPONSE
Thank you for this comment. We believe that we provide a strong rationale for this study within the

introduction section, and mention which elements of our findings resonate with Peters' study in the discussion section. We suggest that our study furthers the work of Peters et al. by highlighting that GPs with a greater understanding of delayed prescribing strategies and experience of using it are more positive towards the approach (Page 18, Line 18-19). Moreover, our study highlights that GPs may not take into account the variation in the natural history of RTI and will issue a prescription with a short delay, regardless of the anticipated duration of the illness (Page 18, Line19-22).

"Although this is a qualitative-based study, the GPs response rate was low. This finding should be discussed more in depth when you discuss the results. You point out the pros and cons of delayed prescribing of antibiotics very clearly but I wonder what these results would have been if more GPs had participated. You paid 50 pounds for the phone interview and despite this, only 32 out of the 156 practices took part in the interviews. Qualitative analysis is a good way to elicit the positive and negative sides of a topic, but I think you might have recruited more favourable GPs in this study and therefore other negative aspects of the delayed prescribing of antibiotics may have been missed. You should better explain this point."
RESPONSE
We appreciate that the GP response rate for the study was low and mention this as a limitation in the discussion section. We mention that analytic saturation was reached after 32 interviews as no new themes or ideas were emerging from the data. (Page 5, Line 50-52). Moreover, we argue that our findings resonate with Peters' et al.'s study, which increases the confidence in transferability of our findings to the literature. Finally, the self-selecting nature of our sample is a limitation and we have mentioned this in the manuscript under the "Strengths and Limitations" section in the discussion. This is however a limitation faced by all studies of this kind.

"Linked to the previous query, and despite being a study based on a qualitative analysis, readers would like to know how many GPs of those you interviewed actually used delayed prescribing on a regular basis."
RESPONSE
All GPs reported that they had used delayed prescribing where they felt it was appropriate. We have included a sentence to reflect this on Page 9, Line 38.

"It is not clear to me if you read the different delayed antibiotic prescribing strategies when you asked them to select the preferred strategy used in their consultations as most of them were more prone to issue the prescription in consultation and advise patients to collect it. You should better explain this part in the text."
RESPONSE
A key aim was to elicit their awareness of the varying delayed prescribing approaches available. Therefore, we did not provide a list of approaches for GPs to select from /discuss. We did not want to influence their responses during the interview. We have clarified the interview process in the manuscript: "GPs were invited to provide their own definition and their method of delaying prescribing" (Page 9, Line 24).

"Why did you consider the 'offer re-consultation if symptoms worsen' as a type of delayed prescribing of antibiotics? In fact, this strategy is not involved in the definition you considered. When a GP asks a patient to reconsult if his/her symptoms worsen he/she is supposed to have another clinical examination and the management will be based on the second history taken plus examination. Please explain."
RESPONSE
GPs interviewed in the study offered this strategy as an approach to delayed prescribing. As mentioned above, we did not provide GPs with examples of delayed prescribing strategies because we wanted to elicit their understandings/perspectives of delayed antibiotic prescribing. As you indicate, it is of interest that some articulated 're-consultation' as a form of delay. Given our

clarification above (Page 9, Line 24) we hope this distinction is clear (i.e. this point reflects GP views and not researcher definition).

"One of the key messages of this study is the low feedback received by GPs when they used the delayed antibiotic prescribing. However, there is no explanation of the strategies used by the GPs themselves to overcome this problem, such as calling patients several days after the visit to know if they cashed in the prescription, or they talked to the patients about this issue in other consultations, etc. Did you get any information about this in the interviews?"
RESPONSE
This is an interesting point. We did not explicitly ask GPs about their strategies to overcome this problem, such as calling patients after the visit. Equally, GPs did not volunteer such strategies. This would be a useful addition in future work. We mention in the concluding comments that approaches to overcoming this problem need to be investigated.

Reviewer 3 Comments:

"Asking a patient to arrange a clinical review if their condition worsens (page 4, line 23 and page 9, line 47) is not really 'delayed prescribing', as has been previously described in the literature. Page 4, line 31 is a little misleading. The evidence (including the evidence cited) suggests that delayed prescribing is associated with antibiotic consumption that is a little bit higher than not prescribing initially."
RESPONSE
Thank you for your comments – we have removed this sentence (page 4, line 23) from the manuscript.
In terms of page 9, line 50, this was a method of delayed prescribing as described by participants. Participants were invited to give their understanding of differing approaches to delayed prescribing, and this was a method described by GPs (not suggested by the researchers).

"There were problems with recruitment. Did this result in participants that are unlike most GPs?
It is not clear to me whether you identified the prescribing level of the practice or the CCG? Ideally, you want the prescribing level of the participating clinician, but failing that surely the practice prescribing level is the next best thing. Within a CCG there will be higher and lower prescribing practices (and clinicians), even if the CCG is a higher prescribing CCG overall."
RESPONSE
Thank you this is an important point. Unfortunately we were unable to obtain individual prescribing data and mention this as a limitation in the discussion section, as well as explaining that we are aware that some GPs will have higher and lower prescribing levels compared to their practice and CCG levels. We have edited the methods section to clarify that we selected practices with the highest prescribing data in the highest prescribing practices, and practices with the lowest prescribing data from the lowest prescribing CCGs, according to STAR-PU data (Page 5, Line 14-15).

"The study was conducted by a team that have conducted lots of trials of delayed prescribing. It would be nice to know if the participating practices had experience of using delayed prescribing as part of a trial?"
RESPONSE
Thank you for this observation. Unfortunately we did not collect data on this. No GPs mentioned participating in past trials of delayed antibiotic prescribing.

"Page 18, line 50 mentions the RCGP TARGET Toolkit, but this is not mentioned in the results. It would help if this was added in parentheses after the sentence on page 14, lines 31-32)."
RESPONSE

Thank you, we have now referenced the TARGET toolkit in the results section as per your recommendation (Page 14, Line 33).

"The sentence on page 18, lines 21-24 could be taken to suggest that delayed prescriptions that are used are 'necessary' or 'beneficial'. There is little evidence to suggest that longer duration of symptoms is associated with greater response to antibiotics, in fact the evidence suggests the contrary. It is helpful to give people an accurate idea of how long their symptoms are likely to last, but perhaps it is not important to give them a 'timeline' for collecting a delayed prescription."
RESPONSE
Thank you for this comment. There is some evidence (from the DESCARTE study, Little et al. 2014) that delayed prescription reduces complications similarly to immediate antibiotics and reduces re-consultations with prolonged symptoms more than either immediate or no antibiotics.

"Suggest revising page 18, line 52 so that it is more relevant to a wider audience and not just those in England."
RESPONSE
Thank you, we have changed the sentence to reflect that implementing guidelines and policies should be on a wider scale, as per your recommendation (Page 18, Line 54).

"More accurate to say reduces unnecessary consumption, rather than prescribing (page 4, line 16)."
RESPONSE
Thank you, we have made this change.

"One of the main things that I got from reading this paper was that if I implement the practice described by GP 17 on page 10 then I will at least get some feedback on how often these prescriptions are collected. You might want to incorporate something along these lines (i.e. GPs might want to consider experimenting with different approaches …) into the discussion?"
RESPONSE
Thank you for this. We have added the sentence: "GPs may want to consider experimenting with different approaches to delayed prescribing to ascertain how best to obtain feedback on how often prescriptions are collected".(Page 19, Line 10-13).

Reviewer 4 Comments:

"My main worry is that it seems to be taken for granted that delayed prescribing is an effective tool for GPs to reduce antibiotics consumption. There is an overwhelming evidence from RCTs that this is the case, however, everyday practice is something different from RCTs, and when it comes to delayed prescribing, this is a crucial point. In connection to this, I miss information on the researchers – what are your opinions on delayed prescribing? (Item 7-8 in COREQ checklist http://intqhc.oxfordjournals.org/content/19/6/349.long) What did you expect to find? This is particularly important, since your conclusion is quite the opposite of the conclusion Peters et al came to. Also – it seems that you postulate a "correct use" of delayed prescribing. What defines how DP "should be used" (P2L20)?"
RESPONSE
Thank you for your comments. There is evidence from the DESCARTE study that although the antibiotic use is higher than the trials would suggest, there is still a reduction in use compared with an immediate prescription, and comparable or better outcomes than with immediate antibiotics. The team approached the research with an open mind and did not anticipate specific findings. We are confident that the rigour of the study and study team safeguarded the integrity of our interpretations and the findings presented.
We believe that our findings are similar to those from the Peters study, and have made comparisons

in the “Comparison with existing literature” section in the discussion section (page 18).
We have changed the sentence in the abstract to “All GPs had a good understanding of RTI management and how the delayed prescribing approach could be used in primary care”, to remove any postulation of a correct use of delayed prescribing (Page 2, Line 19).
Thank you for this comment. As mentioned in the methods section, a semi-structured topic guide was used to interview GPs. Question 3a of the guide asks the GPs to describe whether they use or don't use any form of delayed prescribing in their practice. The use of the guide allowed us to probe further and obtain data on why delayed prescribing is used, and an overview of how GPs tend to use the delayed prescribing strategy in practice.
We believe we have presented information on participant use of delayed prescribing and the kinds of situations when they may elect to use it.

"In the discussion, some points/conclusions are made without letting the reader know how you came to these conclusions (mentioned in detail under Minor points)."
RESPONSE
Thank you – we have responded to this comment within the minor points section.

"The manuscript is quite extensive – more than 7000 words (including the quotes). In my opinion, qualitative manuscripts do not need to be more extensive than quantitative manuscripts, given a thorough analysis. In my opinion (again), the scientific value increases if the analysis and the results presentation focuses on what is new, unexpected and relevant, leaving the obvious out of the manuscript. It seems that you have succeeded in this to a great extent, but there is room for improvement: To me, reporting of theme 1 seems to be unnecessary in this manuscript."
RESPONSE
Thank you for this comment. We appreciate that the manuscript is lengthy but we felt that it was important to be as transparent as possible in explaining how we conducted the study, as well as giving a detailed account of the findings. We feel that the inclusion of Theme 1 “sets the scene” for the reporting of our findings.

"P2L21: “These included GP factors, the role of the patient-practitioner relationship during the consultation, and a lack of an agreed prescribing strategy within and between practices.» You specify the last of these three factors, but not the two first factors. For the reader, it would be nice – even in the abstract – to get to know how GP factors and patient-practitioner relationship are influential."
RESPONSE
This comment reflects that of Reviewer 1 who suggested the same amendments. We have changed the abstract to reflect these comments (Page 2, Line 22-25).

"P2L30: I am afraid that the conclusion does not guide clinicians, researchers and policy makers in what do to next. How to accomplish “greater uniformity” and “greater emphasis”?"
RESPONSE
We have listed some areas for future research and clinical implications in our discussion section, under the sections “Implications for policy, research, and practice”. The conclusion gives an overall summary of the findings of the paper.

"P3L23: “Individual prescribing data was not available and this may have been beneficial to ensure maximum variance of the sample interviewed.” To me, the sentence seems to say that the lack of data was beneficial. I guess you mean the opposite."
RESPONSE
We would like to clarify that being able to access individual prescribing data would have enabled us to select practitioners with differing prescribing rates at an individual level, rather than at a practice level, which may have increased the variance of our sample and potentially provided more generalizable views towards delayed prescribing. This is mentioned in the Strengths and limitations section (Page

16, Line 39-43).

"P4L26: “The use of delayed prescribing can limit the collection of prescriptions by patients to just 40% (9, 10).” The number (40%) and the references seem to have been chosen a bit arbitrarily. I suggest using the Cochrane review."
*Thank you for your comment. We have added the Cochrane as a third source of reference to the manuscript.

"P4L31: “delayed prescribing may be as effective as no prescribing in reducing antibiotic use for RTI,” I find this a bit exaggerated."
RESPONSE
Thank you for this comment. We have changed the sentence to read: “delayed prescribing has the potential to be more effective in reducing antibiotic use for RTI, so long as health professionals provide clear treatment advice to patients” (Page 4, Line 27-29) to emphasise that communication between the patient and practitioner is an important factor for successful delayed antibiotic prescribing.

"P4L42: «Reports suggest that the delayed prescribing technique is not widely or consistently used by GPs (2). I have searched the document (ref 2), but I did not find data on this."
RESPONSE
We have changed the sentence to read: “Reports on antibiotic prescribing suggest that the delayed prescribing technique may not be widely or consistently used by GPs”. (Page 4, Line 39-40)

"P4L44: «Moreover, some GPs have been reported to be critical of the delayed prescribing approach when faced with uncertainty or a lack of clarity concerning the pathophysiology of a condition (14).» I cannot find anything on this in ref 14."
RESPONSE
Thank you for highlighting this error – we have changed the reference to refer to the diagnostic/prognostic uncertainty identified in the Peters et al. paper.

"P6L32: I do not understand why all the 664 GPs in the eligible areas were invited. Even though the participants «varied according to key parameters», an acceptance rate of 6-7% should be discussed more in detail."
RESPONSE
As mentioned in the methods section, we had difficulties in getting sufficient expressions of interest through telephone contact alone. Therefore we approached all GPs within all GP practices identified within the CCGs with a letter from the RCGP National Clinical Champion for Antimicrobial Stewardship. As we did not know the individual prescribing data for GPs we felt it best to approach all GPs within the practice.

"P9L38: I find that table 3 is unnecessary. The sample is not representative, and the numbers give no valuable information."
RESPONSE
Thank you for this comment, however, we feel that keeping this table in the manuscript is preferable as it gives some indication to the reader an idea of GPs preference for particular delayed prescribing strategies.

"P16L39: «One notable finding was that GPs recruited from high-prescribing practices gave responses expected
from GPs with low individual prescribing rates.» This needs some more explanation. Which responses? And what did you expect? Also: I would like to see a definition on high- and low-prescribing. How large is the difference? And does delayed prescribing count as a prescribing in this

high-low dichotomy? In Francis' GRACE- paper, both Southampton and Cardiff had a low no-prescribing rate, but the delayed prescribing rate in Southampton was 10 times that in Cardiff: http://www.ncbi.nlm.nih.gov/pubmed/22947585"

RESPONSE

We have now streamlined the strengths and limitations section for greater clarity to highlight the limitation of not having individual prescribing data and the impact it may have on our findings: "However, one notable limitation was that individual prescribing behaviours of GPs were unknown. Therefore the prescribing rates of the practices obtained from the national prescribing data may not reflect the prescribing rates of the GPs interviewed for the study. Having data illustrating individual prescribing rates of GPs would have been beneficial to recruit a more representative sample." (Page 16, Line 39-43).

We have now included that practices were identified as the highest-/lowest- prescribing practices "according to Specific therapeutic group age-sex related prescribing units (STAR-PU) data" (Page 5, Line 14-15).

Regarding the comment on the Francis paper, there were very small numbers in both sites of Southampton and Cardiff.

DESCARTE as a national study provides useful data and demonstrated more clearly that DP was used in more than 15% of consultations.

"P15L52: «the findings reflect those of another qualitative study investigating delayed prescribing strategies in primary care» I do not fully agree – the respondents in this study seems to be more positive towards DP, compared to the respondents in Peters' study. It might be that you did not succeed in recruiting GPs who were negative towards the method."

RESPONSE

Thank you for this comment, which is similar to that of Reviewer 2. In the discussion section we suggest that the findings are similar to that of Peters et al.'s paper, but we add to their study in that GPs appear to have a positive attitude towards delayed prescribing. In the limitations section we do mention the self-selecting nature of the sample and the possibility that we may have recruited GPs who were more positively inclined than those who did not participate.

"P17L6: «Antibiotic prescriptions would be post-dated with a considerably short delay compared to research suggesting delays of up to 14 days for some RTIs (22).» I can not find anything on this in the results section."

RESPONSE

We have mentioned that GPs would issue delayed prescriptions during a consultation but would not be clear when the script should be used. One example is where GP9 says that "if you're no better in 48 hours" to collect a prescription is a "mixed message" (Page 11, Line 54-56). This plus references to the general nuanced approach to the natural history of RTI indicated that GPs may issue prescriptions with a short delay compared to what guidelines recommend.

"P18L18: «Our findings further suggest that GPs are more positive towards delayed antibiotic prescribing strategies through clearer understanding of the process.» I do not fully understand this. Which results are referred to here?"

RESPONSE

We have edited the sentence to "GPs with a greater understanding of delayed prescribing strategies and experience of using it are more positive towards the approach." (Page 18, Line 17-19). We hope this gives greater clarity.

"P18L19: «Moreover, the current study suggested that GPs were not taking into account the variation in the natural history of RTI» Same as above."

RESPONSE

This point refers to our finding that whilst GP accounts suggested they would utilise the delayed

approach some would do so with a recommended delay that was shorter than the standard natural history of RTI may suggest.

Reviewer 5 Comments:

"The details of the methods need explaining further. Firstly around the sampling (what variables were sampled on for the purposive sampling) and sample size. An n of 50 was suggested, which seems very large and beyond what would be expected for a study of rich data. More justification is needed of this. The abstract says the n was 32, but Figure 2 suggests it was 46."
RESPONSE
We would like to clarify that a target of 30-50 participants was set out in the protocol. We have changed the manuscript to highlight this (Page 5, Line 19).
Figure 2 shows that we received 45 total expressions of interest. 13 were excluded because 10 were not contactable to discuss further and arrange an interview. 1 requested higher payment than the £50 offered which was not possible, and 2 were unavailable for interview before the end of data collection. Therefore 32 GPs were interviewed, 18 from high-prescribing practices, 14 from low-prescribing practices.

"Secondly, more detail is needed about the steps taken to increase trustworthiness of the final analysis, including use of wider research team (and their backgrounds) in establishing the coding framework and its application. It currently looks like it was done entirely by one person, which wouldn't be usual or good practice in qualitative methods."
RESPONSE
Thank you for highlighting this issue. We had mentioned the inclusion of additional researchers during analysis in figure 1. It was indeed an oversight to not include the use of multiple coders in the manuscript. We have now included this information (Page 5, Line 47-50). "RR led the analysis and developed the initial codes. The reviewing and agreement of themes were discussed and confirmed through repeated data sessions with GL and CE, who are both experts in qualitative research."

"How was thematic saturation achieved and how did you know? Mention saturation is in the limitations section."
RESPONSE
Thank you for highlighting this omission. We have now included a sentence on data saturation being reached in the methods section (Page 5, Line 50-51). "Thematic saturation was achieved when no new themes were emerging from new data."

"I do not think that 'face validity' is a meaningful construct in qualitative research and it would be more appropriate to discuss trustworthiness of analysis."
RESPONSE
Thank you for your comment and this has been changed in the document to a more meaningful qualitative construct:
Page 16, Line 56. "This increases the trustworthiness and transferability of the findings"

"Although recruitment was low, how might this have influenced the data, e.g. respondents may be more familiar/use DP so data around the challenges of using it may have been limited. Taking a purposive approach to sampling does, to some extent address this issue."
RESPONSE
This comment has been highlighted by several of the reviewers and has been included as a limitation in the discussion section (Page 16, Line 50-54). "Low recruitment may have influenced the findings as respondents with greater familiarity or a more positive attitude towards delayed prescribing may have been more willing to take part in the study. However more practitioners from high-prescribing

practices were recruited to the study, which may help to minimise this risk."

"Furthermore, interestingly, Figure 2 suggests recruitment was better in high-prescribing practices which would counter this hypothesis. This could be discussed further."
RESPONSE
This is a really relevant observation, thank you for pointing this out. We have added this to our discussion section: "However more practitioners from high-prescribing practices were recruited to the study, which may help to minimise this risk" (Page 16, Line 50-54) .

"The findings are very long and at times descriptive rather than analytical. Sometimes the phrasing suggests a theme is simply a section of the topic guide (e.g. line 55, GPs were invited to reflect on factors that acted as facilitators or barriers… theme being 'factors that influence use of DP). Several sections report what a single GP said, and then another GP. Together this suggests that it would be possible to achieve further synthesis and more analysis was needed. With this number of interviews I would imagine the data were very rich, and I was disappointed the authors haven't taken the analysis further and been more interpretive. I was hoping that more nuanced findings might have emerged. For example, the idea that a DP is a 'contradictory message' (line 46) and 'Muddies the water' (line 41) was raised but not explored in relation to other areas that seem to influence the interaction, e.g. maintaining patient relationship. None of this comes out in the abstract, article summary and is lost in the dense description of the data."
RESPONSE
Thank you for this comment. Data organisation and analysis was systematic and comprehensive (starting with familiarisation, and line by line coding in NVivo) and we were careful to avoid using the interview guide as a pre-ordained framework to help organise, understand, interpret and present the data. The example given (Page 12, line 5) reflects our wish to be transparent in our writing so it is clear how the views represented arose in the context of the interview (e.g. directly solicited (via a question) or volunteered by participants).
We are confident in how we approached analysis, being both analytical and descriptive as appropriate. In places we do offer summaries that stay close to participants' accounts and believe there is a place for this type of descriptive approach (Sandelowski, 2000; Neergaard et al.,2009).
We agree that it is possible that GP views that a DP can convey a confusing message to patients is important. We are currently planning further studies that will allow us to empirically explore GP-patient interactions (focusing on antibiotic talk in particular) and hope to identify how GPs (with patients) attend to / manage this potential tension / contradiction.

"The introduction section suggests the evidence base for DP as an approach is clear, in terms of reassuring patients and validating their concerns around respiratory tract infections. I do not believe the evidence about this is as clear as is intimated. Delayed prescribing potentially provides patients with a confused message (they aren't effective for a viral infection, but here is one just in case), and the patients views on this phenomenon are lacking from the literature. I conducted a very similar study to the one reported here (mentioned in the Discussion, ref 21) and was hoping that this study would have taken that work on further. There is certainly scope for more work in this field, but the authors need to make it clear what is novel here, and how the data and analysis extends current knowledge."
RESPONSE
We have acknowledged that our research is similar and yields similar results to your findings. We argue that our research furthers knowledge in the field in that GPs need to take the natural history of RTI into consideration. Moreover we feel we add to existing literature in that the limited transparency of prescribing strategy within and across practices strongly highlights a need for transparency and consideration of clear standardised guidance and policy in primary care to enhance prescribing decisions. This is highlighted in the discussion section.

VERSION 2 – REVIEW

REVIEWER	Carl Llor University Institute in Primary Care Research Jordi Gol, Primary Healthcare Centre Via Roma, Barcelona. I report receiving research grants from the European Commission (Sixth&Seventh Programme Frameworks and Horizon 2020), Catalan Society of Family Medicine, and Instituto de Salud Carlos III (Spanish Ministry of Health). I also report having had a grant from the Fundació Jordi Gol i Gurina for a research stage at the University of Cardiff in 2013.
REVIEW RETURNED	19-Jun-2016

GENERAL COMMENTS	The paper has clearly improved. No comments now.

REVIEWER	Nick Francis Cardiff University Wales
REVIEW RETURNED	21-Jun-2016

GENERAL COMMENTS	I think the paper is greatly improved. Page 5 lines 11-15 still do not make it clear that, or how, practices with the 'highest prescribing data' were selected from high prescribing CCGs and practices with low prescribing data were recruited from low prescribing CCGs (as indicated in the response to reviewers). I agree with one of the other reviewers that the paper is very long and section 1 of the results does not really address the main aims or contribute much to our existing understanding. I would suggest removing the first section of the results, but this is an editorial decision. I'm not sure that the statement, "the current study suggested that GPs were not taking into account the variation in the natural history of RTI …' (page 17, lines 49-50) is justified by the data. It sounds as though one or two participants mentioned '24 or 48 hours' as a possible delay period. I think the statement should be toned down to, "…some GPs may not be taking into account …". Also, it would be good if the authors could describe whether there is any data on the acceptability of different delay lengths in the Discussion.

REVIEWER	Sarah Peters University of Manchester
REVIEW RETURNED	13-Jul-2016

GENERAL COMMENTS	Thank you for the opportunity to re-review this interesting study. I think it is improved and the points I, and other reviewers, raised about methodology etc largely addressed. My query about the need to further explain purposive sampling has not been addressed - ie what variables were used to sample upon. This is not clear, especially given the sample size fell below that planned.

	I remain of the view that the results section (essentially unchanged since the initial submission) is too long and at times descriptive rather than analytical (not extending far beyond the 'topics' of the interview schedule). I do not doubt that a systematic job has been done in generating the data and performing an analysis, rather that there was scope for further synthesis and interpretation, and that this was a missed opportunity. Nevertheless, the paper does provide a useful addition to a literature that is still in it's early stages and there have been some attempts to pull out what is new and ideas for further work/recommendations.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

The paper has clearly improved. No comments now.

RESPONSE: Thank you for taking the time to review the paper for a second time.

Reviewer: 3

I think the paper is greatly improved.

RESPONSE: Thank you.

Page 5 lines 11-15 still do not make it clear that, or how, practices with the 'highest prescribing data' were selected from high prescribing CCGs and practices with low prescribing data were recruited from low prescribing CCGs (as indicated in the response to reviewers).

RESPONSE: Thank you for your comment. We hope that including the following sentence will clarify this issue:
"The ten practices with the highest prescribing data within each of the high-prescribing CCGs, and the ten practices with the lowest data within each of the low-prescribing CCGs were selected." (Page 5, Line 9-11).

I agree with one of the other reviewers that the paper is very long and section 1 of the results does not really address the main aims or contribute much to our existing understanding. I would suggest removing the first section of the results, but this is an editorial decision.

RESPONSE: Thank you for this comment. The authors have discussed this issue and we feel that theme 1 is useful to providing context for the rest of our findings. However, we are happy to suggest editing the results section in the following ways:
-Leave Theme 1 as it is, in the manuscript and in its entirety.
-Provide a bullet point summary of Theme 1, and omit quotes (see supplement 2).
-Remove Theme 1 from the main manuscript and have it as an appendix (see supplement 3).
We would like to leave the final decision with the editors and would welcome their views on this.

I'm not sure that the statement, "the current study suggested that GPs were not taking into account the variation in the natural history of RTI …' (page 17, lines 49-50) is justified by the data. It sounds as though one or two participants mentioned '24 or 48 hours' as a possible delay period. I think the statement should be toned down to, "…some GPs may not be taking into account …". Also, it would be good if the authors could describe whether there is any data on the acceptability of different delay

lengths in the Discussion.

RESPONSE: Thank you for this comment. We have edited the sentence to read: "…GPs may not be taking into account…". (Page 17, Lines 49-50). We have included the reference (number 23, Little, Rumsby, Kelly, et al. (2005)) which provides data on the acceptability on the lengths of delay for RTI.

Reviewer: 5

Thank you for the opportunity to re-review this interesting study. I think it is improved and the points I, and other reviewers, raised about methodology etc largely addressed.

RESPONSE: Thank you for your comments.

My query about the need to further explain purposive sampling has not been addressed - ie what variables were used to sample upon. This is not clear, especially given the sample size fell below that planned.

RESPONSE: We have now changed the section on sampling to the following:
"It was anticipated that this primary sampling approach of identifying high- and low-prescribing practices would facilitate maximum variation sampling to get a range of differing GP views about the use of antibiotics for RTI and delayed approaches to prescribing." (Page 5, Lines 14-17).

I remain of the view that the results section (essentially unchanged since the initial submission) is too long and at times descriptive rather than analytical (not extending far beyond the 'topics' of the interview schedule). I do not doubt that a systematic job has been done in generating the data and performing an analysis, rather that there was scope for further synthesis and interpretation, and that this was a missed opportunity. Nevertheless, the paper does provide a useful addition to a literature that is still in it's early stages and there have been some attempts to pull out what is new and ideas for further work/recommendations.

RESPONSE: Thank you for your kind comment regarding our systematic job in our analysis. We have responded to the comments about the length of the paper within Reviewer 3's comments, by asking the editors for their recommendations. We have also responded previously to comments about the analytical level of the findings. To clarify, we are confident in how we approached analysis, being both analytical and descriptive as appropriate. In places we do offer summaries that stay close to participants' accounts and believe there is a place for this type of descriptive approach (Sandelowski, 2000; Neergaard et al.,2009).