Author’s response to reviews

Title: The Care Home Independent Prescribing Pharmacist Study (CHIPPS)-A non-randomised feasibility study of independent pharmacist prescribing in care homes

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Author’s response to reviews:
Detailed responses to the reviewer comments.

Reviewer 1

1. This is a well-written paper that has been submitted in a form suitable for publication. It presents the results of feasibility study of a novel pharmacist intervention in care homes. It is rather on the long side (45 pages plus supplementary documentation) and I would suggest the authors see what could be omitted.

   Thank you- in response to comment 8 below we have reduced the level of detail in the Introduction, to reduce the length, but in responding to requests for more information as per other comments we have also had to introduce additional text.

2. My understanding is that the main trial is underway and it would be useful if this could be included in the introduction. Yes – this is underway but won’t complete until mid-late 2020. This information as now been added to the Abstract Conclusion and main Conclusion

3. a. The authors state that this study is part of a programme grant (https://emea01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.uea.ac.uk%2Fchipps%2Fsummary&data=02%7C01%7Crch23%40leicester.ac.uk%7C7C7432b97fb5c5447642a508d6a09375e3%7Caebe6a3144b0195ce8274afe853d9%7C7C0%7C63872952534013586%7C7gtoI6h02n70eWXx6tWdTvIKEWkEDa%2BnXf7OfQRTt9Q%3D&reserved=0) and it would be useful for it to be made clear (in brief) what all the components of the programme are and whether any parts of what has been described in this paper have or will be published separately (apart from 14 and 15).

   b. Reference could be made to the web site or a summary box could be inserted

   c. (instead of the CQC box). a. Details of the steps in the overall programme are in the original paper at the end of the Introduction. We have linked this original text to this comment. In addition to references 14 and 15 two other publications are submitted for publication (on the training programme and the earlier qualitative work) but are not yet in press

   b. We have added the website link (https://www.uea.ac.uk/chipps/)

   c. the box is deleted

4. Abstract
Page 3.

a. Line 25. Could the mixed-methods be clearly defined i.e. 1), 2), 3) etc.

b. Line 27. Up to three is, I think, a result and not a method.

c. Line 29. Referral to other professionals? Is this explained in the main text and are there any results?

4a Now added

4b No this was planned as a practical upper limit for logistical reasons, but recognising that in some areas GP registered care home patients may be spread across more than one home. No change made. We would prefer to retain original text unless otherwise advised by the Editor.

4c. This would mostly be to GPs but did not preclude other HCP a priori. This information was recorded in the pharmaceutical care plans but was not formally analysed as the purpose of the feasibility study was more one of usability to check the plans were filled in not to analyse every item of data. Therefore we have not made any adjustments to the text.

5 Page 4.

Line 11. Should this be in the methods? Is inclusion in the results section because these were chosen as the methods for the main study? If the latter is the reason for choosing number of falls explained in the main body of the text?

Yes – this is here as it was a decision based on the results. Details are in main text of original and revised versions as follows:

Performance of each outcome against the predetermined criteria was combined with data from the literature, and discussed by the Programme Management Group. The outcome measure fulfilling most of the criteria was falls per patient, and it was selected as the primary outcome measure for the definitive trial. DBI, hospitalisations, mortality, Barthel (proxy) and ED-5Q-5L (face-to-face & proxy) and selected items from the STOPP/START guidance also performed reasonably well and were retained as secondary outcomes.

No change made to abstract. We would prefer to retain original text unless otherwise advised by the Editor.
6 Line 14. Are selected items described? How were they chosen?

We have inserted ‘that could be assessed without need for clinical judgement’ This is because some items need an understanding of the patient’s medical history to inform decision making eg stopping a loop diuretic for dependent ankle oedema without clinical, biochemical evidence or radiological evidence of heart failure, liver failure, nephrotic syndrome or renal failure (leg elevation and/or compression hosiery usually more appropriate) but other items eg prescribing of laxatives in patients receiving opioids regularly could be based on records.

7 Line 24. Does "ongoing" mean that it has started?

We have replaced ‘ongoing’ with ‘The full RCT with internal pilot started in February 2018’ and hope this is clearer

8 Pages 5–7 Introduction

This section is far too long. Reference to growth of ageing population and prescribing can be made in two sentences. Issues can also be summarised briefly. Reference could be made to the CQC without the chart.

The Introduction has been reduced and the box has been removed

9 Page 6. Line 30. The reference is to a 2006 publication. Hardly recent! Diagnosis and treatment is not specifically mentioned. What is the scope for this?

There is no line 30 on page 6 of my version. The CHUMS study published in 2009. We assume this is the paper the reviewer is referring to. Whilst we agree that the data is now some 15 years old there has been no study since with such a comprehensive/gold standard methodology to capture medication errors across the medicines management pathway/system i.e. prescribing, monitoring, dispensing, administration! Further this study was the basis of the DoH Immediate Action alert, yet as identified by the CQC the proper and safe use of medicines remains an issue. Therefore we consider that we should retain this key reference to the CHUMS study

10 Page 8 Specific Objectives

The results seem to be presented as if this was a "proper" trial rather than against the objectives as listed. Could the authors review this aspect of the paper?
The results are already presented under the following headings:

Recruitment and retention

Suitability of outcome measures. Note actual values for the outcome measures at baseline and follow-up are reported in table 2 to demonstrate it was feasible to collect them and they were potentially sensitive to change. We have changed the title of table 2 from ‘Outcomes: Table 2. Data generated by proposed measures at baseline and follow-up’ to ‘Table 2. Data generated by proposed outcome measures at baseline and follow-up’ to clarify

Adverse events/serious adverse events

Quality of pharmaceutical care plans

Participant views of service and research acceptability

Refinements to service specification.

We believe these headings already map logically to the objectives as stated earlier in the paper which were originally:

• Test processes for participant identification, recruitment, and consent and assess retention rates.
• Determine suitability of outcome measures, and data collection processes from care homes and GP practices.
• Assess service and research acceptability
• Test and refine the service specification

In the revised version they are amended slightly to reflect comment 39, but extended rather than changed.

11 Page 9 Inclusion Criteria

Well described.

Thank you

12 Page 9 Patient Identification
Line 19. What was the standardized process?

We have removed the term ‘standardised’ from here as the process is already detailed in the recruitment flow chart (figure 1). In summary the process was agreed by the study team and recognised that capacity to give informed consent for taking part in study was different from their capacity to make other decisions. Therefore, for example, whilst a care home manager might suggest a resident had capacity, when the researcher spoke to the resident it might be apparent that they did not understand the research and therefore does not have the capacity to consent. This complies with the best practice recommended in DiazOrdaz K, Slowther A-M, Potter R, et al. Consent processes in clusterrandomised trials in residential facilities for older adults: a systematic review of reporting practices and proposed guidelines. BMJ Open 2013;3:e003057. doi:10.1136/bmjopen-2013-003057

This has now been added to the Discussion.

Line 14. Is the proposed service or what was done in the feasibility study?

Line 27. Did the PIPs have access to the GP records at baseline and on a continuing basis.

We have added to the main text the key roles and confirmed PIPS would have access to GP records.

‘The main tasks were: reviewing a resident’s medication, developing and implementing a pharmaceutical care plan, prescribing and deprescribing, referral to other health care professionals as agreed with GP, improving communication between GP practice and care home and local community pharmacy, supporting systematic ordering, prescribing, and administration
processes and training for care home and GP staff. As members of the GP team PIPs all had access to GP records.

16 Page 12. Suitability of Outcomes

There is no mention of cost yet this is mentioned in the abstract. Has it been dropped?

Cost effectiveness is mentioned in the abstract as part of the aims of the definitive trial. The feasibility study tested whether we could collect health utilisation (GP visits and hospital visits) and medication data and PIP activity data to inform the cost effectiveness estimates in the main trial.

17 Page 13. Assessment of Service and Research No comments.

Thank you

18 Page 14. Results Recruitment and Retention No comments.

Thank you

19 Page 15. Suitability of Outcomes


b. You can't make comments related to MMSE as it was only completed by less than half the sample. Were the 40% and the 35% the same people?

a. We recognise that a study which is not powered cannot assess change in any formal way and as stated in the Methods we have not undertaken any statistical comparison. We believe it is appropriate to describe the findings which we have done, and summarised these by stating in a factual way the direction of change. We have removed the reference to an association between that improvement and the intervention. The sentence now reads

‘The direction of change between baseline and follow-up for most outcome measures suggested improvement.’
We have already noted, in the paragraph below the one the comment refers to, that the MMSE had missing data and so was not taken forward into the RCT. We have also added as a footnote to the table the average MMSE based on those who completed the measure face to face at both time points.

‘Average MMSE for the 12 participants who completed the MMSE face to face at both baseline and follow up was 20.5 and 22.1 respectively’

Falls are multifactorial and their prevention is multifactorial. I am intrigued that you believe preventing falls can be achieved by medicine modification alone.

We agree that falls are multifactorial but medications are generally recognised as a major contributing factor (eg due to postural hypotension, confusion drowsiness). References 20 and 21 cited in the Discussion of the revised paper have previously reported that reducing inappropriate prescribing reduced falls. No change made. We would prefer to retain original text unless otherwise advised by the Editor.

Table 2. The individual items need some comments e.g. does STOPP 3.27 mean that the patients were taking 3.27 drugs that could be stopped. The follow up was lower. Did the PIP stop the drugs?

We have edited the key to the table to explain these more clearly. For STOPPSTART this now reads as:

‘Number of individual medicines which would need to be altered (stopped or started) after researchers with a pharmacy qualification applied STOPPSTART criteria’

As stated in column 1 the figure is both the mean per patient with range and sd, and median with IQR. If values are lower at follow up it means that there are less changes required to increase the appropriateness of the medication regime.

Changes between baseline and follow up may or may not be due the actions of the PIP. We cannot attribute causality for this outcome any more than we can for any other outcome.
No comment.

Thank you

23  Page 18 -23 Participant Views

No comments. What proportion of the actions of the PIP mentioned in comments could be done by a clinical pharmacist as opposed to a PIP.

This information would be in the pharmaceutical care plans and activity logs which we have not analysed in this way for this feasibility study. However in theory, (dependent on individual expertise), a clinical pharmacist could do everything except the prescribing/deprescribing. Both of these are central to medication change. In summary we consider a prescribing pharmacist is potentially key as they can act directly, rather than requesting changes through others (principally GPs). No changes made to paper. We would prefer to retain original text unless otherwise advised by the Editor.

24  Page 23 Service Specifications

Are the original and the revised specifications available to be seen?

The service specification for the feasibility study is already attached as Additional File 1. The service specification for the definitive RCT will be published as part of the study protocol-paper in preparation.

25  Page 24-28 Discussion

a. Choice of falls as primary outcome measure. Are references 19 and 20 relevant to present day UK practice?

b. Has the protocol for the main study been published?

   a. We believe both references are relevant. We have also now added a third reference to support this statement which is a recent systematic review.


   b. The protocol will be published and the paper is in preparation
26  Does initiate referrals mean asking the GP to make a referral or can PIPs make referrals themselves and, if so, to whom?

The PIP could make referrals to some other health care professionals themselves, e.g., practice based nurse or dietitian but not directly to other professionals such as hospital specialists. As detailed in the service specification processes for referral were agreed locally between PIP and GP.

Reviewer 2

27  This manuscript reports on a non-randomised feasibility study of an intervention involving pharmacist independent prescribers in care homes. This work, and any future definitive trial, will be important in providing evidence to support enhancing the scope of pharmacists' current practice.

Overall, the manuscript is well written - I have just highlighted some areas for potential clarification in the comments below.

We thank the reviewer for these positive comments.

28  General comment

There are a few cases where sentences are a little long and hard to follow. I have noted a few examples in the comments below.

Is PIP a commonly used abbreviation for "pharmacist independent prescriber"? Given the scope of practice (i.e., targeting potentially inappropriate prescribing), this could lead to confusion. There is alternating use of the terms intervention and service; I would suggest sticking with one for consistency.

We understand the potential confusion with the use of PIP for potentially inappropriate prescribing but as we have consistently used the abbreviation in all previous aspects of the study including publications and conference presentations and no one else has commented on the potential confusion. We would prefer to retain it here unless the Editor requires it to be changed. The alternative would be to write Pharmacist Independent prescriber out in full every time which becomes very cumbersome for the reader.

29  Abstract
Background: the last sentence on specific objectives is quite long

We have used different punctuation (colon and semi colons) which we hope has addressed this concern

30

a. Methods: it would be good to state/summarise the outcomes of interest; there is mention of the primary and secondary outcomes in the results; this should appear in the methods

b. If this is a non-randomised study is the word "open" necessary?

32a

The outcomes are now listed: (falls, medications, residents’ quality of life and activities of daily living, mental state and adverse events)

32 b We prefer to retain open as although it is not randomised an intervention could still have been delivered in a blinded way

31 Was 10 the max number of participants per home? If so, suggest stating "up to"

Results: Is the word "residents/participants" missing after "forty"

33a 10 was the target sample size for each PIP to manage. It was not ‘up to’. No change made. We would prefer to retain original text unless otherwise advised by the Editor.

33b We have inserted ‘resident’ after ‘forty’ for clarity as suggested

32 Introduction

Paragraph 1: What is an "elderly home bed"? Would "care home" be a more appropriate term?

This sentence has now been reworded

33 a. Paragraph 3: when you refer to "authors" are you referring to authors of the current study or previous CHUMS study?

b. Is there any additional evidence that could be used to back up this claim (e.g. from relevant Cochrane reviews) "despite these recommendations": I don't see reference to any recommendations mentioned in the preceding text Paragraph 6 (p7): a. In reducing the word count the reference to authors has been removed
b. Sentence has been reworded to

‘However, a recent Cochrane Review (7) suggests that despite the recommendations in the Immediate Action Alert, care remains sub-optimal and more effective frequent medicines management interventions in this setting are required’.

We have already referred to the Cochrane review and the CQC and would prefer not to add to the words with further examples.

34 Both the opening sentence and final sentences are long and hard to follow ("Evidence from the UK, (11) suggests...") You state that a similar service model could also improve patient outcomes - what are you basing this on? This statement then appears to be contradicted by the next paragraph where you state that "there is no randomised controlled trial evidence that a PIP can improve the clinical outcomes"

We have shortened and reordered the first sentence and hope the clarity is improved. It now reads

‘Evidence from the UK, (11) suggests practice-based PIPs can prescribe safely and improve patient outcomes for patients with chronic pain compared to both medication review followed by recommendation to the GP, and usual GP led care without any pharmacist review’.

We do not believe there is a contradiction as the absence of an RCT referred to later in this section refers to the care home context. However we have reordered the words slightly to separate the care home context from the participant and hope this is now clearer.

35 Paragraph 7: "to compare the effectiveness"; suggest replacing the word "compare" with "assess"

We have left the word compare as this is describing the ultimate aim of the planned definitive RCT

36 Paragraph 7: "Earlier parts of the programme..." This appears to be the first mention of any preceding work for this specific study; it would be nice to have this outlined more clearly and to inform the reader if CHIPPS is independent of CHUMS or are they linked

Details of the steps in the overall programme are in the original paper in the same paragraph which mentions the programme. We have linked this original text to this comment.
Aim and objectives: I think the terms "pharmacist independent prescribers" and "care homes" should be included "Assess service and research acceptability"; suggest specifying at what level (ie patients, pharmacists etc)

We have added to the first bullet ‘(pharmacist independent prescribers, GP practices, are homers and care home residents)’ and to the third bullet ‘to care home residents, pharmacist independent prescribers, GPs and care home staff”

Trial design

We have added to the first bullet ‘(pharmacist independent prescribers, GP practices, are homers and care home residents)’ and to the third bullet ‘to care home residents, pharmacist independent prescribers, GPs and care home staff”

Patient identification and recruitment

We have now deleted WP1 and just referred to earlier qualitative work.

GPs were paid for their contribution to patient identification and recruitment and for taking part in the interviews, in line with national guidance (http://www.nihr.ac.uk/policy-and-standards/research-costs.htm). This is now added to the text.

The intervention

I don't think Figure 2 is a sufficient overview of the intervention for the reader as it is open to interpretation. Although an additional file is provided, it would be better for the reader to have some overview of the intervention in the main body text

We have added additional text to the narrative highlighting the key areas of the role

See response to point 15 above
41 Outcome measures

It is not clear what records were used to assess outcome measures and who assessed them

Additional information added as requested

‘Potential outcomes and outcome measures were identified in earlier parts of the programme (15) (see Box 2). All were collected by local researchers at baseline and 3-month follow-up for each participant from records held in the care home, or GP practice, and face to face completion of standard outcome tools with residents and care home staff’.

42 "sensitivity to the intervention" is listed as one of the criteria used to assess outcome suitability; how was this determined?

We have added ‘(ie an indication of change)’ after ‘sensitivity to the intervention’,

43 "To inform the final selection, performance against these criteria was combined with information from the literature." ; the last part of this sentence regarding the use of literature is vague

The sentence has been expanded to read:

‘To inform the final selection, performance against these criteria was combined with information on the outcome measure from the literature’

We hope this is clearer

44 a. "The minimum criteria for an outcome to be retained in a subsequent RCT were that it should be objective, discriminating, and efficient to collect.": this would indicate that there were two levels of criteria for assessing outcome suitability? Is this based on an established method for outcome suitability assessment ("pre-determined evidence based criteria" is mentioned in the discussion). It's also not quite clear for the reader how these second set of criteria link in directly with the first set

b. Apart from suitability of potential outcomes for a future study, did the authors consider the use of progression criteria to inform their decisions on whether or not to proceed to a definitive trial?

a. The criteria were predetermined rather than choosing an outcome that showed ‘the best results’ Additional file 3 tabulates the performance of the outcomes/outcome measures against the predetermined criteria. The cells are populated either on the basis of data from this feasibility
study or information in the literature. These were discussed in detail by the Programme Management Group as reported in the Results. We believe that this is clear but would be happy to review this section again if required.

b. We did not have progression criteria in this feasibility study. We did have progression criteria in the subsequent internal pilot phase of the main RCT which is ongoing. We have added a comment to the Discussion regarding this.

‘Whilst feasibility of the service is confirmed and outcome measures agreed, the challenges of blinding and the willingness of participants to be recruited to a randomised study was not explored within this stage of our larger study. These uncertainties will be addressed by the internal pilot phase of the definitive RCT. This internal pilot also has defined progression criteria’.

And to the final conclusion:

‘An internal pilot phase in the main trial will confirm the feasibility of recruiting and randomising sufficient GP practices, PIPs, care homes and residents, the availability of data for primary outcome at 3 months, and that there are no intervention related safety concerns prior to progression to the main trial’.

45 Results

Recruitment and retention

This is a very long paragraph - suggest breaking up

We have made a paragraph break separating recruitment of professionals from recruitment of patients

46 "The data for the PIPs is based on two areas only as in two areas PIPs were approached sequentially and the first one agreeing was recruited" : I don't understand this

We agree this was not clear and have reworded to the following

‘In two areas potentially eligible PIPs were approached sequentially and the first one agreeing was recruited (see Table 1 and Additional file 1). In the other two areas, a larger number of potentially eligible PIPs were identified and all were invited to take part. The response rate for the PIPs is based on these latter two areas only’.
"Participating resident demography is shown in Table 2."; I don't think this is accurate - the table is clearly labelled as outcomes - there is no information on age, gender, number of meds etc…

We apologise- in an earlier draft of the paper this was in a table but it was subsequently converted to the narrative text (age, gender and need for nursing care) and the table was removed. The sentence has now been deleted.

Participant views of service and research acceptability "A full report of the qualitative data will be published separately": I am not clear why this work is included here if this is the intention - I think it would be more beneficial for the reader to have a complete/comprehensive analysis either in this paper or the follow-up paper. In terms of what is presented, I think it is overly reliant on the reader reading through the quotations to figure out what the authors are trying to say (e.g. in a number of instances there is a short sentence followed by a lengthy quote) . There is scope to have more detailed summary points of the substantive findings backed up by relevant illustrative quotes.

There is a proposal to conduct a more in depth analysis of the interviews as part of a PhD programme, possibly combined with similar data from the main RCT. However as this is still just a proposal we have deleted reference to this planned in depth analysis, and would like to retain the reporting of this initial analysis from the feasibility study as it informs the objective of assessing service and research acceptability.

In a number of cases, it would appear that the findings are based on what a single interviewee said "For example, one GP said:" "…noted by a care home manager"

"one GP stated"

As this is qualitative data we have just used illustrative quotes. This phrasing does not mean only one person made this comment or a comment to this effect. However we also note that in qualitative approaches comments made by a single participant are equally valid.

There are a number of cases where a sentence follows on from a quote which I would suggest changing to a new sentence

Eg. "and a dementia nurse highlighted that having a pharmacist who could prescribe was particularly 11 helpful to them"
We have reviewed this sections, tried to streamline it better and removed some quotes.

51 Refinements to Service Specification

"Two of the four PIP pharmacists attended the focus group" - is it correct to call this a focus group if only two participants?

This was planned as a focus group but at short notice two of the four PIPS were not able to attend (as is already reported). Despite only two attending the focus group we believe the interaction was more like a focus group than individual interviews and prefer to retain this description. No change made. We would prefer to retain original text unless otherwise advised by the Editor.

52 Discussion

I think there is scope for greater integration of additional literature to help place the findings in context of current research.

We are not quite sure what this is referring to as there are a number of literature areas which could be tapped into. i.e. challenges of prescribing, primary care pressures, methodological advances in conducting pilot and feasibility studies, exploring the extended role of the pharmacist etc. Given the length of the current paper we suggest we do not add further to the Discussion.

53 "Use of predetermined evidence-based criteria to select the primary outcome for the main trial removed any bias that might have been introduced by a more subjective process."; what do you mean by evidence based?

We have explained evidence based in the Methods in response to comment 43 above. We have edited the text in the Discussion to reflect this, as per below

‘Selection of the primary outcome/outcome measure for the main trial was based on predetermined evidence-based criteria, using data collected during this feasibility study and from the literature. This removed any bias that might have been introduced by a post hoc subjective process’

54 Have the authors considered existing core outcome sets for prescribing for older people and how they could guide outcome selection for any future study?

However the core outcomes do not inform primary outcome selection. No changes made in response to this comment. We would prefer to retain original text unless otherwise advised by the Editor.

55 "In the main trial this process has been standardised with a detailed protocol and reporting templates." Is this trial underway?

Yes the trial has started but won’t complete for another year. Text added to abstract Conclusion and main conclusion and see response to comment 2 above

56 "….participation rates were high, suggesting there had not been selective recruitment": is this based on results from Table 1 - if so, I think this statement might be overly optimistic

We have moderated the statement to say participation rates were good

57 "Falls have a theoretically informed causal link with the intervention," can you elaborate on what you mean/how you have established this?

This has been addressed by reference to the literature. A new reference has been added to the original two


58 ""…selected items from the STOPP/START guidance." - again this hasn't been clearly outlined in the methods section; this has implications in terms of the readers interpretation of results in Table 2

We have added in
‘Some items from STOPP START were identified as needing clinical judgement and detailed knowledge of the patient’s medical history and these were not recommended for retention.’ To the relevant section of the Results’. See also response to comment 6.