Author’s response to reviews

Title: Determinants of intentions to monitor antihypertensive medication adherence in Irish community pharmacy: a factorial survey

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Author’s response to reviews:

Dear Editor/Reviewers,

Thank you for taking your time to consider my manuscript. Apologies for the delay in returning the revisions. Below you will find my responses to your questions. I apologise if they are difficult to distinguish, however the system does not allow adjustment of fonts for this purpose.

Best wishes,
Editor Comments:

1. Please rename the ‘Introduction’ section to ‘Background’.
   Amended.

2. Please include the ethics approval reference number in the ‘Ethics and consent to participate’ statement.
   REC 1356/2017 is now included.

3. Please provide figure titles/legends under a separate heading of 'Figure Legends' after theReferences.
   Section moved as requested.

4. Please add a section "Additional files" (after the References/Figure legends) where you list the following information for each additional/supplementary file in the file inventory:
   - File name (e.g. Additional file 1)
   - Title of data
   - Description of data

   Included as requested
Thank you for the invitation to review this manuscript. The paper addresses the barriers and facilitators to pharmacists undertaking adherence interventions for antihypertensive medication in the community pharmacy setting. In providing a quantitative assessment of the role of various factors in a large sample it offers valuable insight into the next steps required to address implementation of adherence intervention programmes.

Well done on what is an overall thorough approach to the methodology and analysis of the work undertaken. I have some suggestions and points to clarify as follows:

Introduction

A short section giving the estimated prevalence and impact of poor adherence to antihypertensive medication would be useful to frame the importance of the study question.

Added sentence, “Poor adherence to antihypertensive medication is estimated at 40% (1).”


Page 4 Line 40: "most patients with hypertension attend a pharmacy at least once a month" Additional comment is needed to clarify here whether this represents patients with diagnosed hypertension/ patients prescribed antihypertensive medication / all hypertensive individuals.

Amended, “Given that most patients prescribed antihypertensive medication attend a pharmacy at least once a month”

Methods

Page 6 Line 13: the sample size is listed as n=1,543 though the results section states that only 1,153 invitations were sent.

Apologies, this was a transcription error/reusing a flowchart template from another study. 1,543 emails were sent. The error was been corrected. I have also corrected the flowchart of respondent numbers. I have also made revisions to this section to enhance clarity.

Thank you for pointing out this error.
Agreed – clarity could be enhanced in this section and has been revised as follows,

“The TPB framework served as a guide, to ensure important constructs potentially influencing behaviour were evaluated; however social, organisational, political and economic factors [32] must also be included in theoretical models that seek to evaluate the feasibility of implementing a new clinical service such as an adherence intervention in community pharmacy [30, 32]. The current study was designed using items from pre-existing questionnaires, from qualitative discussions with academic pharmacists experienced in community pharmacy practice and a pilot study [18].”

Make it clearer that Table 1 and Fig 2 are related as figure 2 is difficult to interpret when referred to in isolation.

I have included the following at the end of this paragraph “Figure 2 details the final vignette and the eleven factors included in the vignettes are detailed in Table 1”.

I have also amended the legend for Figure 2, “Final vignette with the labels of the factors which were varied systematically highlighted in red. The values for each of the labels are detailed in table 1.”

Page 10 Line 39: change "recommend" to "recommended"

Amended
Page 11 Line 51: explanation for the difference in number between addresses requested and provided? Depending on the reason there may be reflection required on bias introduced here.

The PSI, the regulator of pharmacists/pharmacies in Ireland erroneously provided a smaller sample. The process for obtaining the data was lengthy and was not worth re-applying for the originally requested sample. This error would not introduce bias (differences in characteristics of those emailed v not emailed to participate) as the sample was a simple random sample and was still a significant proportion of the entire population of community pharmacists (40%). It affected the survey – as discussed in the manuscript – by reducing sample size, hampering power and ability to achieve a statistically representative sample of respondents completing the survey.

Page 12 Line 26: change "respondent directly access" to "respondent to directly access"

Amended as follows, “These web links with embedded passwords were included in the invitation to participate and clicking the link provided direct access to a unique password protected survey.”

Page 12 Line 36: explanation for the difference in number between addresses received and invitations emailed? The power calculation indicated that 2,315 pharmacists should be invited therefore it’s not clear why some email addresses weren't used to get closer to this figure. Depending on the reason there may be reflection required on bias introduced here.

I understand that I may have introduced confusion, particularly with regard to the error you pointed out to me. Also note as discussed in the manuscript and appendix there are no established methods for sample size and power calculation of factorial surveys. So essentially if we work backwards. Firstly, the 2,315 does not refer to the power of the survey. This refers to the number of participants that we were required to be invited based on previous response rates of 15%. If 15% of 2,315 responded we would have a sample of 347 responses. 347 responses would be considered statistically representative of a population of 3,600 pharmacists (95% CI, +/- 5%). Secondly, based on 347 responses of 5 vignettes each, and using the data obtained from the pilot survey, we were able to estimate whether the survey would be sufficiently powered for each of the included vignette factors. This again is described in the manuscript and appendix 2. Based on this power calculation we were satisfied to proceed to invite 2315. However finally, rather than providing the requested sample of 2,315 community pharmacist from their registers the PSI erroneously provided a sample of 1,543. This sample although smaller than requested is still a significant proportion of the overall population performed as a simple random sample (thus selection bias unlikely), however it ultimately reduced our survey sample size affecting power and our ability to have a statistically representative sample.
To ensure clarity I have revised this section to read, "A sample of 347 respondents would complete 1,735 randomly chosen vignettes from the 1,797,120 possible vignettes created for this survey. However, there are no well-established power analysis methods for hierarchical models in factorial surveys to determine whether 1,735 completed vignettes would provide adequate statistical power [37]. We took an approach using MLPowSim software package to estimate the power associated with each of the vignette factors for multilevel models (vignettes nested within respondents) which is described in Appendix 3. Based on this approach, assuming 350 respondents complete five vignettes each, all vignette factors are sufficiently powered (>80%) except for gender, number of prescription items and the telephone to collect later value. Rather than there being too few observations to test these factors’ influence, it may be that these factors do not influence responses to the scenario, as is the expected case for gender. Thus, based on the assumption of 350 respondents completing five vignettes each, and based on previous survey response rates, a sample of 2,315 pharmacists was considered sufficient. Permission was sought to obtain email addresses from the PSI for a simple random sample of 2,315 pharmacists from their registers who indicated on their annual registration that they practised in a community pharmacy role. However, following an application process the PSI provided a smaller simple random sample of email addresses for 1,543 pharmacists”

Results

Page 15 Line 3: unclear what is meant by "less true" - that the response was still positive but less strongly so?

These were bipolar adjective 7 point scales, true v false, thus average scores greater or lower than the mid-point depending on the behaviour could be considered as tending to be true or false. I have amended to positive v negative in the text of manuscript.

Discussion

Principal findings: The finding that pharmacists reported being more likely than not to perform each of the three intervention activities is a little lost in the way the principal findings are presented. Clarify that this was the case and then discuss the differences between each intervention. The current format makes it unclear whether the 'moderately positive attitudes' are implied from the MMAM score alone or from the specific responses to each intervention in the vignettes used.
I have rephrased to enhance the clarity,

“In this factorial survey, responses to the MMAM, a validated and structured questionnaire to evaluate pharmacists’ attitudes towards medication monitoring, indicate that community pharmacists in the Republic of Ireland had moderately positive attitudes towards medication monitoring. However respondents’ were neutral about the busyness of the work environment and patient acceptability being conducive towards medication monitoring.

Strengths and limitations: where social desirability bias is discussed there would be value in commenting on whether this is thought to affect respondents differently dependent on their demographics e.g. newly qualified or by gender.

See comments above on disparities between email address numbers requested, received and emailed with invitations. Discussion of any potential resultant bias will be necessary.

This is an interesting observation I had not considered, I would suspect that perhaps social desirability will be higher in those newly qualified. However examining the regression tables, years since qualification does not have a significant influence on the responses to the vignettes and furthermore the estimated coefficients vary in size and direction of effect.

Discuss the relatively high number of surveys (n=72) that were left incomplete - if this was due to busier pharmacists being unable to fulfil them in which case information pertinent to time-pressures may have been lost. If this was due to technical issues or difficulty in pharmacists interpreting what was needed then this should be commented on. Could the partial information have been incorporated into the analyses.

Unfortunately I have no data to determine why some people did not complete the survey – perhaps length was an issue. I could perhaps examine logs to see time of day and length of time taken to complete the survey to see if this relates to incomplete surveys, however I am not sure what value this adds. With regard to the partial completed surveys, following the CHERRIES guidance for e-surveys we specified to only include those reaching the final stage of the survey in the analyses and not to analyse those excluded as result – incorporating these into the analysis would not be recommended, similar to other study designs with prespecified inclusion criteria and statistical plans.
Practice and research implications: Comment on what the actual contractual and professional expectations and responsibilities are for pharmacists in this setting regarding adherence interventions. It is not made clear whether the pharmacists have formal requirements to offer these types of interventions at present and what their awareness is of this aspect on their behaviour. Were any of the pharmacists working in settings where there is an organisational policy requiring action along the lines of these interventions already?

I agree – this is important to convey to readers the current practice of pharmacists in Ireland. The reimbursement of community pharmacists in Ireland is predominantly focused on the supply of prescription medication, and pharmacists are currently not remunerated for providing adherence services or intervention. I have inserted the following to beginning of this section,

“Currently pharmacists in Ireland are not remunerated for providing adherence services and no structured adherence-monitoring program has been implemented in this setting.”

The assertion that the association between offering ABPM and lower likelihood of intervention can be explained by additional time pressure on pharmacists does not seem robust. This would be worth exploring further.

Pharmacists providing ABPM, which can be a lengthy patient encounter, will have less time to thoroughly check through a patients PMR, particularly for less critical issues such as adherence, in comparison to checking for interactions, contraindications (general safety issues that may lead to harm) or ensuring legal obligations have been met. A big issue with pharmacists and enhanced services are they are expected to perform these tasks on top of their current dispensing workload. In some cases where the enhanced services are remunerated and patients can be scheduled in blocks of time (e.g. flu vaccines) a number of pharmacies will deploy extra resources during these times e.g double pharmacist cover. However, I have amended to include perhaps in this sentence.

Very little is made of the fact that the study examines only behavioural intentions towards patients aged 65+. Provide explanation on why this decision was made and also the resultant impact on generalisability for the study.
This survey is part of a larger research study which includes an epidemiological study of determinants, measures, and outcomes of antihypertensive medication adherence in older Irish adults (65+). This criteria for the study was required to be in-line with this epi study which is part of a larger national goal toward improving health in older adults. Specifically, 65 years as a cut-off arose from epi studies utilising American healthcare databases (I think Medicare) to perform analyses, because upon achievement of this age patients achieved automatic enrolment within the specific American health insurance system – thus this age-group could be easily studied. As a result 65 years is a commonly used and accepted cut-off age for epi studies in older people.

Reviewer 2 (Reviewer 2)

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

No - there are minor issues

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are minor issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are minor issues

Statistics - Is the use of statistics in the manuscript appropriate?

No - there are issues with the statistics in the study
INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are major issues

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: REVIEW OF THE MANUSCRIPT TITLED FEASIBILITY OF IDENTIFYING POOR ANTIHYPERTENSIVE MEDICATION ADHERENCE IN COMMUNITY PHARMACY: A FACTORIAL SURVEY

TITLE SECTION:

i. From the content of the manuscript, the study is on feasibility of identifying facilitators and barriers to monitoring anti-hypertensive medication adherence in Irish community pharmacies

ii. The title should be modified to include the response/dependent and independent/influential variables of the survey

iii. The site of the study should be included for epidemiological purposes

iv. Include also the survey design for completeness

v. Note also there is a technical difference between 'a study' and 'a survey'

PLEASE READ THIS……The objectives of this study were to identify facilitators and barriers to monitoring antihypertensive medication adherence of older adults at the point of repeat dispensing.
SUGGESTED TITLE:

FACILITATORS AND BARRIERS TO MONITORING OF ANTIHYPERTENSIVE MEDICATION ADHERENCE IN IRISH COMMUNITY PHARMACIES: A FACTORIAL SURVEY DESIGN

I have modified as follows based on your suggestion, “Determinants of monitoring antihypertensive medication adherence in Irish community pharmacy: a factorial survey”

GRAMMATICAL STRUCTURE

1. Authors should write in active voice appropriately

ABSTRACT SECTION:

1. Write Abstract section for clarity under Background; Aim or Objective(s); Participants and Methods; Results; Conclusion and ± recommendation(s); keywords.

The journals recommended abstract headings are background, methods, results, and conclusions which I have amended abstract to reflect

2. Change 'introduction to 'Background' and separate it from aim/objective(s).

This sentence can form background........... Community pharmacy represents an important setting to identify patients who may benefit from an adherence intervention, however it remains unclear whether it would be feasible and compatible to identify poor adherence within the workflow of community pharmacy.

The journals recommended abstract headings are background, methods, results, and conclusions which I have amended abstract to reflect
3. Aim or Objectives: Re-cast the aim/objective(s) to reflect the suggested title above. Note there is a technical difference between aim and objectives of a study.

Noted, modified objective to aim which is now also reflective of title

4. Change 'Methods' to Participants and methods: This section should be re-written to contain summarily survey design, survey participants, survey period, sampling technique, methods eg medication monitoring attitude measure (MMAM), self-efficacy etc.

The journals recommended abstract headings are background, methods, results, and conclusions which I have amended abstract to reflect

5. Results

i. Start result section with total number of participants, age and sex distribution of the survey participants and any other relevant bio-demographic and work environment variables.

I have amended the results section of abstract as follows.

“Survey invites (n=1,543) were sent via email and 258 completed online survey responses were received; two-thirds of respondents were women, and one-third were qualified pharmacists for at least 15 years. In factorial vignette analysis, pharmacists were more inclined to monitor antihypertensive medication adherence by examining refill-patterns from pharmacy records than asking patients questions about their adherence or medication beliefs. Pharmacists with more positive attitudes towards medication monitoring and normative beliefs that other pharmacists monitored adherence, were more likely to monitor adherence. Contextual factors also influenced pharmacists’ likelihood to perform the three adherence monitoring behaviours, including time-pressures and the number of days late the patient collected their repeat prescription. Pharmacists’ normative beliefs and the number of days late the patient collected their repeat prescription had the largest quantitative influence on responses."

ii. Provide clearly the identify facilitators with their quantitative main and interaction effects

iii. Provide clearly the identify barriers with their quantitative main and interaction effects
Ideally quantitative estimates should be provided in abstract, however as there are numerous factors and multiple models this is not feasible for this manuscript. However I have added a statement of the factors with largest quantitative influences on responses as evidenced from the standardised coefficients which I have added to the regression table.

“Pharmacists’ normative beliefs and the number of days late the patient collected their repeat prescription had the largest quantitative influence on responses”

6. Conclusion

i. Authors have no conclusion. The provided sentence on conclusion is verbose

ii. Please provide conclusion to reflect the identified facilitators and barriers based on the aim/objectives of the survey.

iii. This sentence is not conclusion but recommendation. The use of the word 'potential' is also inappropriate. The is a survey with real-time conclusion. PLEASE READ THIS……. However, there are a number of potential time-barriers, which would need to be overcome, while pharmacists perceptions of their role will also need to be addressed……………………..

Agreed – I have amended conclusion,

“This survey identified that positive pharmacist attitudes and normative beliefs can facilitate adherence monitoring within the current workflow; however contextual time-barriers may prevent adherence monitoring. Future research should consider these findings when designing a pharmacist-led adherence intervention to be integrated with current pharmacy workflow.”
KEYWORDS:

i. Inappropriate and poorly written. Authors should know there is a difference between 'adherence' and 'compliance'

Yes we do know this; but not every clinician (nor researcher) understands the specific evolution of this terminology and the term compliance in fact persists in contemporaneous description of this behavioural phenomena

ii. Focus on the survey variables. Include also the survey design and site

iii. Re-cast based on journal specification or use MeSH guideline

I have expanded the key words as follows adherence interventions, compliance, community pharmacy, factorial survey, medication adherence, medication monitoring, pharmacist attitudes, Republic of Ireland, time-pressures

INTRODUCTION SECTION

1. This SECTION is inadequate and not properly funneled to focus the survey on FACILITATORS AND BAARRIERS TO MONITORING OF ANTIHYPERTENSIVE MEDICATION ADHERENCE IN COMMUNITY PHARMACIES

I would disagree – the rationale for my current approach is as follows. Firstly, I describe the issue (prevalence of poor antihypertensive adherence and difficulty of implementing successful interventions in practice). Next I describe the potential solution (stratifying at risk patients and tailoring of interventions using metrics such refill metrics and standardised questionnaires). Finally, the problem statement; absence of studies evaluating feasibility of identifying poor adherence in clinical practice.

The next paragraph, I funnel down to community pharmacy setting as being the practice setting of interest to solve the problem; firstly, highlighting the advantages of this setting (regular patient contact and access to refill records which can facilitate regular adherence monitoring using objective refill methods and subjective questionnaire methods). Next I highlight potential issues with this setting as identified in previous literature regarding both community pharmacy level interventions and belief-based influences of medication monitoring behaviour (contextual time barriers, attitudes etc.). As there is a paucity of research internationally specifically examining facilitator of adherence monitoring within community pharmacies, I have examined the broader literature of similar intervention and monitoring types.
2. Admittedly facilitators and barriers to medication adherence can be patient-related, pharmacy-related, health-system-related, physician-related, etc. Authors should focus the introduction with appropriate literature on pharmacy led and related facilitators and barriers first before patient-related/health[pharmacy] system factors

I believe there may be some confusion – you appear to be referring to the WHO dimensions of factors influencing medication adherence. My study is not evaluating the effects of community pharmacy workflow systems or community pharmacists (healthcare system/team related barrier) on patient medication adherence. In contrast I am examining the determinants of adherence monitoring by community pharmacists.

3. There is paucity of similar studies from other parts of the world for comparative and consultative purposes

Yes this is a novelty of the study

4. What are pharmacy-related facilitators [pharmacy demographics, contextual factors, behavioural, attitudinal factors, etc] to monitoring of anti-hypertensive medication adherence in community pharmacies in developed nations, developing nations, UK, then Ireland

As noted above there is a paucity of evidence.

5. What are pharmacy-related barriers [pharmacy demographics, contextual factors, behavioural, attitudinal factors, etc] to monitoring of anti-hypertensive medication adherence in community pharmacies in developed nations, developing nations, UK, then Ireland

As noted above there is a paucity of evidence.

6. Provide a sub-section on Theory of Planned Behaviour (TPB), Explain how it forms the basis for the theoretical framework for the study linking contextual, beliefs ad attitudinal factors,[The content of Figure 1 is noted] Justify why your choice of TPB over other models like TRA[theory of reasoned action]?

The Theory of Planned Behaviour is a reasonably well known and used behavioural theory. Ideally I would provide more information within the introduction (see later comments), but I must be cognisant of manuscript length. The fact there is a large literature on the TPB, readers who wish to understand it further can refer to this literature. Furthermore introducing the TPB may confuse some readers that this survey is a an empirical testing of this psychological theory, which it is not and which I want to avoid.
7. Statement of the problem that necessitated the survey is sparsely stated by the authors. The statement of the problem and problem analysis should be provided in order to focus the survey appropriately and dovetail into the aim/objective(s).

To ensure clarity I have summarised the two problem statements from both paragraphs of the background section and inserted at beginning of final paragraph.

“Due to the absence of studies investigating the feasibility of monitoring adherence within the workflow of community pharmacy we undertook a factorial survey of Irish community pharmacists with 1) the objectives to elicit pharmacist beliefs regarding monitoring of antihypertensive adherence, and 2) to identify facilitators and barriers to monitoring antihypertensive medication adherence of older adults at the point of repeat dispensing. The factorial survey was guided by a conceptual model adapted from the Theory of Planned Behaviour (TPB), which has been highlighted as a useful framework to understand barriers and facilitators to extended pharmacist roles in practice [24].”

8. Please in text insertion of references should be done as recommended by the journal

Noted

PARTICIPANTS AND METHODS SECTION

THIS SECTION SHOULD BE RE-ORGANIZED FOR CLARITY AND EASY COMPREHENSION. IT SHOULD BE ORAGANIZED AS ITEMIZED BELOW.

AUTHORS CAN WRITE IN SECTIONS AND SUBSECTIONS OR IN PARAGRAPHE

PROSE PATTERN

1. Change 'Methods' to 'Participants and Methods'.

The journal style guide is Methods
2. Re-write this section in subsection or paragraphed prose with clear emphasis on

i. SURVEY FACTORIAL DESIGN AND APPROACH

-Delete 'study overview' and change to 'survey factorial design and approach'

-The first sentence is the survey design. Elaborate more on the survey design with focus on factorial survey design

-Move the sentences on sampling frame, etc to a subsection on sampling methods

-Move the sentences on sections of the questionnaires to appropriate section on methods section

-Move the sentences on ethics and informed consent to a subsection before statistical analysis.

This is an overview section to give an overview of the survey to the reader prior to going into each of these in detail. This is necessary to give an overall sense of what was done before diving deep into the detail. All of the relevant information you have mentioned is mapped to the correct subsequent subsection and discussed in greater detail.

PROVIDE THE DATE OF APPROVAL OF THE SURVEY.

I am unsure which approval you require?

What was the content of the information study leaflet[Please provide it as an appendix]

ii. Provide survey setting

iii. Provide survey participants

iv. Provide survey period

Leaflet has been appended.

DELETE 'STUDY DESIGN' AND MOVE THE WHOLE PARAGRAPH TO APPROPRIATE PARAGRAPH ON TBP IN THE INTRODUCTION SECTION

PLEASE READ

Survey Design DELETE entire section
I would disagree – I believe this section is in the appropriate section. Introducing this into the introduction would distract from the actual purpose of the survey. The main issue is that some readers, particularly from health behaviour/psychology backgrounds, may be confused by its inclusion in the introduction and may be misled to understand that the survey is testing the TPB, which the survey is not doing. Furthermore the TPB is informing the framework methodology and the constructs to be assessed, whereas the background currently discussed informs the actual contents of these TPB constructs.

Sample size determination:

i. Move the sample size determination and elaboration here

I believe the order of the methods is appropriate and has logical flow. 1st an overview of entire survey, 2nd a description of the framework of the theoretical underpinning of the survey, 3rd a description of the methodology followed by the specific methods applied in this study including the survey outcome responses and contextual factors of interest. Next there is a description of the belief factors of interests and methods of how they were measured, and demographics of respondents to be collected. Subsequently a description of the sample size calculation and how the sample will be obtained and contacted; and how they will complete the survey. Finally, the statistical analysis plan is presented.

ii. Why did you use the 2016 register of community pharmacy instead of 2017 when the main/final study was done?

The application to the PSI to obtain the contact details was in December 2016.

PLEASE READ THIS……. Approximately 3,600 community pharmacists practice in Ireland (December 2016) and a sample of 347 was required to reach a statistically representative sample (95% confidence interval; 5% margin of error)……..
Sampling method:

i. Move the sampling frame and other techniques here

ii. How did you apply random sampling in the selection of community pharmacists in Ireland from 2016 register? What type of random sampling method did you use in the sampling technique

Please see above comments

PLEASE READ THIS…..A random sample (n=1,543) of potential respondents were contacted via email addresses provided by the PSI and were sent a unique password protected web-link to complete the survey online……..

vii. Selection criteria:

a. Inclusion criteria:

i. Provide inclusion criteria with clear statement on how the community pharmacies/pharmacists were identified by Pharmaceutical Society of Ireland?

How was the first and subsequent participants selected? .

b. Exclusion criteria:

ii. Please provide exclusion criteria.

I think the inclusion/exclusion criteria are sufficiently described, particularly for clinicians, pharmacists, registered healthcare professionals etc and researchers who work in these areas. To be a pharmacist you need to be registered with the society (ie board certified). The PSI have a register of all pharmacists in Ireland which also includes information on practice setting (community, hospital, non-patient facing). The PSI provided a simple random sample from their register of those indicating they work in community (pharmacy) settings.
PILOT TESTING

1. Provide a sub-section on pilot testing

I have included some extra details in this section, “Briefly, in the pilot each pharmacy intern completed five factorial vignettes of scenarios focused on repeat dispensing of antihypertensive medication to an older patient, reflective of pharmacy practice in Ireland. The initial vignette, included eight factors and was designed by academic pharmacists experienced in community pharmacy practice and was informed from a previous study [27]. Based on the quantitative results and qualitative feedback received from pharmacy interns during the pilot study, the original eight vignette factors were retained for the current survey with some modifications, and three new factors were added. Two of the new factors were based on qualitative feedback from the pilot study that indicated that further competing tasks exist in the form of administrative tasks (paperwork to claim reimbursement) and non-dispensary related patient interactions.”

2. Why was the pilot testing done in May and June 2016. And the main/final study was done August 2017? [More than a year after the pre-testing]

A large amount of data was collected in the pilot study, which needed to be sorted, cleaned and analysed to yield insights for the final study. Next a protocol needed to be developed incorporating the findings of the pilot study and amending as necessary. In particular, we had to spend a lot time developing a power calculation method which we discuss in the manuscript. Next we had to apply for ethics approval (IRB). After ethics amendments and approval an application had to made to the PSI to obtain respondent contact details. Finally a new survey software vendor had to be procured which provided the capacity to automate the factorial survey in comparison to the manual entry within the pilot study.
METHODS:

- Move the sentences from the first paragraph on sections of the questionnaires to appropriate section on methods section

- Move information on demographic and workplace questions here

- Move information on five factorial vignettes here

- Move information on Medication Monitoring Attitude Measure here. Was the MMAM pre-tested or pilot tested in Ireland before use?

- Move information on subjective norms, self-efficacy and perceived behavioural control questions here

- Move information on Survey Administration here

See previous comments on section order

MOVE THIS SUB-SECTION ON RESPONSE RATE TO FIRST PARAGRAPH ON THE RESULTS SECTION

Response rates

Section has been moved to results

viii. Ethical consideration: -Move the sentences on ethics and informed consent here. PROVIDE THE DATE OF APPROVAL OF THE SURVEY. What was the content of the information study leaflet[Please provide it as an appendix]

I am unsure who are referring to who provides approval (authors, ethics committee?). Note the PSI do not approve the survey, they just review that it is in line with their functions as defined in legislative acts and the request for data access is reasonable in line with functions
ix. Statistical analysis:

a. What type of linear regression did you do? Multiple or multivariate?

Multilevel multivariable (aka multiple) linear regression was performed to allow simultaneous consideration of vignette-level and pharmacist-level variation – this allows analysis of clustered/grouped/repeated responses i.e. that respondents provided multiple responses. I have however clarified that it is as multivariable, as includes multiple respondent-level and vignette level predictor variables in model.

b. Specify the response and explanatory/influential variables for the linear regression?

The response to the vignettes are indicated to be the outcome being tested in the model (which are listed in the section describing the vignette and in the regression table), and pharmacist-level and vignette-level factors are the predictor variables (listed in the section describing the vignette and in the regression table). It would be preferable to spell this out however I must consider length of the manuscript and the fact that this can be interpreted from the regression tables, and avoid duplication of information within the manuscript.

c. Provide statement on Confidence Intervals, Odds Ratios and p-value for acceptance and rejection of null hypothesis.

Specifying a p-value threshold to define statistical significance is a discouraged practice. My analysis did not generate odds ratios. For clarity I have included the standardised coefficients, and added following to this section, “To aid identification of factors which have the largest influence on adherence monitoring behaviour, standardised coefficients were also obtained by standardising all predictor variables (level-1 and level-2 variables) so that each predictor variable have a mean of zero and a standard deviation of one (i.e. z-transformation). To perform transformations, categorical variables were dummy coded. The resultant standardised coefficients represent a one unit change in vignette responses expected with a one standard deviation change in predictor variables.”
RESULTS SECTION

[ORGANIZE THIS SECTION FOR CLARITY EITHER IN SUB-SECTIONS TO REFLECT THE TABLE TITLES OF PARAGRAVED PROSE]

i. Move the sub-section on response rate here

ii. Respondents should be changed to 'Demographics and work environment of the study participants

The participants are technically survey respondents rather than study participants

iii. Medication Monitoring Attitudes scores

iv. Subjective norms and self-efficacy

v. Factorial Vignette-examining dispensing records to assess adherence

vi. Questioning patients about adherence

vii. Explore beliefs about medication that influence adherence

The results are now organised as you have described

FIGURE 1: APPROPRIATE

FIGURE 2: APPROPRIATE

FIGURE 3: APPROPRIATE

TABLE 1: APPROPRIATE

TABLE 2: APPROPRIATE

TABLE 3: APPROPRIATE
TABLE 4

a. What type of linear regression did you do? Multiple or multivariate?
See previous response – added multivariable to be clear

b. Specify the response and explanatory variables for the linear regression in the methods section?
See previous response

c. Indicate the significant variables with asterisks. The bolding is not clear.

I agree asterisks would aid quick visualisation of important variables however these would necessitate the reduction of font to keep each variable to a single line on the table

d. Provide appropriate interpretations for the coefficients that didn't cross the unity 1
Examples
Interpret and include in the results section appropriately

NOTE THAT P=0.000 is not mathematically. Write based on journal of submission recommendation
Corrected to <0.001 and standardised coefficients added.

DISCUSSION

1. Delete the first paragraph titled 'Principal Findings'. The paragraph is occupying space inappropriately

I would disagree with this point. Most style guides within the Equator network recommend this subsection at the beginning of every Discussion section e.g. Strobe. Cherries guidance however does not cover this section but is limited to guidance on reporting of methods/results for e-surveys. In relation to your next question I have reorganised this important paragraph - however I have limited to the themes most relevant to the study objective (pharmacists beliefs, and barriers and facilitator to adherence monitoring), so as not to be overly lengthy and overwhelm readers with more minor findings.
”In this factorial survey, responses to the MMAM, a validated and structured questionnaire to evaluate pharmacists’ attitudes towards medication monitoring, indicate that community pharmacists in the Republic of Ireland had moderately positive attitudes towards medication monitoring. However respondents’ were neutral about the busyness of the work environment and patient acceptability being conducive towards medication monitoring. In factorial vignette analysis, respondents’ attitudes towards medication monitoring were important influences to whether they would monitor antihypertensive medication adherence by examining refill-patterns from pharmacy records, by asking patients questions about their adherence or their medication beliefs. Additionally, respondents’ normative beliefs, whether other pharmacists also performed these behaviours, were important influences. Furthermore, a number of contextual factors influenced respondents’ likelihood to perform the three adherence monitoring behaviours, including time-pressures and the number of days late the patient collected their repeat prescription.”

2. Focus discussion on objectives with focus on the thematic findings as stated in the result section in consideration with the tabular and textual components of the results.

Start first with

- 'Demographic and work environment influences
- Pharmacist beliefs about adherence monitoring
- Contextual Influences
- Facilitators towards adherence monitoring
- Barriers towards adherence monitoring
- Attitudes, normative beliefs and self-efficacy

See above. Note I have arranged the discussion to reflect the main objectives 1) evaluation of pharmacists’ beliefs (attitudes, norms, self-efficacy) and 2) influences of adherence monitoring which have been divided into appropriate themes a) attitudes, norms and beliefs, b) contextual factors which reflect the vignette factos and c) demographic details
3. Include discussion on objectives with focus on significant variables at linear regression analysis considering all the levels and models of measurements.

With regard to my comments above I have focussed on variables which I was specifically interested in pre-analysis a) beliefs and b) contextual factors, while demographic details were included to adjust for potential confounding. For these factors, in light of 3 separate models a single finding of “statistical significance” may not equate to clinical/real world meaningfulness.

4. You may include discussion on other thematic findings that are absolutely or marginally or relatively relevant for discussion[clinical relevance]

See previous comments

5. There is paucity of similar studies [on-line factorial study design] for international comparisons and discussion?

This a novel study applying this method to answer this specific question.

Strengths and limitations

i. Separate strengths of the study from the limitations of the study

Strengths and limitations are already discussed separately. Strengths of the methodology are first discussed followed by weakness of the methodology. In the subsequent paragraph specific limitations to the study are discussed.

ii. Focus the strength of the study on your study findings and contribution to knowledge. Delete the references inserted in the strength of your study.

I do not agree with deleting the references – they back up my arguments countering potential weakness in my study. A check of the current journal’s most recent articles reveal most articles contain references within this subsection.
Practice and research implications

1. Change 'Practice and research implications' to 'implications of the survey'
This section implies implications of survey on practice and research

Conclusion

iv. Authors have no conclusion. The provided sentence on conclusion is verbose

v. Please provide conclusion to reflect the identified facilitators and barriers based on the aim/objectives of the study.

This sentence is not conclusion but recommendation.

PLEASE READ THIS………..Monitoring adherence through pharmacy records appears the most feasible approach within the current workflow to identify poor adherence however there are number of potential time-barriers, which likely require extra resourcing to overcome, while pharmacists perceptions of their role will also need to be addressed……..

Agreed it is repetition of the recommendations in the section, practice and research implications. I have amended as follows,

“Pharmacists potentially can play a role in identifying appropriate patients for adherence interventions and their reasons for non-adherence. This survey identified that positive pharmacist attitudes and normative beliefs can facilitate adherence monitoring within the current workflow; however contextual time-barriers may prevent adherence monitoring. Future research should consider these findings when designing a pharmacist-led adherence intervention to be integrated within current pharmacy workflow; alternatively novel working arrangements to facilitate adherence interventions within this setting should be considered.”
PROVIDE SUB-SECTION ON

a. RECOMMENDATIONS

b. RECOMMENDATION FOR FURTHER STUDIES if any?

Both well discussed in the section titled, “Practice and research implications.”

REFERENCES

1. SOME REFERENCES ARE INCOMPLETE
2. Most references are not related to the FACTORIAL SURVEY DESIGN AND APPROACH
3. Provide more international references for global readership
4. Authors should re-write base on journal recommendation

Noted