Author’s response to reviews

Title: Impact of Pharmacy-Led Medication Reconciliation on Admission to Internal Medicine Service: Experience in Two Tertiary Care Teaching Hospitals

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Version: 3 Date: 23 May 2019

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BHSR-D-19-00003R2
Response to Editor’s and Reviewers’ Comments:
Technical Comments:

Editor Comments:

Please standardize the reporting of results in the manuscript. For example, proportions are sometimes reported with no decimal places while in others they are presented with up to two decimal places. I recommend reporting proportions to one decimal place and odds ratios to 2.

Thank you for your comment.

Proportions are now reported to one decimal place in text and tables, and odds ratios to 2 decimal places.

As for the p-values, p-values larger than 0.01 are reported to two decimal places, and values between 0.01 and 0.001 are reported to three decimal places. Please specify if it should be reported otherwise.
Also, carefully consider reviewer two’s comments regarding a discussion item of how pharmacists may be introduced into the current system. A cost-effectiveness analysis may be outside of the scope for this manuscript, but could be a consideration for a future study. Given reviewer two’s concerns that this study is confirmatory and not novel, a discussion item should address how the experience in Lebanon is different from experiences in other countries and how those experiences may influence the acceptance of pharmacy services. An important consideration for a future study might be an evaluation of the culture of healthcare in Lebanon and perceived roles for pharmacists.

Thank you for your comment.

The authors enriched the discussion, addressed the above discussion items and added the following sentences to the manuscript:

- “Moreover, in 2019, the Ministry of Public Health in Lebanon in collaboration with the Haute Autorité de Santé (HAS France) updated the Accreditation Standards for Hospitals in Lebanon and emphasized the need for medication reconciliation at admission, and discharge. The medication management chapter within the standards also reinforces that this reconciled list should be shared with the healthcare providers and the pharmacy.” (Discussion section, lines 429-433, pages 19-20)
- “In context of the updated mandatory hospital accreditation standards, the findings of this pilot study were reported to the individual hospital sites, to further support the integration of the pharmacy team in the medication reconciliation process. In collaboration with the study sites, the authors are further planning to assess patient outcomes on transitions of care when comparing pharmacist-driven medication reconciliation versus standard of care medication reconciliation (completed by nurse, physician etc.) in each site. In today’s challenging and fast-paced healthcare environment, healthcare institutions are urged to optimize resources and eliminate duplication of efforts from the patient care process. Although outside the scope of this study, a future research focusing on the cost effectiveness of pharmacist-led medication reconciliation, with or without student pharmacists, in comparison to other health care professionals, may also bring insight to hospital administrators on to how to allocate limited resources.” (Discussion section, lines 446-458, pages 20-21)

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Reviewer reports:
Amy Shaver (Reviewer 1): The authors present an interesting paper that could help to inform future standardized practice in Lebanon with application of the use of student pharmacists as pharmacist extenders applicable worldwide.

A few areas if expanded would increase the robustness of the paper. My comments and questions are below.

1) Pilot studies are run so as to gather the necessary information to perform a larger study. Please provide some details about whether the sites involved plan on implementing larger studies or the chance of implementing a more pharmacist and student pharmacist driven
medication reconciliation process. In other words, how has this study helped to influence policy at the study sites, and if not what more could be done to implement a standardized process?

Thank you for your comment.

The authors added the following sentences to the discussion:

- “In context of the updated mandatory hospital accreditation standards, the findings of this pilot study were reported to the individual hospital sites, to further support the integration of the pharmacy team in the medication reconciliation process. In collaboration with the study sites, the authors are further planning to assess patient outcomes on transitions of care when comparing pharmacist-driven medication reconciliation versus standard of care medication reconciliation (completed by nurse, physician etc.) in each site. In today’s challenging and fast-paced healthcare environment, healthcare institutions are urged to optimize resources and eliminate duplication of efforts from the patient care process.50 Although outside the scope of this study, a future research focusing on the cost effectiveness of pharmacist-led medication reconciliation, with or without student pharmacists, in comparison to other health care professionals, may also bring insight to hospital administrators on to how to allocate limited resources.” (Discussion section, lines 446-458, pages 20-21)

2) Could the authors discuss the reasons for 25.6% of the recommendations being rejected (line 274) or if one type of recommendation was rejected more than another. The reasons that were given for the rejection, if known, may be useful for other practitioners. Further, the fact that 64.6% of recommendations were accepted should be more greatly emphasized in the discussion as it bolsters the argument of expanding the utilization of pharmacists and student pharmacists in the medication reconciliation process.

Thank you for your comment. The authors added the below sentence to the discussion:

“Most of the medication-related recommendations relayed by the pharmacy team regarding the unintended discrepancies were accepted (64.6%), and resulted in an alteration in the patient’s pharmaceutical care plan. This finding further supports the role of pharmacists and students pharmacists in the medication reconciliation process. Most of the rejected recommendations were related to the omission of a dietary supplement which were assessed by the physicians as unnecessary during acute illness and hospitalization.” (Discussion section, lines 410-415, page 19)

3) Would it be possible to provide the unadjusted odds ratios (see Table 4) in supplemental materials?

Thank you for your query. The authors added the unadjusted Odds ratios to the table since there are only two values.

Kindly advise if you prefer to exclude them from the table and include them in a supplemental appendix.

4) Although the authors state there is no PDMP in Lebanon, please give a reason as to why outpatient pharmacies were not contacted in completing the BPMH (lines 293-295)?

Thank you for your query. The authors added the below sentence to the discussion:

“In Lebanon, these sources may not provide excellent information to improve BPMH due to the practice of medicine in the country where there is a tendency for patients to seek care directly from specialists (often multiple) without the oversight of a primary-care provider.33
Furthermore, many patients might not have loyalty to a single community pharmacy and to date, a prescription drug monitoring program database does not exist in Lebanon.” (Discussion section, lines 365-369, page 17)

5) The authors mention an ADE from an omitted medication leading to hospitalization (lines 306-307); please elaborate on this concept and if possible provide an example from the study population. Though it is a possibility such an ADE could have resulted from previously poor medication reconciliations, it cannot be the result of med recs occurring on day one of said hospitalization. The authors could make the case for the need for future study on how having a BPMH at the point of transition from inpatient to the outpatient setting may aid in avoiding such ADEs.

Thank you for your comment. The authors would like to clarify that they did not observe any patient case with an ADE from an omitted medication leading to hospitalization; what the authors are trying to say is: previous literature identified that discrepancies in medication history, such as the omission of medications and or incomplete information about adherence or non-adherence, may derail clinicians from identifying drug-induced diagnoses that may have led to the current hospital admission.

The authors amended the sentence in the text, which now reads: “On another note, discrepancies in medication history, such as the omission of medications and or incomplete information about adherence or non-adherence, may delay or prevent clinicians from timely identification of drug-induced diagnoses that may have led to the current hospital admission.17” (Discussion section, lines 380-382, page 17)

6) The discussion lines 308-328 is currently disjointed and is in need of better organization. The authors appear to be emphasizing that although many discrepancies were not judged to be clinically significant over one-third were including some involving narrow therapeutic index medications such as NOACs. This point is somewhat lost in jumping from low clinical significance (line 308) to high (line 309) to low (line 314) to clinically significant again (line 316) and on to narrow TI drug discussion (318-328).

Thank you for your comment. The authors reorganized this section of the discussion as follows:

“When assessing potential severity, most of the unintended discrepancies (63%) were judged as clinically significant over one-third were including some involving narrow therapeutic index medications such as NOACs. This point is somewhat lost in jumping from low clinical significance (line 308) to high (line 309) to low (line 314) to clinically significant again (line 316) and on to narrow TI drug discussion (318-328).

The potential severity was classified as serious since antiarrhythmic therapy is useful in reducing the frequency and shortening the duration of arrhythmias, and decreasing arrhythmia-related hospitalizations.42 Although amiodarone has a long half-life, its omission may be serious as it puts the patient at an increased risk of developing another arrhythmia, or worsening of the original arrhythmia. This also requires additional monitoring including laboratory or diagnostic tests, which may increase length of hospital stay and associated costs. The second serious unintended discrepancy involved the detection of a wrong dose of apixaban, a new oral anticoagulant (NOAC). This severity classification was based on a review of previous studies
which showed that off-label dosing of NOACs was associated with morbidity and mortality, and underdosing NOACs was associated with increased cardiovascular hospitalization, and higher stroke rates.43, 44” (Discussion section, lines 392-409, page 18).

7) The authors list the pharmacist as the medication expert and indicate that they should always be involved in the medication reconciliation process. Do they have any plans on comparing this process with the 'usual care' process at each site? (lines 350-352)

Thank you for your question.

The authors added the following sentence to the manuscript:

“In context of the updated mandatory hospital accreditation standards, the findings of this pilot study were reported to the individual hospital sites, to further support the integration of the pharmacy team in the medication reconciliation process. In collaboration with the study sites, the authors are further planning to assess patient outcomes on transitions of care when comparing pharmacist-driven medication reconciliation versus standard of care medication reconciliation (completed by nurse, physician etc.) in each site.” (Discussion section, lines 446-451, page 20)

8) The authors mention using an inter-professional medication reconciliation process, please describe this. (lines 354-355)

Thank you for your comment. The authors added the following: “An interprofessional medication reconciliation process revolves around communication, teamwork, and involves different healthcare professionals in the medication reconciliation process to ensure optimal patient outcomes. For example, pharmacists taking BPMH should not work in silos and need to communicate with the treating physicians to clarify medication orders, and relay any interventions. Moreover, pharmacists are expected to reach out to the patients’ nurses to verify monitoring parameters.” (Discussion section, lines 435-440, page 20)

Alexandra Perez Rivera (Reviewer 2): This is a single arm descriptive and exploratory analysis of a pilot medication reconciliation service led by pharmacists. The authors are to be commended as they are trying to deliver optimal pharmaceutical care in Lebanon. However, I think this study has significant limitations and the manuscript is not well organized. The authors should consider the following: If medication reconciliation has been proven to be an effective service already (regardless of the setting or country), then the next question would be: In Lebanon, how can pharmacists be introduced in the current system/flow of patient care to deliver specialized pharmaceutical care and is it cost-effective for the hospital?

Thank you for your comment.

The authors added the below paragraphs to the discussion:
- “Moreover, in 2019, the Ministry of Public Health in Lebanon in collaboration with the Haute Autorité de Santé (HAS France) updated the Accreditation Standards for Hospitals in Lebanon and emphasized the need for medication reconciliation at admission, and discharge. The medication management chapter within the standards also reinforces that this reconciled list should be shared with the healthcare providers and the pharmacy.49” (Discussion section, lines 402-406, page 18)
- “In context of the updated mandatory hospital accreditation standards, the findings of this pilot study were reported to the individual hospital sites, to further support the integration of the pharmacy team in the medication reconciliation process. In collaboration with the study sites, the authors are further planning to assess patient outcomes on transitions of care when comparing pharmacist-driven medication reconciliation versus standard of care medication reconciliation
(completed by nurse, physician etc.) in each site. In today’s challenging and fast-paced healthcare environment, healthcare institutions are urged to optimize resources and eliminate duplication of efforts from the patient care process. Although outside the scope of this study, a future research focusing on the cost effectiveness of pharmacist-led medication reconciliation, with or without student pharmacists, in comparison to other health care professionals, may also bring insight to hospital administrators on to how to allocate limited resources.” (Discussion section, lines 446-458, pages 20-21)

Here are my specific comments:

**Background:**

1. 144-158: The authors should clearly state where the background information that exists on medication errors and medication reconciliation in coming from (United States? other countries?) and then contrast with the lack of data from Lebanon.

   Thank you for the remark. The authors revised the text to read: “Medication errors remain a significant patient safety concern and a financial burden in hospitalized patients in the United States and Europe” (Background section, line 145, page 5).

   Lines 178-187 and 189-190 now address the available data in Lebanon and the lack of studies addressing medication reconciliation.

   Background section, lines 181-187, pages 6-7: “A recent survey evaluating general hospital pharmacy practice in Lebanon revealed that around 41% of hospitals perform medication reconciliation upon admission, transfer of care, and discharge. Teaching hospitals were more likely to perform medication reconciliation than non-teaching hospitals; and pharmacy services in teaching hospitals seemed to be more advanced cooperating with affiliated medical schools. A previous study, not directly focusing on medication reconciliation, showed that student pharmacists and faculty identified more than 1000 medication-related problems, 4.3% of which were related to medication reconciliation.”

   Background section, lines 189-190, page 7: “To our knowledge, there are no published studies addressing medication reconciliation in Lebanon.”

2. 144-165: Provide documented epidemiological data to show the impact of medication errors and effects of medication reconciliation.

   Thank you for your input. The authors added the following epidemiological data:

   Background section, lines 150-156, page 5: “In a recent randomized controlled study conducted in Oman, the implementation of medication reconciliation on admission and discharge reduced rates of preventable adverse drug events from 16% to 9.1%, p = 0.009. In another recent prospective interventional study conducted to determine the effect of medication reconciliation in two ICU settings in the Netherlands, the proportion of patients with ≥ 1 medication transfer error at ICU admission was reduced from 45.1 to 14.6% (ORadj 0.18 [95% CI 0.11-0.30]) and after ICU discharge from 73.9 to 41.2% (ORadj 0.24 [95% CI 0.15-0.37]).”

   Background section, lines 170-175, page 5: “In a meta-analysis that compared the effectiveness of pharmacist-led medication reconciliation interventions to usual care, the pooled analysis from 17 studies involving 21,342 adult patients showed a substantial reduction of 67%, 28% and 19% in adverse drug event-related hospital revisits (RR 0.33; 95% CI 0.20 to 0.53), emergency department (ED) visits (RR 0.72; 95% CI 0.57 to 0.92) and hospital readmissions (RR 0.81; 95% CI 0.70 to 0.95) in the intervention group as compared to the usual care group, respectively.”
3. 152: Add an official definition of medication reconciliation
Thank you for your comment. Please see definition of medication reconciliation: “Medication reconciliation is defined as a formal multistep process in which healthcare professionals (HCPs) work together with patients and families to ensure that accurate and complete medication information is communicated consistently across transitions of care. It requires a comprehensive review of all the medications that a patient is taking, known as Best Possible Medication History (BPMH), to ascertain that medications added, changed or discontinued are carefully evaluated. In medication reconciliation, a clinician compares the medications that a patient should be using (and is actually using) to the new medications that the medical team prescribes for the patient. The clinician identifies, clarifies, critically evaluates, and resolves any unintended discrepancies.8-10”

Note: The authors agree that having a clear definition of medication reconciliation improves readability; the authors initially included this statement but were asked twice to rephrase this section to avoid overlap with previously published work, given that the authors are citing the Institute of Safe Medication Practices Canada which provides this exact definition of medication reconciliation. The authors leave it to the Editor’s discretion to re-include above statement or not.

4. 167: “standardized medication reconciliation” was not defined.
Thank you for your feedback. The authors meant to state that the implementation of medication reconciliation is not consistent across hospitals in Lebanon. The authors removed the term “standardized” to avoid confusion. The sentence now reads: “The implementation of medication reconciliation in Lebanese hospitals does not keep pace with international standards.” (Discussion section, lines 178-179, page 6)

5. 173-176: The primary and secondary objectives do not match all the results that were provided. The population is not defined, and the outcomes were not all included.
Thank you for your comment. The primary and secondary objectives were revised to include all study outcomes, and the population was specified. The section now reads as follows: “The primary objective of this study was to assess the clinical impact of pharmacy-led medication reconciliation performed on adults patients admitted to the Internal Medicine (IM) services with ≥1 chronic medication, on day one of hospital admission, measured by the incidence of unintended medication discrepancies identified. The secondary objectives were to assess the time needed for medication history, and the information sources used to complete the Best Possible Medication History (BPMH). Other secondary objectives were to classify the unintended discrepancies by medication class and route of medication administration, by potential ADE severity, and by proximal cause leading to the discrepancy. The study also assesses potential determinants of unintended discrepancies.” (Background section, lines 191-198, page 7)

Methods:
1. I suggest a section titled: Participant selection: 181-182: how were they patients identified?
   Through the medical record? On admission? 182-183: what is the definition of unresponsive? May be change to patients which you were not able to do an interview in English or Arabic were excluded, instead?
Thank you for your suggestion. The authors reorganized the details in the manuscript that address the above questions. Please see changes to the Methods section: “Participant Selection: Participants were included in the study if they were inpatients aged ≥18 years old, admitted to the Internal Medicine (IM) services, and had ≥1 outpatient medications. Eligible patients were identified on day one of hospital admission through a list generated daily by the Pharmacy Department at each participating hospital. Participants were excluded if they were unresponsive i.e. comatose or patients who could not be interviewed in English or Arabic. Data Collection Process: Third- and fourth-professional-year student pharmacists at the Lebanese American University School of Pharmacy were properly trained to assist in the process… verified all students’ findings.”(Methods section, lines 205-228, pages 7-8)

2. The intervention was not described in one place/section. How were patients identified? Who made the first encounter? How were any interview proxies identified? Which were the steps to be followed as the medication history was being obtained? An overview of which questions were asked? When did the supervising pharmacist come in? How long were the interviews supposed to take?

Thank you for your input. The authors clarify how patients were identified under the newly proposed section entitled Participant Selection. The authors are labeling this section of the Methods as “Data Collection Process” and “Main Outcomes and Measures” that incorporate responses to the questions Mrs. Rivera Perez is posing. The student pharmacist makes the first patient encounter. Proxy interviews were identified when the patient is not capable of answering questions. The stepwise approach for the med rec process is detailed herein. The questions asked are available under Appendix 1. Upon completion of the data collection, the student pharmacist relayed all findings to the pharmacist at the corresponding site. The on-site pharmacist and/or supervising faculty verified all students’ findings. This confirms that all student interventions were cross-checked by the on-site pharmacist or supervising faculty. The authors report that the time needed to obtain medication history ranged from 3 – 35 minutes. Such finding highlights the level of time commitment that a pharmacist should exhibit when performing medication reconciliation.

Methods section, lines 214-272, pages 8-10:
“Data Collection Process
Third- and fourth-professional-year student pharmacists at the Lebanese American University School of Pharmacy were properly trained to assist in the process. The student pharmacist obtained written consent from eligible patients, and performed face-to-face interviews with patients and/or family members who were willing to participate. Proxy interviews were identified when the patient was not capable of answering questions. In addition to the interview, the student pharmacist was trained to use multiple sources to obtain the BPMH including (but not limited to) examination of home medication bottles or boxes, communication with the treating physician, or review of the patients’ previous medical record, during a previous hospital admission, as applicable. Dietary supplements including vitamins, minerals, and herbal products were also assessed. The information obtained about patients’ medical and medication history was documented on the patient medication reconciliation assessment form (Appendix 1). Subsequently, the student pharmacist checked the medication list in the patient’s medical chart, and compared it to medications he/she had already collected using the assessment form. Upon completion of the data collection, the student pharmacist relayed all findings to the pharmacist at
the corresponding site. The on-site pharmacist and/or supervising faculty verified all students’ findings.

Main Outcomes and Measures
The pharmacist identified, analyzed, and classified discrepancies according to the Medications at Transitions and Clinical Handoffs (MATCH) Toolkit for Medication Reconciliation: no discrepancies (one-to-one match), intended discrepancies (discrepancies were appropriate based on the patient’s plan of care) and unintended discrepancies (discrepancies required clarification because there was no explanation based on the patient’s clinical condition or care plan).12 The MATCH Toolkit for Medication Reconciliation is a public document developed through the support of the Agency for Healthcare Research and Quality (AHRQ), in collaboration with the Joint Commission. This toolkit promotes a successful approach to medication management and reconciliation that emphasizes standardization of the process for doctors, nurses, and pharmacists within the facility to document.12 It is also among the tools recommended by the Institute for Healthcare Improvement (IHI) as a guiding material for developing a medication reconciliation process in the hospital or outpatient practice setting.6 In order to limit the bias during categorization of the discrepancies, the pharmacist relied on multiple sources including the BPMH collected by student pharmacists, a review of current and past medical records, and open communication with the interprofessional team to clarify ambiguities when needed. When all home medications, as per the BPMH, were listed on the patients’ medication list, this was deemed to be a one-to-one match with no discrepancies. If the discrepancy was warranted by the clinical condition and plan of care, as documented in the chart, this was deemed to be an intended discrepancy. In case the discrepancy was not justified by the patients’ clinical condition or plan of care, this was deemed to be an unintended discrepancy.

Interventions related to unintended discrepancies were shared with the interprofessional team caring for the patient, including nursing, medical staff and students. The pharmacist communicated directly with the most senior member on the interprofessional team, either an attending physician or senior resident, as available. The pharmacist documented whether the intervention was accepted, rejected or pending review.

The unintended discrepancies were classified by type, medication category, therapeutic/pharmacological class, route of medication involved, and whether or not the discrepancy relates to a high-alert medication as per the Institute of Safe Medication Practices (ISMP).30 In addition, the pharmacist estimated the proximal cause leading to the medication discrepancy. In the context of this study, the proximal cause is defined as the apparent reason, or the cause closest in time or sequence to the medication discrepancy, estimated to be the immediate cause of the discrepancy. In contrast to identifying the root causes which usually required conducting structured, robust auditing and feedback method, the proximal cause was estimated by a quick assessment of the pharmacist after review of the unintended discrepancy and soliciting the feedback of the frontline personnel involved the error, during relaying the intervention.31,32

Three of the investigators reviewed all unintended discrepancies and came to a consensus to classify each one according to its potential severity. Severity definitions were adapted from a previous study.19 As such, discrepancies were classified into one of four categories: clinically insignificant (error that would not likely cause harm); clinically significant (error that has the potential to cause harm, and may require increased monitoring); serious (error that has potential to cause harm and 1) likely to require additional intervention or 2) could result in prolonged
hospital length of stay); and life-threatening (error having the potential to cause death or likely lead to death without the use of life-sustaining interventions). In case of disagreement, the investigators adopted the least severe classification based on their conservative clinical judgement, in order to avoid overestimation of the study findings.”

3. I separate section for: main outcomes and measures. Outcomes presented in the results section were not introduced in the methods section.

Thank you for your comment. Section for main outcomes and measures is now separated:

Methods section, lines 230-272, pages 8-10:

“Main Outcomes and Measures

The pharmacist identified, analyzed, and classified discrepancies according to the Medications at Transitions and Clinical Handoffs (MATCH) Toolkit for Medication Reconciliation: no discrepancies (one-to-one match), intended discrepancies (discrepancies were appropriate based on the patient’s plan of care) and unintended discrepancies (discrepancies required clarification because there was no explanation based on the patient’s clinical condition or care plan).12 The MATCH Toolkit for Medication Reconciliation is a public document developed through the support of the Agency for Healthcare Research and Quality (AHRQ), in collaboration with the Joint Commission. This toolkit promotes a successful approach to medication management and reconciliation that emphasizes standardization of the process for doctors, nurses, and pharmacists within the facility to document.12 It is also among the tools recommended by the Institute for Healthcare Improvement (IHI) as a guiding material for developing a medication reconciliation process in the hospital or outpatient practice setting.6 In order to limit the bias during categorization of the discrepancies, the pharmacist relied on multiple sources including the BPMH collected by student pharmacists, a review of current and past medical records, and open communication with the interprofessional team to clarify ambiguities when needed. When all home medications, as per the BPMH, were listed on the patients’ medication list, this was deemed to be a one-to-one match with no discrepancies. If the discrepancy was warranted by the clinical condition and plan of care, as documented in the chart, this was deemed to be an intended discrepancy. In case the discrepancy was not justified by the patients’ clinical condition or plan of care, this was deemed to be an unintended discrepancy.

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Three of the investigators reviewed all unintended discrepancies and came to a consensus to classify each one according to its potential severity. Severity definitions were adapted from a previous study. As such, discrepancies were classified into one of four categories: clinically insignificant (error that would not likely cause harm); clinically significant (error that has the potential to cause harm, and may require increased monitoring); serious (error that has potential to cause harm and 1) likely to require additional intervention or 2) could result in prolonged hospital length of stay); and life-threatening (error having the potential to cause death or likely lead to death without the use of life-sustaining interventions). In case of disagreement, the investigators adopted the least severe classification based on their conservative clinical judgement, in order to avoid overestimation of the study findings.”

4. Why was the MATCH Toolkit selected? Is this validated?

Thank you for your question. The authors added the below sentence to the manuscript: “The MATCH Toolkit for Medication Reconciliation is a public document developed through the support of the Agency for Healthcare Research and Quality (AHRQ), in collaboration with the Joint Commission. This toolkit promotes a successful approach to medication management and reconciliation that emphasizes standardization of the process for doctors, nurses, and pharmacists within the facility to document. It is also among the tools recommended by the Institute for Healthcare Improvement (IHI) as a guiding material for developing a medication reconciliation process in the hospital or outpatient practice setting.” (Methods section, lines 235-242, page 9)

5. 203-204 and 209-210: who was in the medical team? How did these communications occur?

If the pharmacists were the ones doing the categorization, was there any bias introduced?

Thank you for your comment. The authors added the following two paragraphs to the manuscript:

- Methods section, lines 242-249, page 9: “In order to limit the bias during categorization of the discrepancies, the pharmacist relied on multiple sources including the BPMH collected by student pharmacists, a review of current and past medical records, and open communication with the interprofessional team to clarify ambiguities when needed. When all home medications, as per the BPMH, were listed on the patients’ medication list, this was deemed to be a one-to-one match with no discrepancies. If the discrepancy was warranted by the clinical condition and plan of care, as documented in the chart, this was deemed to be an intended discrepancy. In case the discrepancy was not justified by the patients’ clinical condition or plan of care, this was deemed to be an unintended discrepancy.”

- Methods section, lines 250-254, page 9: “Interventions related to unintended discrepancies were shared with the interprofessional team caring for the patient, including nursing, medical staff and students. The pharmacist communicated directly with the most senior member on the interprofessional team, either attending physician or senior resident, as available.”

6. 204-205: was this documented in the results section?

Thank you for your comment. This was documented in the results section.

Results section, lines 342-348, pages 15-16: “Based on the discrepancies found, the pharmacy team recommended a total of 195 medication-related interventions, where 64.6% of these interventions were accepted, 25.6% were rejected, and around 10% pending review. The most common types of medication-related interventions included: the addition of a medication (71.8%), dose adjustment (12.8%), discontinuation or switching of a medication (7.2%), and
frequency adjustment (5.1%). Other interventions were giving medication from home supply (1.5%), and adjustment of medication route (1%).”

7. 209: what was the framework used to make the proximal cause categorization?
Thank you for your query. The authors added the below sentence to the text:
Methods section, lines 258-263, page 10:
“In the context of this study, the proximal cause is defined as the apparent reason, or the cause closest in time or sequence to the medication discrepancy, estimated to be the immediate cause of the discrepancy. In contrast to identifying the root causes which usually required conducting structured, robust auditing and feedback method, the proximal cause was estimated by a quick assessment of the pharmacist after review of the unintended discrepancy and soliciting the feedback of the frontline personnel involved the error, during relaying the intervention.”

8. The statistical plan was poorly described. The authors only talk about the dependent outcome but did not mention any independent variables.
Thank you for your comment. The authors better described the regression analysis in the methods, under the “Data Management and Statistical Analysis” section (lines 276-288, pages 10-11) where we clarified the dependent and independent variables. The section now reads as follows:
“The data collected was coded, entered into SPSS version 25 software, verified for data entry errors, and analyzed. Descriptive statistics were used to report all participants’ responses. The dependent variable was the incidence of unintended discrepancies. For the bivariate and multivariable analysis, the “total number of unintended discrepancies” was dichotomized into yes (≥ 1 unintended discrepancy) or no (0 unintended discrepancies). Independent variables tested for their association with the dependent variable consisted of the following: gender, age, creatinine clearance, number of home medications, allergies, previous Adverse Drug Reactions (ADRs), and number of information sources used to obtain the BPMH. The association between categorical variables were evaluated using the Pearson χ2 test or Fisher’s exact test where the expected cell count < 5. Binary logistic regressions were performed using a Backward LR method. Variables with a p-value of 0.2 or less in the bivariate analysis were included in the initial models. Results were assumed to be significant when p was <0.05 for all statistical analysis.”

Results:
1. 240: how was a previous medical record defined? Communication with which physician?
   This was not introduced in the methods section.
Thank you for your feedback. A previous medical record is defined as the patient’s medical record/chart during a previous hospital admission. The authors included this detail under the Methods section (lines 219-222, page 8):
"In addition to the interview, the student pharmacist was trained to use multiple sources to obtain the BPMH including (but not limited to) examination of home medication bottles or boxes, communication with the treating physician, or review of the patient’s previous medical record, during a previous hospital admission, as applicable.”
2. 254-259 and 265-269: this section was confusing as written. I wasn't sure what was being presented and then figured out it was the unintended discrepancies. Thank you for this comment. The authors made sure to clarify that this section is focusing on the unintended discrepancies. The section now reads as:

“When classifying the unintended discrepancies by route of administration, 92.3% were found to involve an oral medication. Only 3.6% of the unintended discrepancies involved an inhaled medication and 1.5% involved a subcutaneous medication. The most common agents involved in unintended discrepancies consisted of dietary supplements (27.7%). Other medication classes involved were antihyperlipidemic agents (7.2%), medications for reflux disease (7.2%), and medications for asthma/COPD (7.2%). Further details are included in table 3. Moreover, around 8% of the unintended discrepancies involved a high-alert medication, including oral hypoglycemic agents, insulin, anti-arrhythmic agents, and anticoagulants. When assessing potential severity of all medication-related discrepancies by the investigators, 122 discrepancies out of 195 were judged as clinically insignificant, 71 (36.4%) were judged as clinically significant, and only 2 (1%) were judged to be serious. No life-threatening interventions were identified.” (Results section, lines 321-337, page 14)

3. 260-264: should be presented after describing unintended discrepancies. Thank you for your comment. The authors moved this paragraph up, and it is now presented after describing the unintended discrepancies (Results section, lines 316-320, page 13).

4. Table 3: when presenting the drug classes a heading saying prescription and OTC medications were being presented. Thank you for your comment. The authors added “prescription and OTC medications” to the heading in table 3, when presenting the drug classes. (Results section, pages 14-15)

5. I was not able to follow the regression analysis results at all, mostly because it was poorly described in the methods section. Thank you for your comment. The primary and secondary objectives were revised to include all study outcomes, and the population was specified. The section now reads as follows:

“The primary objective of this study was to assess the clinical impact of pharmacy-led medication reconciliation performed on adults patients admitted to the Internal Medicine (IM) services with ≥1 chronic medication, on day one of hospital admission, measured by the incidence of unintended medication discrepancies identified. The secondary objectives were to assess the time needed for medication history, and the information sources used to complete the Best Possible Medication History (BPMH). Other secondary objectives were to classify the unintended discrepancies by medication class and route of medication administration, by potential ADE severity, and by proximal cause leading to the discrepancy. The study also assessed potential determinants of unintended discrepancies.” (Background section, lines 191-198, page 7)

Discussion:
Overall, this is a repetition of the results and new results are presented as well. This section should focus on the implications of the observed results. There is very little focus on the limitations which are big: no control arm and high risk of bias.
Thank you for your comment. The authors revised the discussion which now focuses more on the implications of the results and the limitations of the study. (Discussion section, lines 355-474, pages 16-21)