Author's response to reviews

**Title:** Drug cost by a multidisciplinary approach to potentially inappropriate medications for older patients in home care settings: cross-sectional study and propensity score analysis

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**Author's response to reviews:** see over
Dear Dr. Christopher Morrey

Re: “Drug cost by a multidisciplinary approach to potentially inappropriate medications for older patients in home care settings: cross-sectional study and propensity score analysis,” by Jun Hamano et al.

We are most grateful to you and the reviewers for your critical comments and useful suggestions that have helped us improve our manuscript considerably. As indicated in our responses below (indicated with the ■ symbols), we have taken all of these comments and suggestions into account in the revised version of our manuscript.

We hope that the explanations and revisions of our work are satisfactory.

Reviewer: 1

1-1. The information provided does not present a clearly defined question. Neither the structure of “nurse home visiting programs” nor of the “pharmacist home visiting programs” in Japan are defined for the reader. When the question is proposed it is unclear whether or not the question intends to examine something that is currently in place in Japan or if the nurse home visits and pharmacist home visits are a new intervention. However, this becomes apparent later on in the discussion of the limitations.

■ We have corrected the question of this study in page 2, line 33 to line 36 and in page 6, line 94 to line 97.

■ We have explained the structure of nurse and pharmacist home visit program in Japan in page 6, line 104 to in page 7, line 114.

■ The programs of nurse home visits and pharmacist home visits have been used extensively in Japan.

1-2. As a scientist I would not know how to set up the same scenario to replicate the results.

■ We have revised the Methods section in page 6, line 100 to in page 8, line 134.

1-3. I am not competent to assess whether or not they applied the use of propensity scores correctly to the data.

■ We performed our analysis to adjust the potential confounders as possible as we could by using
propensity scores. There might have been other confounders, which we could not adjust and thus further research is needed to consider all potential confounders that can affect the drug cost of PIMs in home care setting and the effectiveness of home visit program. We have added these points in page 14, line 235 to 236 and in page 14, line 251 to page 15, line 253.

1-4. There is no definition as to what these pharmacists and nurses are doing in the home visiting programs. There is no background information offered as to why some patients see pharmacists, some see nurses, and some see both?

We have added the definition and the background information of nurse and pharmacist visit program in page 6, line 104 to in page 7, line 115.

1-5. My hypothesis is that pharmacists see patients which are more complex and that the underlying differences between the population seen by the pharmacist and the population seen by the nurse are probably not reconcilable.

We have added the interpretation of our result as “pharmacist home visit programs tend to involve patients with complicated conditions and PIMs might have been actually appropriate in these circumstances.” in page 12, line 213 to line 215.

1-6. I wonder if high cost of prescriptions at baseline is a predictor for those who see a pharmacist?

Our study did not assess all potential confounders that might affect the using home visit program. Therefore, further research is needed to consider not only other potential confounders of drug cost of PIMs but also the potential confounders associated with using home visit program.

1-7. In line 132 and 133 it mentions categorizing the patient age into three groups. However, I don’t know why this is mentioned. Based on my very limited knowledge about propensity scores, there are 4 ways to apply the scores to the data (matching case to controls, stratifying cases and controls, using propensity score as independent variable in multivariable model, and using propensity scores to weight observations). The mentioning of these classifications would seem to indicate the data would be stratified;

We used patient age groups as a risk factor variable potentially associated with the increased number of medications. We used propensity score as independent variable in multivariable model.

1-8. Were matched propensity scores tried first? Matching produces the least amount of bias. It would be interesting to see the results published from both approaches… this would strengthen the
The matching by propensity scores was not used in our study since the matching by propensity scores requires the equally large number of both groups in study samples and our sample sizes were considered as not large enough to conduct this.

1-9. Prices seem very low especially since the Brand name prices were used.
We estimated the drug cost based on actual pharmaceutical prices listed by the regulatory committee at the Ministry of health, Labour and Welfare, Japanese government. We used “Brand name price” in the sense of actual pharmaceutical prices. Then we have changed the description in page 8, line 132 to line 134.

1-10. Does table 1 need permission of the authors of the STOPP criteria to reproduce it?
The criteria were published and distributed extensively and thus we cited the original work in the reference.

Below is response for comment in attached file from Reviewer: 1

[Major Compulsory Revision]

1-11 (JC1). Regarding the title
We have changed the title of our article to “A comparison of estimated drug costs of PIMs between older patients receiving nurse home visit services and patients receiving pharmacist home visit services: a cross-sectional and propensity score analysis”

1-12 (JC7&JC8). Regarding the conclusion
We have corrected the conclusion as “Patients who were using nurse home visit program have a trend towards lower drug costs of PIMs than those who were using nurse and pharmacist home visit program or pharmacist home visit program alone. Although, this study tried overcoming the limitation of study design by using propensity score analysis, caution may be need about interpretation of this study.” in page 4, line 55 to line 59 and as “those who were using nurse home visit program have a trend towards lower drug costs of PIMs than those who were using nurse and pharmacist home visit program or pharmacist home visit program alone.” in page 14, line 247 to 249.

1-13 (JC13). By multidisciplinary approach, I would expect that you would be trying to show whether or not having a pharmacist + a nurse reduces the cost.
Our study did not assess the multidisciplinary approach using both a pharmacist + a nurse. Our study only assessed the relations of either nurse or pharmacist home visit program to drug cost
of PIMs. Thus we have changed the sentence as “estimated the relations either nurse or pharmacist home visit program to drug cost of PIMs identified by the STOPP criteria for older patients in home care settings.” in page 6, line 92 to line 93.

1-14 (JC22). What kind of home visit service?

We have changed the sentence as “patients received home visit services regularly by doctor at least twice a month for over a month” in page 7, line 19 to line 20.

1-15 (JC26). What medication list was used for the purpose of detecting PIMs?

We used the copies of prescription contents of one month during the survey period, which was sent from each clinic. We have added the sentence as follows: “We had collected the copies of prescription contents by single monthly basis during the survey period which was sent from each clinic and confirmed the medication.” in page 8, line 128 to line 129.

1-16(JC26). Was this list check against medications actually present in the home?

We have checked the copies of prescription contents of one month during the survey period, which was sent from each clinic. Thus we have changed the sentence as “We had the copies of prescription contents of one month during the survey period which was sent from each clinic and confirmed the medication.” in page 8, line 28 to line 29.

1-17(JC26). Was the list updated after each pharmacist / nursing visit?

We could recognize update of the list after the one-month period and analyze accordingly.

1-18(JC26). Did the number of visits have an impact on the list?

We did not assess the impact of the number of visits for the drug list. As the reviewer points out, this point seems to an important factor to have influence on medication list and further study may be needed to clarify to this point.

1-19(JC27). What is meant by the survey period? Were the patients followed from May – December?

We assessed the copies of prescription contents by single monthly basis during the survey period (from May to December). Thus we have revised as “We had collected the copies of prescription contents by single monthly basis during the survey period which was sent from each clinic and confirmed the medication.” in page 8, line 128 to line 129.

1-20(JC28). Why did you choose to estimate cost based off of brand name drugs rather than use actual costs?
We estimated the drug cost as actual pharmaceutical prices listed by the regulatory committee at the Ministry of health, Labour and Welfare, Japanese government. We used “Brand name price” in the sense of actual pharmaceutical prices. Thus we have changed the description in page 8, line 132 to line 134.

1-21(JC34). Please explain why you would call this a multidisciplinary approach.

Our study did not assess the multidisciplinary approach but assessed the relations of nurse and pharmacist home visit program to drug cost of PIMs. Thus we have changed the sentence as “estimated the relations of nurse and pharmacist home visit program to drug cost of PIMs identified by the STOPP criteria for older patients in home care settings.” in page 6, line 92 to line 94.

1-22(JC35). Please explain why from this data you could conclude increasing the use of nursing home visits would result in lower PIM costs.

We agree with the points that our study could not conclude increasing the use of nursing home visits would result in lower PIM costs. The relations of nurse or pharmacist home visit program to drug cost of PIMs were assessed in our study. Thus we have changed the description of discussion in page 12, line 207 to page 14, line 244.

1-23(JC36). Why do you think this finding is generalizable to other “home care settings?”

We agree that our study may not be generalizable to other “home care settings”. We have described the limitation as “our study may not be representative of older home care patients, because it was carried out with only a few institutions in Japan” in page 14, line 237 to line 238.

1-24(JC37). There was a trend towards lower costs, that may warrant further research, but I wouldn’t say that it was a finding of this study.

Our study may not show such a trend towards lower costs. Thus we have described this limitation of our study as “we cannot draw conclusions about the effectiveness of nurse and pharmacist home visit program to drug cost of PIMs, because our study was not an intervention study.” in page 14, line 240 to line 242.

1-25(JC43). Please revise conclusion to ensure it doesn’t extend past what the data supports.

We have changed the description of conclusion in page 14, line 247 to page 15, line 253.

1-26(JC44). There is no discussion of barriers to information that pharmacists may have.

We have added the sentence about the barrier to information that pharmacists may have in page
12, line 216 to page 13, line 225.

1-27(JC44). Is something preventing pharmacists from having access to this clinical information?

We have added this point about pharmacist home visit programs in Japan in page 13, line 219 to line 225.

【Minor Essential Revision】

1-28(JC3). This tool identifies potentially inappropriate medications, not the costs. After the PIMs were identified with STOPP, using the drug cost was estimated using the cost of the brand name drugs.

We have added the following sentence into the method section: “After the potentially inappropriate medications were identified with the Screening Tool of Older Persons’ potentially inappropriate Prescriptions (STOPP) criteria, we estimated the drug cost as actual pharmaceutical prices” in page 3, line 39 to line 42.

1-29(JC9). Regarding the types of drug therapy problems

We agree with the point: “not prescribing medicines that are indicated” is not the category of PIMs. Thus we have deleted this sentence.

1-30(JC12). Based on the citation, I was expecting you to show a multidisciplinary intervention aimed at reducing PIMs and costs.

Our study did not assess the multidisciplinary approach. Our study assessed the relations of nurse and pharmacist home visit program to drug cost of PIMs. Thus we have revised the sentence as “it was not clear about the relations of pharmacist intervention to drug cost of PIMs” in page 5, line 90 to page 6, line 91.

1-31(JC16). Regarding the using the word “enrolled”

Using the word “enrolled” was not appropriate for this study. Thus we have deleted this sentence.

1-32(JC17). “All patients” were not enrolled, but only those meeting the inclusion criteria below.

We have revised the sentence as follows: “We included all patients who were 65 years or older and who satisfied our inclusion criteria,” in page 7, line 117 to line 118.

1-33(JC18). If prospective, how was consent obtained?

The study was based on the retrospective review and thus we have deleted this sentence.
1-34(JC21) Does this mean no one at the clinic, or none of the clinicians that would be visiting the patient? How did you assess their familiarity with the STOPP criteria? Was this asked before or after the enrollment window? If asked before, do you think it influence the results? Were there any educational interventions?

- Few at the clinic were familiar with the STOPP criteria.
- We assessed their familiarity with the STOPP criteria based on analysis of copies of prescription contents of one month.
- We did not conduct any educational interventions for clinicians.

1-34(JC23) Can you be more specific for “regularly.”

- Patients received home visit services regularly by their doctors at least twice a month for over a month. We have added this sentence in page 7, line 119 to line 120.

1-35(JC25) What did you verify them against?

- We had collected the copies of prescription contents of one month during the survey period, which was sent from each clinic and confirmed the medication. We have described this point in page 8, line 128 to line 129.

1-36(JC31) I don’t see mention of these 123 patients in table #2

- “123 patients” was not shown in Table 2. These “123 patients” were obtained by subtracting the number of patients who used nurse home visit programs (203 patients) and those who used only pharmacist home visit programs (104 patients) from all patients (430 patients). Thus we have changed the sentences of page 10, line 176 to line 178 as “Almost one fifth, 78 patients (18.1%) had used both nurse and pharmacist home visit programs (Table 2). Over one quarter, 123 patients (28.6%), had not used either program.”

1-37(JC38) Could it also imply that there is a confounding variable that hasn’t been adjusted for and that pharmacists see more complex patients?

- Our result implies that there might have been a confounding variable that has not been adjusted for and that there is possibility that pharmacists see more complex patients. Thus we have revised the sentences of the discussion section as: “There are several explanations about this finding. First, pharmacist home visit programs tend to involve patients with complicated conditions and PIMs might have been actually appropriate in these circumstances.” in page 12, line 213 to line 215 and as “Third, there might have been other unidentified confounding variables that might affect the effectiveness of home visit program to the drug cost of PIMs.” in page 13, line 226 to line 227.
1-38(JC39) please explain the nature of the pharmacist interactions with the patient so as to shed some more light on why you think this might be an issue.

We have described the nature of pharmacist home visit program and revised the sentences of discussion in page 13, line 218 to line 225.

1-39(JC40) Do you have a reason why pharmacist home visiting programs do not improve communication in Japan?

Pharmacists of home visit programs usually did not receive the details of patients’ medical history from doctors and were not expected to give advice to doctors about prescription. This background may prohibit the improvement of pharmacist’s communication in Japan. We described this point in page 13, line 221 to line 225.

1-40(JC41) There is probably an unidentified confounding variable

The possibility of an unidentified confounding variable may exist in our study. Thus we have described this point in page 13, line 226 to line 232.

1-41(JC42) It might not be that they “have no choice,” but rather that the PIM is actually appropriate in these circumstances and that the pharmacist is using his judgment to help them use the medication safely.

We have added the sentence: “pharmacist home visit programs tend to involve patients with complicated conditions and PIMs might have been actually appropriate in these circumstances.” in page 12, line 213 to line 215.

【Discretionary Revision】

1-42(JC4) When compared to what?

We have revised the sentence as “Patients who used the nurse home visit programs had lower drug cost of potentially inappropriate medications than who did not use, but it was not significantly different” in page 3, line 44 to line 46.

1-43(JC14) Drug cost to whom? The patient? OR The insurer?

We have changed “drug cost” as “actual pharmaceutical prices” in page 4, line 95 to line 96. The actual pharmaceutical prices means the prices which is listed by the regulatory committee at the Ministry of health, Labour and Welfare, Japanese government.

1-44(JC19) Were these clinics, providing primary care?
We have changed the sentence as “These clinics provide primary care by ambulatory service and home visit services for community residents” in page 6, line 101 to line 102.

1-45(JC20) Were the patients followed during this time?
1-46(JC29) What drugs are prescription drugs in Japan? Does this differ from U.S.?

The prescription drugs in Japan are similar to those in U.S. However, drug names and prices of Japan would be differed from those of U.S.

【Comment】
1-47 (JC11) Do you mean in detecting DRPs?

The cited article (References 26) suggested that the STOPP criteria are more sensitive in detecting PIMs than the Beers’ criteria. On the other hands, the cited article (References 25) indicated that the STOPP criteria have high sensitivity for detecting potential drug-related problems.

Reviewer: 2

【Major Compulsory Revisions】
2-1 It would be helpful if the nursing and pharmacy home visit programs could be described in some detail. Please include what each discipline’s role/service is and what they typically evaluate in the home visits.
2-2 Did nursing and pharmacy both have equal access to clinical records?
2-3 What is the frequency of home visits by each discipline?
2-4 What constitutes regular home visits, and how often were patients seen during the study period by either discipline?

We have provided the definition and the background information of nurse and pharmacist visit program in page 6, line 104 to in page 7, line 114.

2-5 What constitutes a “regularly prescribed by the clinic” medication?
2-6 What point were medication lists considered for inclusion in the study?

We had the copies of prescription contents of one month during the survey period, which was sent from each clinic and confirmed the medication. We have added this sentence in page 8, line 128 to line 129.
2-7 Why was brand name medication cost used over generic?
- We estimated the drug cost based on actual pharmaceutical prices listed by the regulatory committee at the Ministry of Health, Labour and Welfare, Japanese government. We used “Brand name price” for indicating actual pharmaceutical prices. Thus we have revised the description in page 8, line 132 to line 134.

2-8 It seems questionable that the total monthly cost of PIM (as brand name medication) should be as low as it is reported. Could this be due to cost differences of medication between the markets in United States and Japan?
- As described in 2-7, we estimated the drug cost based on actual pharmaceutical prices listed by the regulatory committee at the Ministry of Health, Labour and Welfare, Japanese government. We used “Brand name price” for indicating actual pharmaceutical prices. Therefore, there would be some differences of medication costs between the markets in United States and in Japan.

2-9 What reference was used to estimate the cost of medication?
- As described in 2-7, we estimated the drug cost based on actual pharmaceutical prices listed by the regulatory committee at the Ministry of Health, Labour and Welfare, Japanese government.

2-10 The title is misleading. The primary intervention evaluated was not a multidisciplinary approach.
- We have revised the title of our article as “A comparison of estimated drug costs of PIMs between older patients receiving nurse home visit services and patients receiving pharmacist home visit services: a cross-sectional and propensity score analysis”

2-11 The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.
- We have corrected the label on figures (title legend of Table 4 and 5), spelling and terms.

【Minor Essential Revisions】
2-12 I will list the manuscript line number and my recommended changes below.
We have corrected the manuscript as reviewer recommended. Some of terms and sentences have been completely replaced by other terms and sentences (indicated with the * symbols).
*46 – In patient groups…
49 – In patient groups…. (in page 3, line 48)
*54 - …visiting programs did not have the…
63 – Prescription medications are an essential… (in page 4, line 67)
74 - …countries with an aging… (in page 5, line 77)
75 - …population, such as Japan,… (in page 5, line 78)
83 - …reduce the number of patients with PIMs… (in page 5, line 87)
181 – In patient groups who used nurse home… (in page 11, line 198)
183 – In patient (in page 12, line 201)
184 – groups who did not… (in page 12, line 201)
*240 - …in multidisciplinary teams.

【Discretionary Revisions】

2-13 if further clarification is given to define what the nurse and pharmacist home visiting programs entail.
We have provided the definition and the background information of nurse and pharmacist visit program in page 6, line 104 to in page 7, line 114.

2-14 The conclusion, however, seems somewhat disjointed, particularly the second half. Perhaps some reference to the need for future study to better elucidate or further clarify the findings presented in this study would be merited.
We have revised the conclusion as “Patients who were using nurse home visit program have a trend towards lower drug costs of PIMs than those who were using nurse and pharmacist home visit program or pharmacist home visit program alone. Although, this study tried overcoming the limitation of study design by using propensity score analysis, caution may be need about interpretation of this study.” in page 4, line 55 to line 59 and as “those who were using nurse home visit program have a trend towards lower drug costs of PIMs than those who were using nurse and pharmacist home visit program or pharmacist home visit program alone.” in page 14, line 247 to 249.

2-15 Perhaps some further discussion of the limitations of these tools would be helpful.
We have revised four main limitations in page 13, line 230 to page 14, line 242.

We hope that the revised version of our manuscript is now suitable for publication in BMC Health Services Research.