PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Trends in the receipt of medicines information among Finnish adults in 1999–2014: a nationwide repeated cross-sectional survey
AUTHORS	Mononen, Niina; Airaksinen, Marja; Hämeen-Anttila, Katri; Helakorpi, Satu; Pohjanoksa-Mäntylä, Marika

VERSION 1 – REVIEW

REVIEWER	Assoc Prof. Dr. Narumol Jarernsiripornkul Division of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Khon Kaen University, Khaon Kaen, Thailand
REVIEW RETURNED	24-Sep-2018

GENERAL COMMENTS	General comments This manuscript is logically organized and well written. However, there are some comments that the authors need to address. Specific Comments 1. Abstract a. Design: Longitudinal study should be mentioned. b. Conclusion: Line 53-56: These sentences are not necessary to include in the Conclusion part. Suggestions related to the main findings of this study are preferred. 2. Methods: a. Study design: Longitudinal study should be included in this section. b. Line 46-48: Please clarify the health behavior of the population that is related to the outcomes of study. c. Please explain more detail how to select and random the 5000 patients to be representatives of the population. Also, how to distribute the questionnaires to cover all different groups of patients. d. Why did the researchers choose the use of medication within the past 7 days? e. Data on the indication for use was shown in the Results, however this data was not mentioned in the Methods. f. Page 7, Line 37-88: How many people was piloted by convenience sampling? 3. Results a. According to the medicines list mentioned in the Methods, no finding of the medicines was shown in Results or Tables. Please briefly provide the common medicines in use.

	b. Appendix A: if possible, percentages should be presented for each main group of the respondents, i.e female/ male, individual age group, etc. This will make it easy to understand the texts in Results. 4. Discussion a. Page 13; Line 27-28: this sentence needs to further explain and discuss in more detail. b. Page 13, Line 42-43: In term of “Influence”, it seems that these factors are statistically associated with the receipt of MI. Please consider to modify this sentence. c. Based on the legislation of EU for providing the patient package inserts for all patients receiving medicines, please give possible explanation or reason for the decreased rates of MIs distributed over time. d. The sentence indicates that the receipt of MI from internet is still quite “rare”. In my opinion, 16% is not indicated as “rare”. 5. Conclusion a. Please modify the conclusion, not repeat same sentences as the conclusion in Abstract part. Again, the last sentence should not be included in the conclusion. Further brief suggestion should be emphasized on the main findings of this study.

REVIEWER	Ragnhildur I. Bjarnadottir University of Florida, College of Nursing, Gainesville, FL, USA
REVIEW RETURNED	07-Nov-2018

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript, describing a study of an important and timely topic: the provision of medication information to patients. The study has some strengths, most notably the use of a large national sample. However, there are notable weaknesses in the design and reporting that raise concerns. Firstly, the authors neither distinguish between prescribed and over-the-counter medication, nor between active medication information-seeking or passive receipt of information. This is of particular importance as it relates to the interpretation of the results and the potential implications. For example, the implications or interpretation of a gender difference in reported receipt and/or sources of medication information differ significantly depending on whether these are discrepancies in the information being provided or gender differences in information-seeking behaviors. Similarly the implications of the finding that up 28% of participants did not receive any medication information differ substantially depending on whether these participants were taking prescription medication (where the responsibility of the prescribing clinician is well defined) or over-the-counter medication. Secondly, the researchers describe a robust body of literature exploring receipt of medication information but indicate that a gap in the literature is the lack of a longitudinal examination on the subject. The authors do not communicate well why this is an important gap to address or what the implications of such longitudinal analyses might be for practice, policy or research. In addition, the researchers appear to have chosen to conduct the data analysis using purely descriptive cross-sectional methods, and therefore it is unclear how (if at all) the study is filling this gap in the literature.

	Finally, the authors describe descriptive statistics, including means and percentages, but do not report any comparative statistics to determine whether the reported differences from year to year are significant or not. Overall, the analytical methods use appear to be somewhat lacking in robustness. In light of these three key weaknesses, I am unable to recommend that this paper be accepted for publication without major revisions to address them.

REVIEWER	Elaine Walsh University College Cork, Ireland
REVIEW RETURNED	09-Nov-2018

GENERAL COMMENTS	This is a large population based study with interesting findings pertaining to medication information. There are some concerns relating to methodology however. Major concerns: • The methods state that the annual sample “was made nationally representative”. The reference to support this is in Finnish however. How was this achieved? Could the authors provide additional information about sampling? There are considerable variations between the samples from individual years e.g in 1999 11% of the sample were taking 3 or more medications versus 20% in 2014, 1999 13% of the population had 2 or more co-morbidities versus 32% in 2014. The analysis is purely descriptive and though detailed (e.g Appendix B), it doesn’t adequately assess how such variations may have impacted the outcome being assessed It can’t be ascertained from the results if the differences noted in receipt of medication information over time are statistically significant and if they are does the difference remain if the variability in number of meds, co-morbidities, education in different years etc is controlled for? It would seem that a regression analysis should be conducted • How relevant is it to include information from 1999 when 2 sources of medication information were omitted? • The study excludes the older adult population of >65 years. In view of the association of increasing age with multimorbidity and polypharmacy, the study excludes the group potentially taking the greatest number of medications to whom the findings are potentially most relevant. This should be addressed. Minor concerns • Though the introduction provides a good review of the literature there are grammatical errors and the meaning of certain phrases is unclear. Examples: Page 4: Lines 13 and 14 Lines 41 and 42 Page 5: Line 11 and 12 • There is data missing from 6 years-more explanation of this is required. The use of the word “annual” is not appropriate in view of this

	• Could the rationale for the ratio calculations between the mean number of medications and co-morbidities/MI be explained?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

General comments

This manuscript is logically organized and well written. However, there are some comments that the authors need to address.

Specific Comments

1. Abstract

a. Design: Longitudinal study should be mentioned.

Authors' response: Thank you for this important comment concerning the study design. However, this study did not follow the same people as a cohort throughout the study period 1999-2014. Each study year, a new independent random sample of 5000 Finns aged 15-64 years was derived. Therefore, our understanding is that this study cannot be considered as a longitudinal follow-up study, but it is a repeated cross-sectional study. For this reason, we would like to suggest to leave the study design as "repeated cross-sectional survey". We have clarified the text in the Abstract and in the Methods section of the manuscript as follows:

ABSTRACT/Setting (page 2, lines 18-19):
"Each study year, a new nationally representative sample of 5000 Finns aged 15-64 years was drawn from the Population Register Centre of Finland."

METHODS/Study design (page 5, lines 39-40):
"The study was conducted as a repeated cross-sectional postal survey using each year a new nationally representative sample (n=5000) of the Finnish adult population aged 15-64 years."

1

b. Conclusion: Line 53-56: These sentences are not necessary to include in the Conclusion part. Suggestions related to the main findings of this study are preferred.

Authors' response: Thank you for this important comment. The conclusion has been rewritten as recommended to better reflect the key findings of this study as follows:

ABSTRACT/Conclusion (page 2, lines 48-56):
"Healthcare professionals and package leaflets had still a dominating importance in 2014 despite the growing number of MI sources over time, but still a minority of adult medicine users reported receiving MI via the Internet in 2014. Worrying is that the proportion of adult medicine users who did not receive MI from any of the sources became 7-fold during the study period."

2. Methods

a. Study design: Longitudinal study should be included in this section.

Authors' response: Please, see our response to the comment 1a (above).

b. Line 46-48: Please clarify the health behavior of the population that is related to the outcomes of study.

Authors' response: The national health behavior survey used in this study has its origins in the wellknown North Karelia Project, started in 1972, which has been instrumental in improving public health in Finland (Puska et al. 1981, 2009, 2016). The Project aimed at understanding etiology and factors related to high prevalence of cardiovascular diseases in Finland, also regional differences in the prevalence and associated mortality.

The annual national health behavior survey was established in 1978 to perform as an indicator for changes in the population health and related risk factors, such as smoking, food and alcohol consumption and physical activity (Helldán & Helakorpi 2015). The survey has been targeted to the adult working age population of 15-64 years old. The survey has been repeated every year in the same way to yield comparable results. In addition to the original standard set of structured questions, some other questions have been added to the survey instrument over the years. One of the added questions was the one used in our study concerning receipt of medicines information from different sources available for consumers/medicine users in Finland (added to the survey instrument in 1999).

Of the variables included in the survey instrument, we have used gender, age, diagnosed diseases and medicines in use as background variables to understand possible differences in the receipt of medicines information in different medicine user groups. The question related to the morbidity was focused on the most common public health concerns in Finland, and was worded in the following way (Methods/Survey instrument and measures; page 6, lines 33-34): "Within the past year (12 months), have you had any of the following diagnosed diseases or diseases treated by the physicians?" This question was followed by a list of chronic and acute diseases/conditions common in Finland. Respondents could indicate from the list as many diseases as they had been suffering from within the year prior to the survey. It was not possible to report any other diseases than those mentioned in the list. The list was composed by the leading public health experts in Finland knowledgeable of the morbidity rates.

In the survey, use of medicines was assessed by the question (Methods/Survey instrument and measures; page 5, lines 26-27) "Have you used any tablets, powders, or other medicines within the past week (7 days)?" This question was followed by a list of commonly used prescription and nonprescription medicines for common chronic and acute conditions. Respondents could indicate

from the list as many medicines as they had been using within 7 days' time frame prior to the survey. It was not possible to report any other medicines than those mentioned in the list.

To clarify above mentioned issues related to the health behavior of the study population included in our study, the following clarification has been added to the Methods section:

METHODS/Study design (page 5, lines 45-48):
"The annual "Health Behaviour and Health among the Finnish Adult Population" survey was established in 1978 to perform as an indicator for changes in the population health and related risk factors, such as smoking, food and alcohol consumption and physical activity. The survey has been targeted to the adult working age population of 15-64 years old. "

c. Please explain more detail how to select and random the 5000 patients to be representatives of the population. Also, how to distribute the questionnaires to cover all different groups of patients.

Authors' response: For the "Health Behaviour and Health among the Finnish Adult Population" survey, every year, a random independent sample (n=5000) of the Finnish population aged 15–64 years has been derived from the Population Register Centre of Finland (Helldán & Helakorpi 2015). The Population Register Centre of Finland is a government-based register where all Finnish citizens and permanent residents are obliged to be registered (Population Register Centre 2018). Thus, it is the register that has the most reliable coverage of the Finnish citizens and permanent residents. A random sample of 5000 drawn from the Register's database by using its routine sampling method was big enough to represent the population under interest.

The "Health Behaviour and Health among the Finnish Adult Population" survey has been conducted every year (1978-2014) as a postal survey (Helldán & Helakorpi 2015). The distribution of the questionnaires by mail has assured better coverage of the entire study population than e.g., using online surveys. This is because every Finn or a person living permanently in Finland is obliged to register their current address to the Population Register Centre. Therefore, all citizens and permanent residents in Finland can be reached by mail. In order to maintain response rate high enough for generalizable results, more reminders have been sent since 1986 (one reminder in 1978-1985, two reminders in 1986-1998, three reminders in 1999-2014). Thus, the number of reminders has remained the same during the study period covered in our study (1999-2014).

The Population Register of Finland contains the following basic information about all the Finnish citizens and permanent residents: name, personal identity code, address, citizenship, native language, family relations, and date of birth and death (if applicable).

As the sample was derived from the entire population aged 15-64 years each year, it is expected to cover different patient and population groups according to their existence in the target population. However, the response rate has decreased, being 67% in 1999 and 53% in 2014. At the same time, an increasing trend was found that non-respondents were young men, unmarried or single and with a lower level of education (Tolonen et al. 2006).

These issues have been added to the Methods section and to the Discussion as follows:

METHODS/Study design (page 5, lines 39-57, page 6, lines 3-4):
"The study was conducted as a repeated cross-sectional postal survey using each year a new nationally representative sample (n=5000) of the Finnish adult population aged 15-64 years. The

national health behavior survey used in this study has its origins in the North Karelia Project, started in 1972, which has been instrumental in improving public health in Finland. The annual “Health Behaviour and Health among the Finnish Adult Population” survey was established in 1978 to perform as an indicator for changes in the population health and related risk factors, such as smoking, food and alcohol consumption and physical activity. The survey has been targeted to the adult working age population of 15-64 years old. The survey has been repeated every year in the same way to yield comparable results.
In addition to the original standard set of structured questions, some other questions have been added to the survey instrument over the years. One of the added questions was the one used in our study concerning receipt of MI from different sources available for consumers/medicine users in Finland (added to the survey instrument in 1999).

The sample has been derived from the Population Register Centre of Finland which is a governmentbased register where all Finnish citizens and permanent residents are obliged to be registered. The survey has been conducted every year (1978-2014) as a postal survey. The distribution of the questionnaires by mail has assured better coverage of the entire study population than e.g., using online surveys. This is because the Population Register Centre has the current address available for all Finns and permanent residents. In order to maintain response rate high enough for generalizable results, three reminders were have been sent during the study period covered in our study (1999-2014). Data from the years 1999, 2002, 2005, 2008-2014 was compared as these are the years when the survey instrument included the question on the receipt of MI.”

DISCUSSION/Strengths and limitations of this study (page 14, line 31):
“The non-respondents more often tended to be young men, unmarried or single and with a lower level of education.”

d. Why did the researchers choose the use of medication within the past 7 days?

Authors’ response: The use of medication within the past 7 days was used as a measure in order to control recall bias. The researchers who designed the “Health Behaviour and Health among the Finnish Adult Population” survey took into consideration experience and evidence from the methodological studies assessing the influence of question structure on the recall of self-reported medicine use (Gama et al. 2009). They ended up using one week’s period (7 days) as it is a period over which people can still quite well recall their medicine use. This question was complemented with another question that assessed use of specific medicines within the same one week’s period (7 days). Use of medicines was assessed by the question “Have you used any tablets, powders, or other medicines within the past week (7 days)?” This question was followed by a list of commonly used prescription and non-prescription medicines for common chronic and acute conditions. The other option for a question would have been to ask medicine use at the point of the survey, i.e., on that day (24 hours) when the respondents filled the questionnaire (Mitchell et al. 1986, Klungel et al. 2000). The following sentence has been added to the Methods section:

METHODS/Survey instrument and measures (page 6, lines 32-33):
“The use of medication within the past 7 days was used as a measure in order to control recall bias.”

e. Data on the indication for use was shown in the Results, however this data was not mentioned in the Methods.

Authors' response: In the Methods section (page 6, lines 24-31), we have mentioned that the respondents were asked to report their medication use with a list of commonly used prescription and non-prescription medicines for common chronic and acute conditions. These results are shown in Table 1 (pages 9-10) and presented in the Results (page 8, lines 16-19) as follows:

METHODS/Survey instrument and measures (page 6, lines 24-31):
"Use of medicines was assessed by the question "Have you used any tablets, powders, or other medicines within the past week (7 days)?" This question was followed by a list of commonly used prescription and non-prescription medicines for common chronic and acute conditions (Table 1). Respondents could indicate from the list as many medicines as they had been using within 7 days' prior to the survey. It was not possible to report any other medicines other than those mentioned in the list."

RESULTS (page 8, lines 16-19):
"The respondents used most commonly one medicine, ranging from 63% in 1999 to 54% in 2014 (included prescription and non-prescription medicines). The respondents reported using medicines most commonly for headaches (range 50% to 53%), other aches or pains (28% to 31%) and high blood pressure (15% to 23%)."

f. Page 7, Line 37-38: How many people was piloted by convenience sampling?

Authors' response: The "Health Behaviour and Health among the Finnish Adult Population" survey was first conducted as a regional follow-up study as part of the North Karelia Project (Puska et al. 1981, 2009, 2016). Thus, the survey instrument has been developed in a stepwise manner by adding new questions to the original instrument since 1972. The public health experts involved in the North Karelia Project have been responsible for the instrument development and have made use of the best knowledge available of carrying out national population studies as mail surveys.

The question concerning receipt of medicines information was added to the survey instrument in 1999. The question as it appears in the survey instrument is a result of extensive work by senior researchers in public health and medicines information. The question was piloted in several formats with the target group (5-10 individuals from the target group recruited as a convenience sample) and the current version was found to be most valid for the primary purpose of the survey that was to indicate long-term trends. These aspects concerning the instrument development have been described more detailed in the Methods section as follows:

METHODS/Patient and public involvement (page 7, lines 33-37):
"The question as it appears in the survey instrument is a result of extensive work by senior researchers in public health and medicines information. The question was piloted in several formats with the target group (5-10 individuals from the target group recruited as a convenience sample) and the current version was found to be most valid for the primary purpose of the survey that was to indicate long-term trends."

3. Results

a. According to the medicines list mentioned in the Methods, no finding of the medicines was shown in Results or Tables. Please briefly provide the common medicines in use.

Authors' response: Thank you for this comment. We have included information about the common medicines in use in the Results section (page 8, lines 16-19). More detailed information about the medicines in use can be found in Table 1 (pages 9-10). The respondents have been categorized into four groups according to the number of medicines they self-reported using from the given list (Methods section: Analysis, page 7, lines 12-13, please see below). This information was used to analyze whether the number of medicines in use was associated with the receipt of medicines information.

METHODS/Analysis (page 7, lines 12-13):
"The number of medicines in use was counted for each respondent and respondents were divided into following groups: people using one, two, three, and four or more medicines (Table 1). The receipt of MI was compared between all these medicine user groups (Appendix B)."

RESULTS (page 8, lines 16-19):
"The respondents used most commonly one medicine, ranging from 63% in 1999 to 54% in 2014 (included prescription and non-prescription medicines). The respondents reported using medicines most commonly for headaches (range 50% to 53%), other aches or pains (28% to 31%) and high blood pressure (15% to 23%).

b. Appendix A: if possible, percentages should be presented for each main group of the respondents, i.e female/ male, individual age group, etc. This will make it easy to understand the texts in Results.

Authors' response: The percentages of each main group have been added to the Appendices A and B.

4. Discussion

a. Page 13; Line 27-28: this sentence needs to further explain and discuss in more detail.

Authors' response: Thank you for this comment. In order to provide more clarity, we have complemented the paragraph with some examples of the system-based changes that may have led to the diminished physician involvement in patient care. The following sentences have been added to Discussion section:

DISCUSSION (page 13, lines 27-28):
"These findings may indicate that physicians are becoming less involved in actual patient care as the healthcare has become more fragmented. Thus, time allocated for physician office visits has shortened, leading to a situation that physicians do not have time to concentrate on their patients' medications."

b. Page 13, Line 42-43: In term of "Influence", it seems that these factors are statistically associated with the receipt of MI. Please consider to modify this sentence.

Authors' response: Thank you for this comment, which we have taken into account and reformatted the sentence accordingly:

DISCUSSION (page 13, lines 42-43):
"According to the present study, gender, age, number of medicines in use and number of diseases are associated with the receipt of MI."

c. Based on the legislation of EU for providing the patient package inserts for all patients receiving medicines, please give possible explanation or reason for the decreased rates of MIs distributed over time.

Authors' response: Thank you for highlighting this issue. What we mean by our results is that although package leaflets have been obligatory in all medicinal products in the EU, including Finland, since 1999, the proportion of medicine users reporting using them as a source of medicines information has decreased over time. Thus, it is not the distribution, but the use of the package leaflets as a source of medicines information that has decreased. We also found a more general trend that an increasing number of medicine users do not receive medicines information from any sources. This is quite surprising while taking into account that the medicines information sources have remarkably diversified during the study period. Further research should be focussed on identifying reasons and contributing factors to the increased rates of medicines users not receiving medicines information from any sources on the medicines they use.

d. The sentence indicates that the receipt of MI from internet is still quite "rare". In my opinion, 16% is not indicated as "rare".

Authors' response: Thank you for this important comment, As the access to and actual use of the Internet varies a lot between countries the term "rare" can be interpreted differently. Given that in Finland, over 90% of the adult population used the Internet in 2014 (Statistics Finland 2018), 16% using it for searching information on their medications can be considered as a low proportion or "rare". In this context, one might expect the number of medicine users seeking information online be higher. This issue has been clarified in the Discussion section by comparing the Internet use as a source of medicines information to its use in general:

DISCUSSION (page 14, lines 5-6):
"This study indicates that the receipt of MI from the Internet was quite rare as more than 90% of the Finns aged 16-64 years were Internet users in 2014. There are no similar population-based long-term trend studies from other countries to compare our results."

5. Conclusion

a. Please modify the conclusion, not repeat same sentences as the conclusion in Abstract part. Again, the last sentence should not be included in the conclusion. Further brief suggestion should be emphasized on the main findings of this study.

Authors' response: We have revised the conclusions according to the Reviewer's recommendation. However, we would like to suggest to have the conclusion in the same format in the Abstract part and in the actual research report part. This is for assuring coherence of the study as the conclusion gives the answer to the research question under investigation, based on the evidence obtained by that particular research conducted. We are ready to further modify the conclusions according to further instructions by the Reviewer. The conclusion is rewritten as follows:

ABSTRACT/Conclusion (page 2, lines 49-56) and CONCLUSION (page 15, lines 7-15):
"Healthcare professionals and package leaflets had still a dominating importance in 2014 despite the growing number of MI sources over time, but still a minority of adult medicine users reported receiving

MI via the Internet in 2014. Worrying is that the proportion of adult medicine users who did not receive MI from any of the sources became 7-fold during the study period."

Reviewer: 2

Thank you for the opportunity to review this manuscript, describing a study of an important and timely topic: the provision of medication information to patients.
The study has some strengths, most notably the use of a large national sample. However, there are notable weaknesses in the design and reporting that raise concerns.

Firstly, the authors neither distinguish between prescribed and over-the-counter medication, nor between active medication information-seeking or passive receipt of information. This is of particular importance as it relates to the interpretation of the results and the potential implications. For example, the implications or interpretation of a gender difference in reported receipt and/or sources of medication information differ significantly depending on whether these are discrepancies in the information being provided or gender differences in information-seeking behaviors. Similarly the implications of the finding that up 28% of participants did not receive any medication information differ substantially depending on whether these participants were taking prescription medication (where the responsibility of the prescribing clinician is well defined) or over-the-counter medication.

Authors' response: Thank you for these important comments concerning the study design and the survey instrument. This option of separating receipt of medicines information on prescribed and OTCmedicines in the survey instrument was considered but the question was decided to be presented at the general level. The concern was that the respondents may not be capable of differentiating prescription and OTC-medicines/food supplements in their self-administered responses. This may have led to decreased reliability of the responses and more biased results. On the other hand, quite many people use concomitantly prescription and OTC-medicines, i.e., they are not separate population groups, but are overlapping.

One more reasons for using the general level question concerning receipt of medicines information was the nature of the "Health Behaviour and Health among the Finnish Adult Population" survey: it was a population-based survey intended to indicate long-term trends and changes in health behaviors that can be studied more in detail with other methods in other studies. It is obvious that various medication user groups may have different information needs and sources which should be investigated more in detail in future studies. These methodological aspects have been presented in the Methods section (please, see below). They are also more clearly stated in the Discussion section of the current version of the manuscript (please, see below).

METHODS/Survey instrument and measures (page 6, lines 24-31):
"Use of medicines was assessed by the question "Have you used any tablets, powders, or other medicines within the past week (7 days)?" This question was followed by a list of commonly used prescription and non-prescription medicines for common chronic and acute conditions (Table 1). Respondents could indicate from the list as many medicines as they had been using within 7 days' prior to the survey. It was not possible to report any other medicines other than those mentioned in the list."

DISCUSSION/Strengths and limitations (page 14, lines 33-37):
"The respondents did not have the opportunity to report MI from other sources than those listed in the survey, to report separately MI sources on prescription and non-prescription medicines, and to

distinguish between active MI seeking or passive receipt of MI. This should be taken account when interpreting results and potential implications. For example, the gender difference in the use of MI sources may differ depending on whether these are discrepancies in the information being provided or gender differences in information seeking-behaviors. Furthermore, people using prescription vs. nonprescription medicines may differ in the amount and use of different MI sources. However, in Finland all medicine users should receive MI from their healthcare providers while prescribing and dispensing both prescription and non-prescription medicines."

Secondly, the researchers describe a robust body of literature exploring receipt of medication information but indicate that a gap in the literature is the lack of a longitudinal examination on the subject. The authors do not communicate well why this is an important gap to address or what the implications of such longitudinal analyses might be for practice, policy or research.
In addition, the researchers appear to have chosen to conduct the data analysis using purely descriptive cross-sectional methods, and therefore it is unclear how (if at all) the study is filling this gap in the literature.
Finally, the authors describe descriptive statistics, including means and percentages, but do not report any comparative statistics to determine whether the reported differences from year to year are significant or not. Overall, the analytical methods use appear to be somewhat lacking in robustness.

Authors' response: Thank you for this important comment concerning the analytical approach chosen in our study. As previously explained in this response letter, the primary aim of our study was to describe long-term trends in the receipt of medicines information from various sources among Finnish adult medicine users in order to identify changes over time. Indicative trend analysis has been the primary purpose of the entire "Health Behaviour and Health among the Finnish Adult Population" survey from where our data were derived from the period 1999-2014.

As the Reviewer mentioned, there is quite a good number of studies on the receipt of medicines information from various sources that have applied cross-sectional study designs and/or have focused on some specific medicine user/patient groups. The advantage of our descriptive study is that it covers the entire adult population and a long time period to assess the evolution of the use of various medicines information sources. This evidence is useful for evidence-informed strategic development of medicines information practices at the national, local, organizational and patient care level, as well as in policy making. E.g., in Finland, the follow-up data from the "Health Behaviour and Health among the Finnish Adult Population" on medicines information sources of adult population has been actively used for these purposes (Närhi 2007, Närhi & Helakorpi 2007a & b, Pohjanoksa-Mäntylä et al. 2011). It has provided a good understanding of the importance of various medicines information sources and changes over time. One aspect followed has been the changes in the importance of healthcare professionals as medicines information sources over time while the availability of other medicines information sources has remarkably diversified since 1999. Within healthcare professionals, particularly community pharmacists' involvement in medicines information has been of interest to follow because pharmacists' duty to counsel was enacted in 1983, and since then, they have proactively developed their medicines information services to consumers and medicine users (both prescription and OTC-medicine users) (Puumalainen 2005, Pohjanoksa-Mäntylä 2010).

Other high priority aspects to follow have been evolution of the use of statutory medicines information to consumers in the form of package leaflets that became mandatory within the EU (and Finland) in 1999 and use of electronic internet-based medicines information sources which also became available in the beginning of the study period. Thus, our study covers quite a unique period of time in

terms of diversifying medicines information sources to consumers and enabling access to medicines information.

We have elaborated the text to communicate better why the lack of an examination on the medicine users' receipt of medicines information from various sources over a long period of time is an important gap in the literature to address (please, see Introduction; page 4, lines 44-46). We also have added information on the implications of such long-term analyses for practice, policy and research (please, see Article Summary/Strengths and limitations of this study; page 3, lines 11-14). This gives ground for not focusing our analysis on comparing different medicine users or finding associated factors to receipt of medicines information. Please, find the revisions made below:

ARTICLE SUMMARY/Strengths and limitations of this study (page 3, lines 11-14):
"Repeated surveys are necessary to indicate population level changes in the utilization of available MI sources and reveal needs to develop MI practices and policies at the national level."

INTRODUCTION (page 4, lines 44-46):
"Repeated surveys are necessary to indicate population level changes in the utilization of available MI sources and reveal needs to develop MI practices and policies at the national level. In Finland, improving the accessibility and quality of MI have been among the key strategic medicines policy goals over the last decades. The long-term comparative information in the receipt of MI and the proportion of people receiving MI are important measures to indicate whether the desired outcomes are met. Therefore, this study was examined long-term trends in the receipt of MI among Finnish adult medicine users in 19992014."

Reviewer: 3

This is a large population based study with interesting findings pertaining to medication information. There are some concerns relating to methodology however.

Major concerns:

- The methods state that the annual sample "was made nationally representative". The reference to support this is in Finnish however. How was this achieved? Could the authors provide additional information about sampling?

Authors' response: Thank you for this important methodological comment. We have added a detailed response that can be found as a response to the comment 2c (please, see Reviewer 1, above).

There are considerable variations between the samples from individual years e.g in 1999 11% of the sample were taking 3 or more medications versus 20% in 2014, 1999 13% of the population had 2 or more co-morbidities versus 32% in 2014. The analysis is purely descriptive and though detailed (e.g Appendix B), it doesn't adequately assess how such variations may have impacted the outcome being assessed. It can't be ascertained from the results if the differences noted in receipt of medication information over time are statistically significant and if they are does the difference remain if the variability in number of meds, comorbidities, education in different years etc is controlled for? It would seem that a regression analysis should be conducted

Authors' response: Thank you for this another important methodological comment concerning the analytical approach chosen in our study. As previously explained in this response letter (please, see our comments 1a, 2b and 2c to Reviewer 1, and comments to Reviewer 2), the primary aim of our study was to describe long-term trends in the receipt of medicines information from various sources among Finnish adult medicine users in order to identify changes over time. Indicative trend analysis has been the primary purpose of the entire "Health Behaviour and Health among the Finnish Adult Population" survey from where our data were derived from the period 1999-2014. Each study year, a new independent random sample of 5000 Finns aged 15-64 years was derived. Thus, the survey each year is a cross-section of the Finnish adult population reflecting its health behaviors, morbidity, use of medicines and receipt of medicines information at that particular point of time. It was a conscious decision to conduct first a descriptive indicative trend analysis which is presented in this paper. The present study provides a foundation for further analysis that could go deeper in understanding receipt of MI in various population groups, changes over time and factors influencing it, by using multivariate analysis This has been added to the Discussion section as follows:

DISCUSSION/Implications and future research (page 14, lines 18-19):
"The present study provides a foundation for further analysis that could go deeper in understanding receipt of MI in various population groups, changes over time and factors influencing it."

How relevant is it to include information from 1999 when 2 sources of medication information were omitted?

Authors' response: This descriptive trend analysis on the receipt of medicines information among adult medicine users in Finland was first conducted in 1999. The list of possible medicines information sources to consumers was made comprehensive, reflecting availability of medicines information at that time. As the medicines information sources have remarkably diversified since then, it has been necessary to complement the list to reflect the development. Otherwise, the results would have been biased by omitting the new medicines information sources becoming more common after 1999 as the respondents could only select from the medicines information sources given in the survey instrument.

The study excludes the older adult population of >65 years. In view of the association of increasing age with multimorbidity and polypharmacy, the study excludes the group potentially taking the greatest number of medications to whom the findings are potentially most relevant. This should be addressed.

Authors' response: Thank you for this important comment concerning selection of the study population. The "Health Behaviour and Health among the Finnish Adult Population" survey was focused on the working age Finns of 15-64 years in order to identify risks in their health behaviors for establishing preventive health promotion actions (Helldán & Helakorpi 2015). Thus, it was not possible to include older adult population >65 years although association of increasing age with multimorbidity and polypharmacy may increase their need of information on their health, diseases and medication use. A methodological concern related to involving older respondents in selfadministered surveys is how well they are capable of responding by themselves without assistance. In the future, the receipt of medicines information among older adults should be investigated further, and this fact is mentioned in the Discussion as follows:
DISCUSSION (page 13, lines 34-37):
"In the future, special attention should be paid to the receipt of MI among people with multiple diseases and medications and the aging populations whose proportion is growing."

DISCUSSION/Implications and future research (page 14, lines 45-48):
“As part of this work, it is necessary to continue research on trends in the receipt of MI at the population level andand to identify population groups needing special attention, such as older adults.”

Minor concerns

Though the introduction provides a good review of the literature there are grammatical errors and the meaning of certain phrases is unclear. Examples:

Authors’ response: Thank you for pointing out grammatical errors and other unclear sentences in the Introduction and in the Context of our study. We have corrected them as follows:

Page 4: Lines 13 and 14

“These changes have led to improved availability of MI, first on paper and later via the Internet and electronic databases in smartphones and other electronic devices. The applications are evolving fast towards systems enabling customized MI, interactive communications and following up treatments.”

Page 4: Lines 41 and 42

“The use of the Internet as a source of MI has become more common over time, but it is not yet as commonly used source of MI for consumers users as healthcare professionals.”

Page 5: Line 11 and 12

“Until 1983, patients and medicine users received information about their medicines exclusively from their own physicians.”

There is data missing from 6 years-more explanation of this is required. The use of the word “annual” is not appropriate in view of this

Authors’ response: The term “annual” was used to highlight that the “Health Behaviour and Health among the Finnish Adult Population” survey was conducted annually during the period of 1978-2014 (Helldán & Helakorpi 2015). However, not all questions were included each year, e.g., the question concerning receipt of medicines information was one of the rotated questions. Our study covers all the years when the medicines information question was included in the survey. This has been described in the Methods section (please, see below). In order to provide more clarity, we have removed the term “annual” from the manuscript when appropriate (e.g., from the Abstract/Study design section and from the Discussion/Strengths and limitations of this study).

METHODS/Study design (page 6, lines 3-4):
“Data from the years 1999, 2002, 2005, 2008-2014 was compared as these are the years when the survey instrument included the question on the receipt of MI.”

- Could the rationale for the ratio calculations between the mean number of medications and co-morbidities/MI be explained?

Authors' response: Thank you for your comment concerning the ratio calculations between the mean number of medications and co-morbidities/medicines information. As the nature of this paper is a descriptive trend analysis over a 15-year time period with remarkable changes in terms of 1) medicine use (people tend to use more medicines than they did previously which may be seen in the mean number of medications in use per person), 2) co-morbidities (people may tend to have more comorbidities because our population is aging), and 3) receipt of medicines information from multiple sources (people may tend to receive medicines information from more sources than before because availability and access to medicines information sources has remarkably diversified during the study period) we developed this "indicator" to reflect these societal changes over time. We have the following texts in the Methods and the Results section concerning this "indicator":

METHODS/Analysis (page 7, lines 22-27):
"Finally, a ratio between the mean number of medicines in use and the mean number of diagnosed diseases compared to the mean number of MI sources from which MI was received was calculated to indicate whether any remarkable changes were seen over time in the number of MI sources used in relation to morbidity and medicine use."

RESULTS/Receipt of medicines information and associated factors (page 12, lines 45-52):
"Overall, the mean number of medicines in use and the mean number of diagnosed diseases increased slightly among medicine users, while the mean number of MI sources from which MI was received remained relatively stable during the study period 1999-2014 (Fig. 3). The ratio between the mean number of medicines in use and the mean number of MI sources from which MI was received remained relatively stable, but the ratio between the mean number of diagnosed diseases and the mean number of MI sources increased."

If needed, we are ready to add more detailed clarification of the purpose of this part of the analysis and its findings according to further instructions from the Editor/Reviewer. We are also ready to remove this part from the manuscript if it does not add to knowledge.

FORMATTING AMENDMENTS

Required amendments will be listed here; please include these changes in your revised version:

1. Please provide a more detailed contributorship statement. It needs to mention all the names/initials of authors along with their specific contribution/participation for the article. This should list each author's contribution to the paper according to the ICMJE guidelines for authorship. This should be stating how each author contributed to the article. It should discuss on the planning, conduct and reporting of the work in your paper. You may also consider the conception and design, acquisition of data or analysis and interpretation of data, etc.

Authors' response: Thank you for this request of providing a more detailed contributorship statement. Please, find the revised text below (page 16, lines 10-16):

“Contributors: SH has been involved in designing the survey. SH and MA have been involved in developing the survey instrument concerning the receipt of medicines information. NM, MA, KH and MPM planned the analysis and reporting this particular study. The data were applied from the National Institute for Health and Welfare. NM performed the data analysis, and MA, KH, SH and MPM contributed to the interpretation of the data. NM prepared the initial draft of the manuscript. MA, KH, SH and MPM critically reviewed and revised the manuscript. All authors read and gave the final approval of the version to be published.”

2. Please provide another copy of your figures with better qualities and please ensure that Figures are of better quality or not pix-elated when zoom in. NOTE: They can be in TIFF or JPG format and make sure that they have a resolution of at least 300 dpi and 90mm x 90mm of width. Figures in PDF, DOCUMENT, EXCEL and POWER POINT format are not acceptable.

Authors’ response: New copies of the figures with better qualities have been processed and attached to the manuscript as recommended.

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VERSION 2 – REVIEW

REVIEWER	Ragnhildur I. Bjarnadottir University of Florida College of Nursing, USA
REVIEW RETURNED	28-Jan-2019

GENERAL COMMENTS	Thank you for the revisions to this manuscript. I appreciate your responses and find that all major weaknesses have been adequately addressed.

REVIEWER	Elaine Walsh University College Cork, Ireland
REVIEW RETURNED	24-Jan-2019

GENERAL COMMENTS	The authors have provided a detailed response to the comments and have certainly clarified a number of the issues raised. The revised submission does not however address the original concern raised regarding data analysis. Though the authors have provided greater clarity on how the study sample was selected for each year, the fact remains that there were variations between the samples from individual years in terms of medications, morbidity, socio-demographic characteristics etc. The current analysis does not account for these variations, nor does it establish if the reported differences in receipt of MI over time are of statistical significance. In the absence of controlling for potential confounding factors and establishing statistical significance, reporting a

	definitive difference in receipt of MI over time currently lacks justification. In addition, associations have been described without testing for statistical significance. E.g. the following statement has been added by the authors to the discussion in the revised submission: "According to the present study, gender, age, number of medicines in use and number of diseases were associated with the receipt of MI". No statistical test has been applied to determine if an association exists and therefore such a definitive statement lacks justification. The ratio calculations which form the basis for the associations described in the paper are defined by the authors in their response as an "indicator developed to reflect societal changes over time" and were developed de novo by the authors. These calculations in my opinion could supplement, but should not replace, inferential statistics. My major concern is that the results and associations that have been reported definitively by the authors in this paper are not adequately supported by the current analysis. Data from 1999 remains a minor concern. E.g. regarding the result: "Receipt of MI from package leaflets decreased both in women (48% to 38%) and men (36% to 26%)". The authors state that this source of medication information was not included in 1999 survey. Is the comparison here between 2002 and 2014 rather than between 1999 and 2014 as for the other results? This should be clarified. Again clarification is required regarding: "The most commonly reported MI sources were physicians, community pharmacists and package leaflets throughout the study period 1999-2014 among adult medicine users"

VERSION 2 – AUTHOR RESPONSE

Thank you for the reviewers' further comments on our resubmitted manuscript. We have addressed all of them and made additional revisions to the manuscript accordingly. Please find our revisions and responses attached.

We would be happy to clarify any aspect of our response and look forward to your correspondence.

VERSION 3 – REVIEW

REVIEWER	Elaine Walsh University College Cork, Ireland
REVIEW RETURNED	21-Mar-2019

GENERAL COMMENTS	The authors have addressed all concerns with the revised submission