PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	What do European women know about their female cancer risks and cancer screening? A cross-sectional online intervention survey in 5 European countries
AUTHORS	Wegwarth, Odette; Widschwendter, Martin; Cibula, David; Sundström, Karin; Portuesi, Rosalba; Lein, Ines; Rebitschek, Felix

VERSION 1 – REVIEW

REVIEWER	Maria Fiore Department of Medical, Surgical and Advanced Technologies "G.F. Ingrassia", University of Catania. Italy
REVIEW RETURNED	08-May-2018

GENERAL COMMENTS	The manuscript is straightforward and complite. I consider the manuscript valuable to get published in its current state.

REVIEWER	Shino Oba Gunma University Graduate School of Health Sciences, Japan
REVIEW RETURNED	21-May-2018

GENERAL COMMENTS	This study is focusing on the disease knowledge of non-patients general individuals in five European countries. The study is of public health importance. However, the manuscript has serious limitations. 1. The aims of the study includes both intervention and observation of study participants. They should be two different studies. It is impossible to conduct them at the same time to provide scientific evidences. 2. As the intervention of the leaflet is one of the major aims of the study, the comparison group is necessary. 3. Sampling scheme is not clear. It seems that private companies are involved to collect data but detailed sampling methods are not mentioned. It is hard to evaluate if the data represents the European population from the manuscript. 4. Several analyses were conducted as if abruptly without providing background information in Introduction. Were authors aiming to obtain the estimate of European women, or evaluating the differences by country. Were they aiming to make a comparison between core-age group vs. all the others? Were they aiming to reveal the difference between minority vs. majority women? I was even suspicious that the authors compared whatever available factors in data.

	5. The questionnaire used in the study is widely focusing WID. It gives an impression that the study group is promoting WID to European women. The background of developing this questionnaire should be explained in the manuscript. 6. The correct answers of the questionnaire should be clearly defined by scientific evidences with relevant citations. More detailed comments / questions are as follows: Abstract 1. Please clearly define the term “informed choice”, which seems to be the keyword of this study. 2. Explain the Harris Interactive and the Toluna panel. Is it the name of the company that collected data? 3. Please give more information on “the age specific risk of development of cancer”. How this measure was defined and validated? 4. Please explain the reason why the women 40 years old or older were the samples of this study. Cervical cancer is prevalent in much younger age group. Introduction 5. The harm of overdiagnosis and overtreatment of cancer is emphasized, but it is not the only issue studied in this manuscript. 6. P.5, 2nd paragraph The reference articles are not sufficient. These cited articles are only for specific countries, not for all European countries. 7. Need more explanation to designate the core age group for this study. The age risk differ by types of cancer. Methods 8. It needs more detailed information to explain the legitimacy of Harris Interactive and the Toluna Panel. How about the degree of representativeness of female population in Europe. E.g., how did they obtain the e-mail address of the participants? 9. It seems like the leaflet was provided to the participants together with questionnaires. Please explain how the authors made sure that the participants answered the questions before reading the leaflet, then answer the certain questions after that. The process of data collection should be written in details. 10. The good amount of leaflet explains the women’s cancer risk identification test. It is like a promotion of WID. If the questionnaire focus on this issue. Authors needed to re-think the study aim. 11. Provide a background information and importance to study the level of knowledge and its acquisition by country in Introduction before explaining it in Methods. 12. Please explain the core group comprised of 50-69 years old was applied to assess the knowledge of all 4 types of cancer. Cervical cancer is prevalent in younger age group. Please explain the importance to compare the women in 50-69 years and women in the other age group.

	13. P10 line 8- Data on women's age-specific risks for each of female cancer were derived from the Robert Koch Institute. Please explain what this mean to the study design. 14. Please explain the definition of correct answers. The risk of certain cancer in specific age group should be different by country, and with and without risk factors such that smoking status and family history of cancer, obesity etc . Please provide the accurate citations for the correct answers. 15. The participation rate of 61.4% is not that bad for the observational study. However, The authors did not provide the information on their target population. Because of that, the selection bias is a serious concern. Results 16. Please define the "minority women" in methods. As a matter of factor, the reason why the authors included the analysis comparing majority vs. minority women is not clear. Please provide the background information and importance of the study in Introduction. Also, please provide the distribution of minority women in table 1. 17. The second paragraph of Discussion is written as if a review of previous studies. The discussion should be written based on current findings. 18. As the authors discuss, the cross-sectional study design is not appropriate to measure the effectiveness of intervention with a leaflet. Tables 19. Table 1. Distribution of other important characteristics, which would influence on the study results, should be presented. E.g. past history of cancer and family history of cancer. BMI, physical activity and smoking status, as indicators of health conscious individuals. 20. Table 2 -Please define "the correctness of the knowledge". -Please define the "core age" and "over estimation" 21. Table 3 -The purpose of this table analysis is not clear, although it seems like the authors intended to highlight the different knowledge level and intervention effect by country. The title should clearly indicate the contents of the table.

REVIEWER	Abdulmohsen Al-Zalabani Associate Professor College of Medicine, Taibah University, Saudi Arabia
REVIEW RETURNED	01-Jul-2018

GENERAL COMMENTS	This manuscript reported a well-planned, well-conducted study tackling the issue of whether women had overestimated their risk of developing cancer at a certain time in life.

	I have some comments: ==Methods== * Page 7, Line 10: The abbreviation "FORECEE" is used for the first time in the manuscript. So, it needs to be spelled out in the first appearance. * Page 8, Line 15: "The email provided basic information about the study, the link to the survey and the leaflet". This statement lead to an impression that the leaflet was attached to the invitation email. Later description in the manuscript clarified that respondents have access to the leaflet only after they answered the questionnaire for the first time. The statement above needs to be modified. * Some parts of the manuscript may need a bit of rearrangement. For example: a) the part from "page 8 line 55" to "page 9 line 35" (Except page 9, lines 25-27) is better to be under a title of "intervention". b) the part in "page 10 line 8 to 17" belongs to the "outcomes" section rather than "statistical analysis" section. * Page 10, Lines 8-10: Authors stated that "... age-specific risks for each of the female cancers were derived from the Robert Koch Institute ... database in Germany". First, they need to report in the manuscript the exact age-specific risks for each type of cancer they got from the database. Second, I wonder if the age-specific risks for each of the cancers are similar in all of the 5 countries included. Was there a reason not to use the age-specific risk of the country of each respondent? ==Results== * Page 10, Lines 21-27: Numbers reported here are not clearly presented. Median and range of what? What does the abbreviation "m" mean?. I guess the numbers refer to the respondents "estimation of their age-specific cancer risk out of 1000 women". I think it is better to rephrase the paragraph to make it more comprehendible. * Does Figure 1 presents extra information not presented in Table 3? If not, do you still need Figure 1?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Maria Fiore
Institution and Country: Department of Medical, Surgical and Advanced Technologies “G.F. Ingrassia”, University of Catania. Italy
Please state any competing interests or state ‘None declared’: None declared.

Please leave your comments for the authors below
The manuscript is straightforward and complite. I consider the manuscript valuable to get published in its current state.

Thank you for taking the time to review our paper.

Reviewer: 2
Reviewer Name: Shino Oba
Institution and Country: Gunma University Graduate School of Health Sciences, Japan
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
This study is focusing on the disease knowledge of non-patients general individuals in five European countries. The study is of public health importance. However, the manuscript has serious limitations.

1. The aims of the study includes both intervention and observation of study participants. They should be two different studies. It is impossible to conduct them at the same time to provide scientific evidences.

The nature of our study was that of a cross-sectional online intervention survey (before/after design) based on an evidence-based leaflet (intervention). Women were (i) presented with a panel of questions followed by (ii) the presentation of the leaflet, and finally, (iii) the initial questions were asked again without the women having the leaflet at their disposal. The aforementioned is definitely an appropriate strategy in order to gain scientific evidence as to whether the presentation of the risk information on the effectiveness of medical interventions is capable of modulating people's knowledge concerning cancer risk, screening, or other medical interventions and information. This approach has been successfully implemented in a number of studies, including:

Schwartz LM, Woloshin S, Welch HG. Using a drug facts box to communicate drug benefits and harms. Annals of Internal Medicine. 2009;150(8):516-27.

Gaissmaier W, Wegwarth O, Skopec D, Müller AS, Broschinski S, Politi MC. Numbers can be worth a thousand pictures: individual differences in understanding graphical and numerical representations of health-related information. Health Psychology. 2012;3(31):286–96.

Wegwarth O, Kurzenhäuser-Carstens S, Gigerenzer G. Overcoming the knowledge–behavior gap: the effect of evidence-based HPV vaccination lealfets on understanding, intention, and actual vaccination decision. Vaccine. 2014;32(12):1388–93.

Garcia-Retamero, R, Galesic, M, Gigerenzer G. DO icon arrays help reduce denominator effect? Medical Decision Making, 2011;30(6): 672–84.

Wegwarth O, Gaissmaier W, Gigerenzer G. Deceiving numbers: survival rates and their impact on doctors' risk communication. Medical Decision Making. 2011;31(3):386–94.

2. As the intervention of the leaflet is one of the major aims of the study, the comparison group is necessary.

We fully agree that randomization into an intervention (i.e. a new drug) and a control arm is the gold standard in clinical trials. In our case, however, where the test is whether an information leaflet can inform and/or change knowledge, the control group would, by definition, need to be comprised of those subjects presented with exactly the same questions but without access to an information leaflet; this scenario would not be logical, as women in the control group would undoubtedly repeat the responses they provided during the first round of questions.
In addition, women participating in our study were not told they would be presented again with the same questions at a later point of time during taking the survey and, after perusing the leaflet, were

no longer able to return to the initial part of the survey; this strategy was adopted to further reduce any potential bias.
Overall, we are of the opinion that the strategy we implemented was appropriate and valid in order to assess whether an intervention (i.e. providing an information leaflet) has an impact on women's knowledge regarding cancer risk and screening.

3. Sampling scheme is not clear. It seems that private companies are involved to collect data but detailed sampling methods are not mentioned. It is hard to evaluate if the data represents the European population from the manuscript.

As with many scientific online surveys, it is entirely appropriate to seek support from established survey companies in order to gain a large (and/or representative) sample reflecting the target population. With regards to sampling, we are aware of no point in the manuscript where it is claimed that our sample was representative of the entire European population or of the five European countries surveyed. Rather, our goal was to survey national samples of women that would approximate the distribution in age (40 to 75 years of age) of women at highest risk of female cancer and in education of the general population in five European countries that represented Northern, Eastern, Southern, Western, and Central Europe and reflected the nationalities of members of the FORECEE Consortium (www.forecee.eu). Based on these criteria, the following countries were chosen: the Czech Republic, Germany, the United Kingdom, Italy, and Sweden.

4. Several analyses were conducted as if abruptly without providing background information in Introduction. Were authors aiming to obtain the estimate of European women, or evaluating the differences by country. Were they aiming to make a comparison between core-age group vs. all the others? Were they aiming to reveal the difference between minority vs. majority women? I was even suspicious that the authors compared whatever available factors in data.

The core objectives of this study were triggered by the needs described in the FORECEE project (www.forecee.eu) funded by the European Union's Horizon 2020 research and innovation programme:
Objective 1: To assess the knowledge of European women (represented by five countries as specified above) regarding female cancer risks and screening.
Objective 2: To assess whether an intervention (online information leaflet) is capable of modulating knowledge.
Objective 3: To assess whether baseline knowledge and the ability to improve said knowledge with respect to cancer risk and screening varies across the five European countries.
In addition, because only mammography screening has been implemented as a systematic, population-based screening program with the same age core group (50 to 69 years) in all five countries, we decided i) to investigate women's knowledge regarding cancer screening specifically for mammography screening and ii) to compare knowledge on cancer risk and screening specifically for breast cancer and mammography between women of the age core group (50 to 69 years) for that screening program and women outside of that core group as spelled out under the aims of the study in the introduction. We agree, however, that the introduction could make that detail clearer, which is why we have rearranged paragraphs and added information on the mammography screening programs in Europe.
We also agree that the original version of this manuscript did not clearly state that we compare whether baseline knowledge and the ability to improve knowledge with respect to cancer risk and screening varies across the five European countries. This information has now been added at the end of the introduction.

At the same time, we suspect that the reviewer may have misinterpreted the meaning of the terms “majority of women”/”minority of women”. These terms indicate (numerical) proportions, e.g. more than 50% or less than 50% of women. See also our reply to comment 16/ results.

5. The questionnaire used in the study is widely focusing WID. It gives an impression that the study group is promoting WID to European women. The background of developing this questionnaire should be explained in the manuscript.
We assume the reviewer is referring to the leaflet and not the questionnaire. We agree that the manuscript in the current form does not sufficiently explain the background of the study. We therefore add the following paragraph to the method section: “The core objectives of this study were triggered by the requirements of the ongoing FORECEE (Female cancer prediction using cervical omics to individualize screening and prevention) project— funded by the European Union’s Horizon 2020 research and innovation programme—that is going to develop an epigenetic test to predict the risk for breast, ovarian, cervical, and endometrial cancers in women using cervical cells (https://forecee.eu). Part of the FORECEE project is to understand educational and communicative needs from the side of women who might be targeted in the future by the potential introduction of the resulting women’s cancer risks identification (WID) test. The study reported herein investigated the educational aspect in that it sought to learn i) about women’s knowledge of their female cancer risks and cancer screening at base line , and ii) about the effect of an evidence-based leaflet (intervention) on that knowledge. To gain these insights with sufficiently large samples from different European countries, the study was set up as a cross-sectional online survey with two phases (before/after intervention).”

6. The correct answers of the questionnaire should be clearly defined by scientific evidences with relevant citations.

We have added a table (table 1) displaying the actual age-specific cancer risks from the population-based cancer registry database of the Robert Koch Institute in Germany along with more specifications on what counts as a correct answer by modifying the first paragraph of “statistical analyses and data presentation” under methods: “Epidemiological data on age-specific 10-year risks for each of the female cancers were derived from the population-based cancer registry database of the Robert Koch Institute (www.krebsdaten.de) in Germany.23 Details on the age-specific risks for each of the four female cancers derived from the database can be seen in table 1. To accommodate for potential country-specific variations in female cancer risks, women’s estimates to the knowledge questions on cancer risks were rated correctly within a ±50% margin of error. For instance, if the risk of a 55 year-old woman developing breast cancer within the next 10 years was 30 out of 1,000 women, estimates between 15 and 45 were considered correct. Estimates above the upper bound of the 50% margin of error were rated as “overestimations” and those below the lower bound of the 50% margin as “underestimations.” Women’s responses to the question concerning their knowledge of mammography screening were rated correct if they chose the option stating that the screening comes with benefits (reduction of cancer deaths) and harms (e.g., overdiagnosis), as suggested by scientific evidence.(7, 19)”
We have further added three citations (23, 7, 19) to the paragraph to support the data used for judging answers as correct.

7. Autier P, Boniol M, Koechlin A, Pizot C, Boniol M. Effectiveness of and overdiagnosis from mammography in the Netherlands: population based survey. British Medical Journal. 2017;359:j5224.
19. Gøtzsche PC, Jørgensen KJ. Screening for breast cancer with mammography. Cochrane Database Systematic Review. 2013;6(CD001877).
23. Kaatsch P, Spix C, Katalinic A, Hentschel S, Luttmann S, Stegmaier C, et al. Gesundheitsbereichterstattung des Bundes: Krebs in Deutschland 2011/2012 [Public health reports of the goverment: cancer in Germany 2011/2012]. Berlin: Robert Koch Institute; 2015.

More detailed comments / questions are as follows:

Abstract
1. Please clearly define the term “informed choice,” which seems to be the keyword of this study.

“Informed choice” is an established term in the medical setting, which is why we provide no detailed definition in the abstract. However, to remind the readership of the requirements of informed choice in the setting of cancer screening, we rephrased a sentence in the introduction: “But are women sufficiently informed about the their baseline cancer risk and the benefits and harms of mammography screening required to make an informed choice on screening attendance?”

2. Explain the Harris Interactive and the Toluna panel. Is it the name of the company that collected data?

We clearly state in the method section, first paragraph (lines: XX), that Harris Interactive is an established market research institute operating in numerous countries around the world. Their panels have been used in various research studies. For instance, we used their panel for the following study: Wegwarth O, Schwartz LM, Woloshin S, Gaissmaier W, Gigerenzer G. Do physicians understand cancer screening statistics? A national survey of primary care physicians in the U.S. Annals of Internal Medicine. 2012(156):340–9.

In the original submission these panels are explained in a paragraph under “Sample frame.” However, to be more specific, we have now added further details to the paragraph: “The sample frame was the Harris Interactive Panel and the Toluna Panel, maintained and subcontracted, respectively, by Harris Interactive, an established market research institute operating in more than 60 countries worldwide. The panels are representative of the general population with respect to age, education, gender, and regions in each of the countries and comprise about 78,000 and 275,000 female participants of the age group targeted in this study, respectively. Participants have agreed in advance to participate in online research.”

3. Please give more information on “the age specific risk of development of cancer”. How this measure was defined and validated?
Age-specific risks of developing or dying from a specific type of cancer within the next ten years are calculated (by the RKI) with the program DevCan (https://surveillance.cancer.gov/devcan) of the National Cancer Institute in the USA, based on the current cancer incidence and mortality rates. The model implemented in DevCan estimates age-conditional probabilities of developing different types of cancer in a hypothetical cohort based on cross-sectional cancer rates and death rates while accounting for age-dependent competing risks. The detailed method is described in: Fay MP. Estimating age conditional probability of developing disease from surveillance data. Population Health Metrics. 2004;2(1):6.

4. Please explain the reason why the women 40 years old or older were the samples of this study. Cervical cancer is prevalent in much younger age group.

We do not agree that cervical cancer is prevalent in much younger women. It is correct that cervical cancer in situ (a precursor to cervical cancer but with an excellent prognosis if diagnosed) is very prevalent below 40, but in screened populations, invasive cervical cancer occurs mainly in middle-aged and older women. In Sweden, for example, 75% of such cases occur in women above 40 and the average age of debut is 55 years. Furthermore, because our budget accommodated only a certain number of women we had to compromise between the power of the study and investigating a wider age range. Nevertheless we believe that our approach is justified because:

1) All four female cancers (including cervical cancer) for which we studied women's knowledge of their age-specific cancer risks are prevalent in the age group 40 to 75 years.
2) We specifically studied women's knowledge of cancer screening for mammography, which is offered at the earliest from the age of 40 years onwards and usually not after the age of 75 years.

Introduction
5. The harm of overdiagnosis and overtreatment of cancer is emphasized, but it is not the only issue studied in this manuscript.

We spend some more words in the introduction on overdiagnosis and overtreatment because this aspect of screening is mostly overlooked by/unknown to screening participants. However, we also emphasize other issues: We explain that screening can both have benefits and harms and discuss the current state of female cancer screening in Europe and current evidence on what women might know about cancer screening in Europe/specific European countries.

6. P.5, 2nd paragraph
The reference articles are not sufficient. These cited articles are only for specific countries, not for all European countries.

Currently no studies on this particular aspect of women's knowledge exist for all European countries.

7. Need more explanation to designate the core age group for this study. The age risk differ by types of cancer.

In the method section under the heading "statistical analysis and data presentation" we define the core age group as such: "To define the core age group, we decided upon women eligible for mammography screening for breast cancer (50–69y) because this is an implemented, systematic population-based screening program in each of the 5 European countries, for which women in these countries receive an invitation letter every second year supplemented with information material."
We emphasize again that differences between women belonging/not belonging to the age core group were studied solely with regards to knowledge on breast cancer risk and knowledge on mammography screening (target population of the population-based mammography screening is 50- to 69-year-old women). This is clearly stated in the aims of the study in the introduction and under "outcomes" in the methods. These analyses are therefore not affected by the fact that age-specific risks differ for different types of cancer.

Methods
8. It needs more detailed information to explain the legitimacy of Harris Interactive and the Toluna Panel. How about the degree of representativeness of female population in Europe. E.g., how did they obtain the e-mail address of the participants?

For clarification, we included the following specifications in the sample frame description under methods: "The sample frame was the Harris Interactive Panel and the Toluna Panel, maintained and subcontracted, respectively, by Harris Interactive, an established market research institute operating in more than 60 countries worldwide. The panels are representative of the general population with respect to age, education, gender, and regions in each of the countries and comprise about 78,000 and 275,000 female participants of the age group targeted in this study, respectively. Participants in the panel have agreed in advance to participate in online research."
Emails of participants are obtained by online recruiting via web applications, public relation activities, and recommendations via websites, social networks, affiliate marketing, and emails.

9. It seems like the leaflet was provided to the participants together with questionnaires. Please explain how the authors made sure that the participants answered the questions before reading the leaflet, then answer the certain questions after that. The process of data collection should be written in details.

The questionnaire and the leaflet were both programmed online and presented in a consecutive order online: 1) Questions, 2) leaflet, and 3) questions again. At each step, women were no longer able to go back to the previous step, that is, after accessing the leaflet online, they could not return to the initial question and when leaving the leaflet and entering the questions asked for the second time, they could not return to the leaflet.
We have now added some more details in the method section under “survey questionnaire” to make the procedure clearer.

10. The good amount of leaflet explains the women’s cancer risk identification test. It is like a promotion of WID. If the questionnaire focus on this issue. Authors needed to re-think the study aim.

At the end of the section “survey questionnaire” under methods we are clear about the reasons for this: “The leaflet was part of a larger study on 1) women’s knowledge about female cancers and cancer screening and 2) their attitude towards a forthcoming epigenetic predictive test on female cancer risks (WID test). Results from the second part of the study, which do not deal with women’s knowledge of current risk and clinical practice, go beyond the scope of this article and will be presented elsewhere.”

11. Provide a background information and importance to study the level of knowledge and its acquisition by country in Introduction before explaining it in Methods.

We believe that the introduction sufficiently explains why studying women’s knowledge on female cancer risks and screening is important in the following paragraph: “But are women sufficiently informed about their baseline cancer risk and the benefits and harms of mammography screening, which is a prerequisite to making an informed choice on screening attendance? In 9 European countries, 92% of the women overestimated the benefit of mammography by at least an order of magnitude, and less than 10% of a national US sample regularly attending one or more cancer screenings had ever heard of overdiagnosis due to screening.(15, 16) The European study additionally revealed that the nature of health information provided largely influenced overestimation. Moreover, as a German national study documented, a considerable number of women incorrectly assumed that mammography screening prevents incidence of cancer.(17) What remains unaddressed in these studies is whether these women had already greatly overestimated their risk of developing cancer at a certain time in life. Misperceiving one’s own risk of developing cancer as being particularly high may trigger unreasonable assumptions about cancer screening.(15, 17)”

12. Please explain the core group comprised of 50-69 years old was applied to assess the knowledge of all 4 types of cancer. Cervical cancer is prevalent in younger age group. Please explain the importance to compare the women in 50-69 years and women in the other age group.

Please see our reply to comment 7.

13. P10 line 8-
Data on women’s age-specific risks for each of female cancer were derived from the Robert Koch Institute. Please explain what this mean to the study design.

As pointed out in our reply to comment 6/ general issues, we rated women’s provided estimates to the knowledge questions on cancer risks as correct within a ±50% margin of error to accommodate for

potential country-specific variations in female cancer risks. Neither we nor the clinical experts (including epidemiologists from different European countries) of the FORECEE project are aware of any substantial variation in female cancer risk among women from the studied five European countries. Moreover, although we cannot claim comparability of female cancer risks across the five countries for each of the four cancer types studied here, the randomized controlled trials on mammography done in some European countries suggest no considerable differences in base line risk for breast cancer. We are thus confident that using the German baseline risks for female cancer with a 50% margin of error when evaluating women's estimates on their risks should well capture the range of actual baseline risks in the five European countries.

14. Please explain the definition of correct answers. The risk of certain cancer in specific age group should be different by country, and with and without risk factors such that smoking status and family history of cancer, obesity etc . Please provide the accurate citations for the correct answers.

For the definition of correct answers, please see our reply to comment 6/ general issues. Our study did not aim to investigate whether women know highly individualized cancer risk estimates stratified by risk factors such as obesity or smoking status. We therefore did not collect data on these risk factors. What we did collect was information on whether women had a cancer diagnosis in the past; analyses including/not including these women did not show any differences in the proportion of correct/incorrect responses as described in the method section under "statistical analyses and data presentation."

15. The participation rate of 61.4% is not that bad for the observational study. However, The authors did not provide the information on their target population. Because of that, the selection bias is a serious concern.

We already acknowledged the potential existence of nonrespondent bias in the limitation section with the following statement: "Fourth, we cannot rule out the existence of nonrespondents' bias. Although we achieved a reasonable response rate and stratified the sample to match women's characteristics for age and education in our sample to the general population at survey completion, we cannot exclude the likelihood that women with higher cancer risks due to close family history or a greater interest in the topic of cancer and screening were more likely to respond to our survey, which might have influenced our results and limit the generalizability of our results."

Results

16. Please define the "minority women" in methods. As a matter of factor, the reason why the authors included the analysis comparing majority vs. minority women is not clear. Please provide the background information and importance of the study in Introduction. Also, please provide the distribution of minority women in table 1.

We speak not of "minority women" or "majority women" but "minority of women" or majority of women," that is, to proportions of women with correct responses. For instance, when saying that the "minority of women" correctly answered the question, we mean that a proportion of less than 50% of the sample provided the correct response. Because we assume that this is conventional terminology, we have left these phrases as is.

17. The second paragraph of Discussion is written as if a review of previous studies. The discussion should be written based on current findings.

It is common practice to set new findings of a recent study in context to existing studies in the discussion – we believe this adds significant value to the clarity and context of the finding.

18. As the authors discuss, the cross-sectional study design is not appropriate to measure the effectiveness of intervention with a leaflet.

This appears to be a misunderstanding. What we said in the discussion/ limitations is the following: "Third, the cross-sectional design of the study prevented us from assessing durability of improvements in knowledge. We thus are not able to judge whether women maintain over a longer run the improvements in knowledge we found in our study."
However, because our study did not aim at investigating durability of improvements at the current point of time, we consider our design as appropriate to investigate the effect of an information intervention on baseline knowledge.

Tables
19. Table 1.
Distribution of other important characteristics, which would influence on the study results, should be presented. E.g. past history of cancer and family history of cancer. BMI, physical activity and smoking status, as indicators of health conscious individuals.

We collected data on personal cancer history only, which did not effect results as stated in the method section under "statistical analyses and data presentation."

20. Table 2
-Please define "the correctness of the knowledge".
-Please define the "core age" and "over estimation"

We have added the following details at the end of the table: "*n core = women in the core age group (50 to 69y) eligible for mammography screening in the five European countries, § correct response of age-specific cancer risk = 50% margin of error of the actual age-specific cancer risk based on the population-based cancer registration dataset of the Robert Koch institute (www.krebsdaten.de), ¶ overestimation of age-specific cancer risk = > 50% margin of error of the actual age-specific cancer risk based on the population-based cancer registration dataset of the Robert Koch institute (www.krebsdaten.de)"

21. The purpose of this table analysis is not clear, although it seems like the authors intended to highlight the different knowledge level and intervention effect by country. The title should clearly indicate the contents of the table.

We believe that the original legend to Table 3 (now Table 4) was clear, but to make it even more specific we have now slightly changed it to the following: "European women's knowledge regarding mammography screening; presented as the proportion of women choosing the correct and the incorrect options out of the choice set of three possible answers before and after leaflet presentation."

Reviewer: 3
Reviewer Name: Abdulmohsen Al-Zalabani
Institution and Country: College of Medicine, Taibah University, Saudi Arabia
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
This manuscript reported a well-planned, well-conducted study tackling the issue of whether women had overestimated their risk of developing cancer at a certain time in life.

I have some comments:

==Methods==
* Page 7, Line 10: The abbreviation "FORECEE" is used for the first time in the manuscript. So, it needs to be spelled out in the first appearance.

Thanks for noticing. We have now spelled out what the abbreviation “FORECEE” means and provided some more background information on the project in the beginning of the method section: “The core objectives of this study were triggered by the requirements of the ongoing FORECEE (Female cancer prediction using cervical omics to individualize screening and prevention) project— funded by the European Union’s Horizon 2020 research and innovation programme—that aims to develop an epigenetic test to predict the risk for breast, ovarian, cervical, and endometrial cancers in women using cervical cells (https://forecee.eu). Part of the FORECEE project is to understand educational and communicative needs from the side of women who might be targeted in the future by the potential introduction of the resulting women’s cancer risks Identification (WID) test. The study reported herein investigated the educational aspect in that it sought to learn i) about women’s knowledge of their female cancer risks and cancer screening at base line, and ii) about the effect of an evidence-based leaflet (intervention) on that knowledge. To gain these insights with sufficiently large national samples from different European countries, the study was set up as a cross-sectional online survey with 2 phases (before/after intervention).”

* Page 8, Line 15: "The email provided basic information about the study, the link to the survey and the leaflet". This statement lead to an impression that the leaflet was attached to the invitation email. Later description in the manuscript clarified that respondents have access to the leaflet only after they answered the questionnaire for the first time. The statement above needs to be modified.

We agree and have now modified the phrasing of the sentence to “The email provided basic information about the study, the link to the study (with a personalized password) in the nation-specific language of the target population…” We hope this makes it clearer now.

* Some parts of the manuscript may need a bit of rearrangement. For example:
a) the part from "page 8 line 55" to "page 9 line 35" (Except page 9, lines 25-27) is better to be under a title of "intervention".

Because we found it difficult to disentangle lines 25 to 27, which describe the procedure of implementing the intervention, from the remaining lines, which describe the development and content of the intervention, we extended the subheading of this part of the manuscript to “Survey questionnaire and intervention” and hope that this change satisfies.

b) the part in "page 10 line 8 to 17" belongs to the "outcomes" section rather than "statistical analysis" section.

Our wording in these lines may have led to a misunderstanding. The data on women’s age-specific cancer risk derived from the Robert-Koch-Institute were not an outcome measure of our study reported here. Instead, we are referring to data derived from a large population-based cancer registry on actual cancer risk, which served as an external criterion of the actual size of female risks for evaluating the correctness of women’s estimates of their expected cancer risk. In order to avoid potential confusion with BMJ open’s readership we have slightly modified the sentence:
“Epidemiological data on age-specific 10-year risks for each of the female cancers were derived from the population-based cancer registry database of the Robert Koch Institute (www.krebsdaten.de) in Germany.”

* Page 10, Lines 8-10: Authors stated that "... age-specific risks for each of the female cancers were derived from the Robert Koch Institute ... database in Germany".
First, they need to report in the manuscript the exact age-specific risks for each type of cancer they got from the database.

We agree and have now included table 1 in the method section, which provides the actual age-specific risks for each of the female cancer types.

Second, I wonder if the age-specific risks for each of the cancers are similar in all of the 5 countries included. Was there a reason not to use the age-specific risk of the country of each respondent?

For one, not all of the European countries included in our study have population-based cancer registries, meaning that sufficient information on country-specific risk is missing. Although we cannot claim comparability of female cancer risks across the five countries for each of the four cancer types studied here, the randomized controlled trials on mammography conducted in some European countries suggest no considerable differences in base line risk for breast cancer. Nevertheless, to accommodate for potential country-specific variations in female cancer risks, women's estimates to the knowledge questions on cancer risks were rated as correct within a ±50% margin of error.

==Results==

* Page 10, Lines 21-27: Numbers reported here are not clearly presented. Median and range of what? What does the abbreviation "m" mean?. I guess the numbers refer to the respondents "estimation of their age-specific cancer risk out of 1000 women". I think it is better to rephrase the paragraph to make it more comprehendible.

We assume that reviewer 3 is referring to the results on page 13, lines 21-27. We agree and have now clarified that the median and the range refers to the overestimates provided by women to the questions on the age-specific risks for each of the cancers by adding the word "overestimation" next to median and range. "m" is a common abbreviation for median and, to the best of our knowledge, can be used after the word "median" is introduced in the first place. However, to avoid confusion we have decided to spell it out throughout.
In addition we decided to better specify what we mean by "overestimation" and have now included the following additional sentence under "statistical analyses and data presentation": "Estimates above the upper bound of the 50% margin of error were rated as "overestimations" and those below the lower bound of the 50% margin as "underestimations."

* Does Figure 1 presents extra information not presented in Table 3? If not, do you still need Figure 1?

We agree and have eliminated figure 1.

VERSION 2 – REVIEW

REVIEWER	Abdulmohsen Al-Zalabani College of Medicine, Taibah University, Saudi Arabia
REVIEW RETURNED	09-Aug-2018

GENERAL COMMENTS	All previous comments were satisfactorily addressed.