



STUDY PROTOCOL

REVISED Evaluating adults' health-related values and preferences about unprocessed red meat and processed meat consumption: protocol for a cross-sectional mixed-methods study [version 2; peer review: 2 approved]

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Abstract

Background: People need to choose from a wide range of foods, and in addition to availability and accessibility, people's values and preferences largely determine their daily food choices. Given the potential adverse health consequences of red and processed meat and the limited knowledge on individuals' health-related values and preferences on the topic, such data would be useful in the development of recommendations regarding meat consumption.

Methods and analysis: We will perform a cross-sectional mixed methods study. The study population will consist of adult omnivores currently consuming a minimum of three weekly servings of either

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unprocessed red meat or processed meat. We will explore participants' willingness to stop or reduce their unprocessed red meat, or their processed meat consumption through a direct-choice exercise. This exercise will consist of presenting a scenario tailored to each individual's average weekly consumption. That is, based on a systematic review and meta-analysis of the best estimate of the risk reduction in overall cancer incidence and cancer mortality, we will ask participants if they would stop their consumption, and/or reduce their average consumption. We will also present the corresponding certainty of the evidence for the potential risk reductions. Finally, we will measure their meat consumption three months after the interview and determine if they have made any changes to their average consumption.

Ethics and dissemination: The research protocol was approved by the ethics committees in Canada (Research Ethics Board, Dalhousie University), Spain (Comitè Ètic d'Investigació Clínica de l'IDIAP Jordi Gol), Poland (The Bioethics Committee of the Jagiellonian University), and Brazil (National Research Ethics Commission). The study is based on voluntary participation and informed written consent. Results from this project will be disseminated through publications and presentations.

Keywords

health, values and preferences, red meat, processed meat, cross-sectional study, mixed methods



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REVISED Amendments from Version 1

We would like to thank the reviewers for taking the time to review our protocol (version 1) and for their comments. We have considered each comment in the new published version (version 2).

We would like to clarify that due to the COVID-19 pandemic, all sites are conducting the study remotely; only the pilot study was conducted in-person since it was implemented before the start of the pandemic.

We have improved the manuscript by clarifying the difference between the pilot study and the sites in which the study was actually conducted.

Further, given the pandemic, some changes in the study's methods and procedures were made, which are now reported in the new published version of the protocol (version 2). For this reason, all methodological aspects related to the in-person interviews and questionnaire administration have been removed and only the online/remote procedures are instead explained and reported in the manuscript.

Additionally, we have corrected some errors in Table 1, we've clarified some procedural aspects in the "Study procedures" section, and, finally, we have provided additional supplementary material as suggested by the reviewers.

Any further responses from the reviewers can be found at the end of the article

Introduction

Food choices are important for the overall health of each individual¹. On a daily basis, people need to choose from a wide range of food in order to meet their nutritional requirements². People's dietary values and preferences influence the types of foods they consume, as well as the quantity of consumption^{3,4}. However, nutritional guidelines have consistently ignored the systematic identification and incorporation of people's values and preferences in the development of their recommendations^{5,6}.

In light of recent studies showing an association between unprocessed red meat and processed meat consumption and adverse health outcomes, such as all-cause mortality, cardiovascular mortality, cancer risk, and stroke⁷⁻¹², dietary guidelines have generally endorsed limiting meat intake (e.g. limiting processed meat)¹³⁻¹⁵. However, limited information exists regarding how much people value meat in their diet and their willingness to reduce meat consumption in the face of undesirable health effects¹⁶. Recently, an international panel of 14 members noted the low quality evidence supporting the causal relation of meat and adverse effects, and the small protective effect of reducing meat consumption if indeed such an effect exists. The panel formulated a weak recommendation in favor of continuing usual consumption¹⁷. The recommendation was also based on a systematic review of studies addressing peoples' values and preferences regarding meat consumption; however, the evidence was also judged to be of low quality given identified issues with risk of bias and indirectness¹⁶.

We have therefore designed a study to evaluate adults' values and preferences regarding meat intake and their willingness to

change their consumption in the face of possible undesirable health consequences. Given the general importance of reducing cancer, the recent claims on cancer risk associated with meat consumption from the International Agency for Research in Cancer and the World Cancer Research Fund^{8,18}, and in an attempt to avoid overwhelming participants with too much information, based on a systematic review of the literature¹¹, we chose the risk estimates for two cancer outcomes to share with participants, specifically cancer incidence and cancer mortality.

This study is part of NutriRECS (Nutritional Recommendations; www.nutriRECS.com)¹⁹, an initiative that aims to: 1) apply rigorous systematic review and guideline methods using the GRADE approach to investigate the association between diets, foods and nutrients and health outcomes; 2) incorporate patient and community values and preferences to inform guideline recommendations; 3) apply strict and transparent management of conflicts of interest, and; 4) disseminate nutritional recommendations via open-access peer-reviewed publication.

Methods and analysis

Study design and setting

We are conducting an international cross-sectional mixed-methods study including: i) a quantitative assessment through an online survey; ii) a qualitative evaluation through semi-structured interviews and, iii) a follow-up quantitative assessment through a questionnaire in three different sites in three countries (Spain, Brazil, and Poland). Study settings will include universities, and the general community. The study began in 2019 with recruitment and data cleaning ongoing, with expected completion in early 2021. In 2019, we conducted a pilot study in a sample of 32 participants recruited in the general community in Nova Scotia and Prince Edward Island, Canada²⁰. The results and feedback of this pilot study were used to inform and improve the study's procedures.

Study population and eligibility criteria

We will enroll adults 18 to 80 years of age who currently consume a minimum of three serving per week of either unprocessed red meat or processed meat. Unprocessed red meat is defined as mammalian meat (e.g. beef, pork, lamb), and processed meat is defined as white or red meat preserved by smoking, curing, salting, or by the addition of preservatives (e.g., hot dogs, charcuterie, sausage, ham, and cold cut deli meats)²¹. We will exclude adults who have active cancer; those who have severe cardiovascular disease (history of stroke, acute coronary syndrome, heart failure, and symptomatic peripheral arterial disease); those who are pregnant; and participants unwilling or unable to provide informed consent.

Recruitment strategy

We will recruit convenience samples of participants from the general population or people studying or working at universities. We will recruit participants from the general population using social media postings on the Cochrane website, Twitter, and Facebook pages. We will recruit people studying or working at universities by email. The social media posting and the emails will include information on study's details, eligibility

criteria, contact information of the researcher carrying out the study, and the related link to access the online survey.

Sample size

For the quantitative assessment, we have made a best estimate of the proportion willing to reduce their meat intake of approximately 0.5 using the response distribution results from our pilot study based on a proportion of 0.53 of pilot participants willing to reduce unprocessed red meat and 0.44 of participants willing to reduce processed meat²⁰. We decided that a margin error around this estimate of as much as $\pm 0.1\%$ is acceptable. We can achieve this precision with a 0.5 estimate in our primary outcome, the proportion of individuals ready to reduce or stop eating meat. Our sample size estimate is 96 participants at each site (95% confidence interval with $\pm 0.1\%$ margin error)^{22,23}.

For the qualitative evaluation, through a maximum variation sampling strategy, in each site, we will include participants until data saturation. Data saturation is achieved when no additional concepts emerge²⁴. During data collection and analysis, if the research team determines that we have not reached data saturation, recruitment will be extended to include more participants until saturation is achieved. The maximum variation technique consists of the inclusion of a highly heterogeneous sample, and a description of the variability or dispersion for the relevant variables^{3,25}. We will attempt to include an approximately equal number of participants with the following characteristics of these variables: gender (men and women); age (those between 18 to 66 years old, and those between 67 and 80 years older); education level (those with some high school or less, those with a high school degree, and those with a college degree) and willingness to stop or reduce meat consumption (willing ≥ 5 from the Likert-Scale and unwilling ≤ 4 from the Likert-Scale).

Study procedures

For the quantitative assessment, participants interested in participating will access the online survey and will be able to complete the questionnaire, including demographic characteristics, medical history information and meat consumption beliefs and behavior. The questionnaire will also include a direct choice exercise that will consist in presenting scenarios tailored to each individual's typical weekly meat consumption. These scenarios will reflect the best estimate of absolute risk reduction in overall cancer incidence and cancer mortality over their lifetime based on our systematic review and dose-response meta-analysis¹¹. This will allow us to assess participants' willingness to: a) stop or b) reduce their unprocessed red meat and processed meat intake in the face of overall cancer incidence and cancer mortality risks.

After presenting participants with the cancer incidence scenario tailored to their consumption, participants will be asked regarding their willingness to stop their unprocessed red meat intake. If participants will be unwilling to stop (≤ 4 of the Likert-scale), they will be presented with an additional question about their willingness to reduce. Similarly, participants

will be then presented with the cancer mortality scenario and related questions for unprocessed red meat. Finally, participants will be presented with the cancer incidence and mortality scenarios tailored to their processed meat consumption with the same logic of questions explained above.

Participants will be presented with both scenarios of unprocessed red meat and processed red meat. If participants declare to consume less than one serving of one type of meat per week, for example unprocessed red meat, they will skip the questions on red meat and will be presented with the scenarios and questions of processed meat only and vice versa. Finally, we will conduct a follow-up assessment, either by phone or by email, at three months to ask participants, who agreed to be contacted, if they have made any changes in their meat consumption.

Questionnaire. Based on our pilot study, we further developed and piloted a questionnaire in each site to collect the following data: age, sex, socioeconomic status, educational level, employment status, household size, religious beliefs, the presence of chronic and other health conditions, and family history of cancer, and meat consumption beliefs and behavior information. We asked both men and women with different educational backgrounds and of different ages (those between 18 to 66 years old, and those between 67 to 80 years older) to complete the questionnaire in order to identify ways of improving the content and/or structure of the questionnaire.

We will assess participants' current weekly consumption of unprocessed red meat and processed meat. We will facilitate these questions related to their meat consumption habits by providing pictures illustrating types of meats and serving size to determine the typical number of servings they consume of each meat weekly. In addition, we will determine which factors participants take into account when choosing their diet, whether their food choices influence or are influenced by other people (e.g. preparing food for children) and to what extent they are satisfied with their current diet. See *Extended data* for the Spanish version of the online survey.

Serving size estimate and participant's current meat consumption assessment. We estimated that each serving of unprocessed red meat is equal to 120g, and 50g for processed meat¹¹. In Spain, the mean \pm standard deviation of meat intake, according to 2016 Spanish National dietary survey in adults, conducted by the Spanish Agency for Consumption, Food Safety and Nutrition, is $37 \pm 63\text{g/day}$ (2 servings/week) of unprocessed red meat and $32 \pm 65\text{g/day}$ (4 servings/week) of processed meat²⁶. In Brazil, according to the Health Survey conducted in São Paulo in 2008, the mean \pm standard error of meat intake is $71 \pm 2 \text{ g/day}$ (4 servings/week) of unprocessed red meat and $28 \pm 1 \text{ g/day}$ (4 servings/week) of processed meat²⁷. In Poland, according to the domestic deliveries and consumption report of 2017, the average intake of both unprocessed meat and processed meat is 115 g/day (9 servings/week)²⁸. In Canada, according to the Statistics Canada's Canadian Community Health Survey, the mean intake among

Canadians is 52 g/day (3 servings/week) of unprocessed red meat and 22 g/day (3 servings/week) of processed red meat²⁹. Based on these data, we defined the average intake of both unprocessed red meat and processed meat as 3 servings per week to calculate the baseline risks of cancer incidence and cancer mortality. In order to assess participant's current meat consumption, we determined the absolute risk reduction for all meat consumption frequency categories (servings/week) as follows: 3 to 4, 5 to 6, 7 to 8, 9 to 10, 11 to 12, 13 to 14, and more than 15 servings per week. We will report in servings per week their current meat consumption for both unprocessed red meat and processed meat.

Direct choice exercise. Following standard methodologies used in previous work in the field of obstetrics from members of our team^{30,31}, we will use a direct choice experimental design to assess the proportion of people willing to change their consumption when faced with a risk reduction of overall cancer incidence and cancer mortality based on a seven point Likert- scale from 1 (meaning definitely not) to 7 (meaning definitely yes).

To ensure that participants have a similar understanding of these two outcomes, we will describe the development of each outcome through the use of health states examples (Table 1 and Table 2). We will present our data from our systematic review that addressed the possible impact of reducing meat intake on overall cancer incidence and mortality¹¹. We will first present the baseline risk and the risk reduction participants might achieve by stop eating meat and its certainty. We will develop an interactive electronic decision aid using MagicApp software (<http://magicproject.org/research-projects/share-it/>) to show the probabilities of reducing the risk of overall cancer incidence if participants' would stop eating unprocessed red or processed meat (three servings/week scenarios in Figure 1 for processed meat and Figure 2 for unprocessed red meat intake – see *Extended data*³² for all servings/week scenarios). In addition to the risk reductions, the overall certainty of evidence based on the GRADE approach for cancer and incidence and mortality will be shared with the participant³³. For the direct choice exercise in the online survey, we will provide an explanatory video that will describe to participants how to read and

Table 1. Health states - Cancer incidence.

Cancer incidence	
Symptoms & Signs	<ul style="list-style-type: none"> • Cancer is wide group of diseases and may cause many signs or symptoms • Some signs and symptoms are common for different cancers while others are more specific for each type of cancer • Not explained loss in body weight, night sweats, fever • Problems with eating, loss of appetite • Weakness/ fatigue • Sometimes bleeding or discharge, blood in stool or urine • Change in bowel habits, difficult or painful urination • Pain • Unexplained anemia • Persistent cough or blood in saliva • Persistent lumps or swollen glands • Changes on the skin
Treatment	<ul style="list-style-type: none"> • There are different types of treatment that will depend on the type of cancer and how the cancer is advanced. • You may receive only one treatment, but in most cases a combination of subsequent is needed: surgery and/or hormone therapy (giving hormones or drugs that block hormones to slow down cancer growth), chemo or immunotherapy (drugs that kill cancer cells or flag them for immune system to destroy) and/or radiation therapy (radiation in high doses to kill cancer cells or slow their growth).
Consequences	<ul style="list-style-type: none"> • You can experience side effects of cancer treatment, such as anemia, loss of appetite, fatigue, hair loss, nausea • You can experience pain, gastrointestinal problems, urinary problems • It will affect your social life short term and possibly long term • You can experience long-term consequences of cancer and its treatment, such as problems with heart, lungs, endocrine system, bones and joints, digestion, memory • You may experience anxiety, depression and other emotional problems • You may no longer be able to participate in your regular activities • You may die

Table 2. Health states – Cancer mortality.

Cancer mortality	
Symptoms & Signs	<ul style="list-style-type: none"> • Before you die you experience symptoms related to cancer and its spread, such as pain, weakness/fatigue; those symptoms may have various duration, you may suffer those symptoms for several years • Before you die you experience unwanted effects of treatment you received for cancer. • You are dead and you do not feel any pain or breathlessness.
Treatment	<ul style="list-style-type: none"> • There is no need for any treatments and they are stopped
Consequences	<ul style="list-style-type: none"> • You lose your vital bodily and mental functions, ending your life. • You will leave everything that was important in short time span.

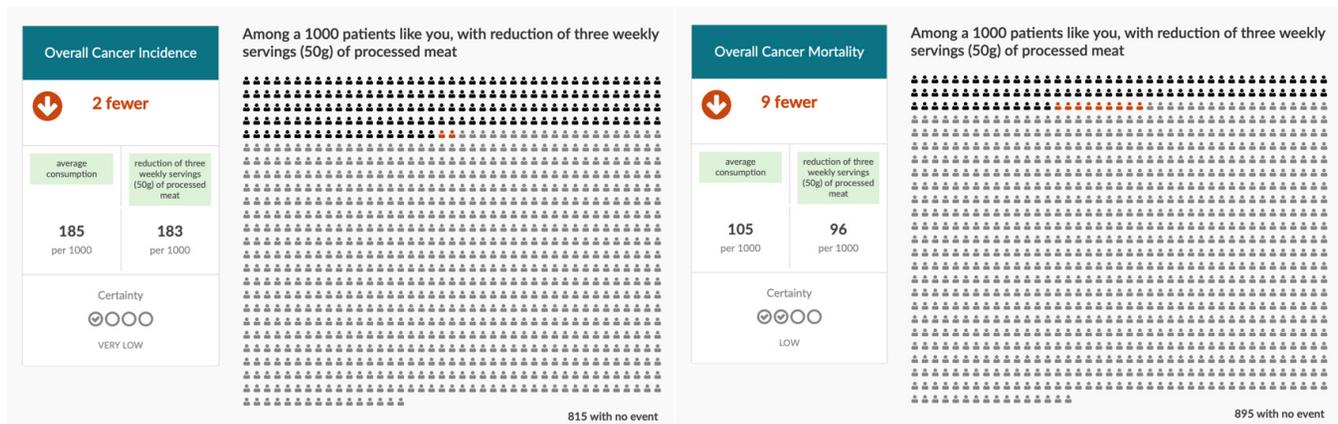


Figure 1. Three servings/week scenarios for processed meat.

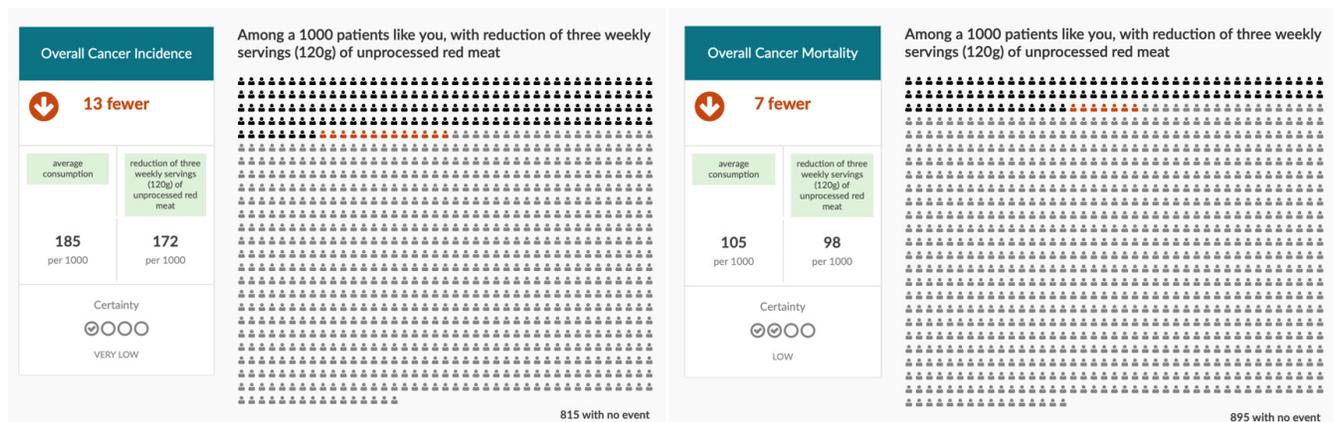


Figure 2. Three servings/week scenarios for unprocessed red meat.

interpret the data presented in the scenarios. In addition, we will provide participants with explicit text tailored to their average weekly meat consumption. If participants are unwilling

to stop eating meat to achieve the possible associated health benefits, we will ask them if they would be willing to reduce their meat intake but remind them that the cancer risk

reduction, they might anticipate will be less by reducing their meat intake then stopping completely.

Semi-structured interview. We will also develop and pilot a script in each site for a semi-structured interview. We will conduct these interviews in order to explore peoples' motives regarding their willingness to change their meat consumption. Based on our pilot study, interviews will take approximately 30 minutes. See *Extended data* for the Semi-structured interview script.

Follow-up assessment. We will contact participants by phone or by email three months after the online survey and ask them if they have made any changes in their meat consumption. In case of the phone follow-up, we will follow a semi-structured telephone script previously piloted; in instances where participants prefer to be contacted by email, we will send them a questionnaire with the same content we will use for the phone interview. See *Extended data* for the Follow-up assessment script.

Outcomes

The primary outcome measure for all included participants will be willingness to change meat consumption in the face of the undesirable cancer health risks. We will show participants the cancer risk reduction they may achieve if they would stop eating unprocessed red meat or processed meat tailored to their weekly consumption and ask them if they are willing to stop, on a scale from 1 (meaning "definitely not") to 7 (meaning "definitely yes"). If participants are not willing to stop eating meat (≤ 4 from the Likert-scale), we will ask them if they will be willing to reduce any amount of their weekly meat intake, on a scale from 1 (meaning definitely not) to 7 (meaning definitely yes). As a secondary outcome, we will explore participants' values and preferences regarding meat intake and the related motives around their willingness or unwillingness to make any changes. We will ask participants in the qualitative evaluation, which factors determine their unprocessed red meat or processed meat intake, and to what extent these factors influence their willingness/unwillingness to stop/reduce their meat consumption. Finally, we will estimate their meat consumption at three months after the online survey and determine if they have made any changes.

Data synthesis and analysis

Quantitative analysis. We will describe participants' demographic and medical history information as well as meat consumption behaviors using means and standard deviations or frequencies and proportions, as appropriate.

We will describe the distribution of the continuous dependent variables: a) "willingness to stop unprocessed red meat consumption in the face of cancer incidence risk"; b) "willingness to stop unprocessed red meat consumption in the face of cancer mortality risk"; c) "willingness to reduce unprocessed red meat consumption in the face of cancer incidence risk"; d) "willingness to reduce unprocessed red meat consumption in the face of cancer mortality risk", by presenting histograms and using means and standard deviations or median and IQR, as appropriate. We will do the same analysis for processed meat. Then,

we will conduct an exploratory linear regression analysis using the above dependent variables and the participants' characteristics (sex, age, level of education, occupational status, religious belief, and family history of cancer) as the independent variables. We will calculate the beta coefficients and the associated 95% confidence interval of participants who are willing to avoid, and for those willing to reduce unprocessed red meat and processed meat consumption in the face of undesirable cancer risks.

Additionally, we will conduct an exploratory logistic regression analysis using the dependent variables on willingness as categorical variables: those willing (≥ 5 from the Likert-Scale) and unwilling (≤ 4 from the Likert-Scale). We will calculate the odds ratio and the associated 95% confidence interval of participants who are willing to avoid and reduce meat consumption in the face of undesirable cancer risks.

Using our three-month follow-up assessment data, we will calculate the frequency and proportion of participants who made any changes in their meat consumption.

Qualitative analysis. We will audio-record and transcribe verbatim all semi-structured interviews and use thematic analysis for the qualitative analysis^{34,35}. For our iterative analysis, we will use constant comparison within and across cases to identify any patterns. We will code all transcripts and then the codes will be sorted into themes. We will subsequently compare the identified themes with demographic and participant characteristic information collected to demonstrate any patterns among groups such as sex, age, and education level.

Integrating qualitative and quantitative analyses. We will conduct a sequential analysis of the quantitative and qualitative components of the data. We will analyze each dataset separately and then, at the end of the study, draw meta-inferences informed by the findings from both data sets. We expect the qualitative results to provide a better understanding of the decision-making process than if the quantitative results were considered alone.

Ethics and dissemination

Research approval was obtained by the Research Ethics Board, Dalhousie University (Canada; 2019-4715), the Clinical Research Ethics Committee of the Jordi Gol University Institute for Primary Care Research (IDIAP; Spain; 19/121-P), the Bioethics Committee of the Jagiellonian University (Poland; 1072.6120.141.2019), and the National Research Ethics Commission (Brazil; CAAE 21826419.4.0000.8527), and if needed will be obtained from all other participating sites. We will explain the entire process of the study to the participants and we will present the potential benefits and risks of participation. The potential benefits of this study to participants include gaining an understanding of the current research regarding overall cancer mortality and incidence based on an up to date high quality dose-response systematic review and meta-analysis¹¹, which participants could use in future dietary decisions. There are no potential physical or psychological risks to participating in this study.

Participation in the study is voluntary and participants may withdraw from the study at any time without penalty. Should they choose to withdraw; participants will decide whether they want us to discard all or some of the data they have provided. Participants willing to participate will have to sign a written consent form, and they will be assigned a number to anonymize all data collected. Consent forms will be kept separately in a secure cabinet. All interviews will be audio-recorded and transcribed onto a computer file. The recording device will be stored in a secure cabinet and the recordings will be deleted upon completion of the study. Participants will not be identified by name nor otherwise identified when research results are shared. It is possible that a participant could be quoted to highlight results, however, they will be anonymized and neither their name, nor their assigned alphanumeric code, will be shared. Participants will be made aware of this possibility during the consent process and may, if they wish, choose not to allow the use of direct quotations. No compensation will be provided to participants. We will share with participants a copy of our published final results by email or by postal service.

We will adhere to the checklist of good practice in the conduct and reporting of survey research³⁶ when reporting our results. Results will be disseminated through publications and presentations.

Discussion

Our international mixed-methods study will be the first to explicitly explore peoples' health-related values and preferences, and their willingness to stop and/or reduce meat consumption when informed of the potential adverse cancer risk, and the uncertainty around this evidence. The information patients will receive will be based on a recent systematic review and dose-response meta-analysis¹¹.

Our study in the context of previous research

Because there is limited information in the literature on how people value their health in relation to their diet, developing nutritional recommendations based on health-related values and preferences of community members is a major challenge. Previous studies addressing people's meat preferences did not adequately present the undesirable health effects of meat consumption in ways that captured the current evidence and its uncertainty^{37,38}.

In the context of the NutriRECS initiative, our team conducted a systematic review that summarized evidence that omnivores are attached to meat and are reluctant to reduce their meat consumption. However, we rated the certainty of evidence as low due to issues with risk of bias, indirectness, and because of the small number of participants and limited information regarding data analysis¹⁶.

A NutriRECS international panel using an individual patient perspective formulated a weak recommendation in favor of continuing current unprocessed red meat and processed meat consumption, acknowledging the low certainty regarding the

values and preferences evidence¹⁷. This experience triggered the design of the present study, aiming to overcome the limitations of the studies to date¹⁶.

Limitations and strengths

Our study has some potential limitations. Our sample includes participants living in high-income countries or from high income strata in low to middle income countries. Therefore, we cannot generalize these findings to low-income populations. We will, however, collect information on participants' socioeconomic status and education level in order to explore the effect of these characteristics on participants' dietary values and preferences.

A second limitation of our study is the exclusive focus on cancer outcomes, despite evidence suggesting that reducing meat consumption may reduce the risk of diabetes and cardiovascular outcomes^{12,39}. However, due to the recent claims of meat consumption and cancer risks^{8,40}, the inconsistency in data on cardiometabolic risk associated with both unprocessed and processed meat^{10,39}, and to not overburden participants with too much information, we prioritized two cancer outcomes.

Regarding strengths of our study design, we will address some of the limitations in the previous studies by following a systematic and transparent approach with the use of questionnaires, direct choice exercises and open-ended questions to assess peoples' health values in relation to their unprocessed red meat and processed meat consumption. We will inform people of the most recent evidence of meat consumption and its related cancer risks¹¹, including the certainty of evidence for these risks, according to their current weekly average consumption. In addition, we will explore their willingness to make any changes to their diet based on the potential risk reduction in cancer.

Our international multicentre study will help ensure generalizability of the results. In addition, the collection of both quantitative and qualitative data will enable an accurate identification of the current health values and preferences regarding meat consumption. In addition to our initial pilot study²⁰, we have further piloted the questionnaires and scripts in each center among both men and women, both with different educational backgrounds, and of different ages to ensure readability and understandability in the general population. We have trained research staff and we will monitor study procedures to ensure quality implementation throughout the interview process. Ultimately, we will follow-up participants to determine if they have made any changes in their meat consumption according to what they have reported during the initial interview; this will allow us to assess the consistency and reliability of our study findings.

Implications for practice and research

Our international study has direct implications for decision makers, guideline developers and policy makers in the development of nutritional recommendations. Up to now, this aspect

has been neglected when formulating recommendations. Panels will now have access to international research evidence on values and preferences specific to actual estimated risk reductions in cancer, and the relevant certainty, associated with decreased meat intake. Based on international GRADE standards⁴¹, this information will prove crucial for guideline panels moving from the evidence to recommendations on red and processed meat.

One potential area of further research will be the evaluation of how panels are using this new evidence when formulating recommendations. This work will also inform clinicians regarding community values and preferences when considering the implementation of diet related changes with their patients. Our proposal will use innovative approaches to assess people's health values and preferences in relation to their diet. The study will provide a rigorous and transparent methodology that can be further utilized in the context of other nutritional scenarios.

Data availability

Underlying data

No data are associated with the article.

Extended data

- Open Science Framework: <https://doi.org/10.17605/OSF.IO/4HKXQ>³²

- o All servings/week scenarios for processed meat and for unprocessed red meat intake,
- o Semi-structured interview script
- o Follow-up assessment script.

- Spanish version of the online survey available here.

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Acknowledgments

This study will be conducted using MagicApp software (<http://magicproject.org/research-projects/share-it/>). MAGIC (Making GRADE the Irresistible Choice) is a non-profit Foundation, aiming to increase value and reduce waste in healthcare through a digital and trustworthy evidence ecosystem. MAGIC is the core platform in the evidence ecosystem bringing digitally structured guidelines, evidence summaries and decision aids to clinicians and patients.

Claudia Valli is a doctoral candidate for the PhD in Methodology of Biomedical Research and Public Health (Department of Paediatrics, Obstetrics, Gynaecology and Preventive Medicine), Universidad Autònoma de Barcelona, Barcelona, Spain.

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Tomás Meroño 

Biomarkers and Nutrimentalomics Laboratory, Department of Nutrition, Food Sciences and Gastronomy, Food Technology Reference Net (XaRTA), Nutrition and Food Safety Research Institute (INSA), Faculty of Pharmacy and Food Sciences, University of Barcelona, Barcelona, Spain

The authors improved the manuscript and answered all the points raised.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Nutrition, nutritional epidemiology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 19 May 2021

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Mary Dicklin

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Kevin Maki

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This paper has been revised to address the comments from the reviewers, and I have just a few, relatively minor, suggestions for revisions as described below.

1. It might be useful to define the range of the Likert Scale (e.g., a 7-point scale from 1 [meaning definitely not] to 7 [meaning definitely yes]) where it is 1st mentioned (i.e., in the Sample size section). It currently isn't defined until later in the Direct choice exercise section, but it is mentioned earlier in both the Sample size and Study procedures sections.
2. In the 3rd paragraph of the Study procedures section: In the sentence beginning, "If participants declared..." the word "unprocessed" is missing where it says the participants "will skip the questions on red meat".
3. There appear to be some errors in the Semi-structured interview script available online: a) "unprocessed red meat" should be "unprocessed red meat"; b) perhaps "In which way" should be "In which ways do"; c) should the question that begins with "Are these factors..." refer to both processed meat and unprocessed red meat? d) "What could motivate" should be "What could motivate"; e) The last question, "Do you think it is something that we would be interested in learning from the interviewees?" is unclear. Should this instead say something like "Is there anything that you think we would be interested in learning from the interviewees?"

Competing Interests: Received research funding from the National Cattlemen's Beef Association/Beef Checkoff.

Reviewer Expertise: Design and conduct of clinical studies in human nutrition, metabolism and chronic disease risk factor management.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 23 February 2021

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Tomás Meroño 

Biomarkers and Nutrimetabolomics Laboratory, Department of Nutrition, Food Sciences and Gastronomy, Food Technology Reference Net (XaRTA), Nutrition and Food Safety Research Institute (INSA), Faculty of Pharmacy and Food Sciences, University of Barcelona, Barcelona, Spain

The study protocol presented by Valli *et al.* aims to evaluate the willingness to change their consumption of unprocessed and processed red meat in light of risk reductions in cancer incidence and mortality. The "mixed-methods" refers to the combination of quantitative and

qualitative research methodologies. The qualitative research aims to study the factors behind the willingness or not to modify red meat consumption.

In addition, they propose to evaluate the preferences of consumption of the participants; however the relevance for this data is not clear in the actual version of the protocol.

General comments

- From a participant point of view, the tables with information of cancer incidence and mortality are more shocking than the low certainty estimates produced by the MAGICApp. Also, the figure is not of easy understanding. It does not translate in a clear message of what will happen to me if I do not reduce my red meat consumption.
- The meta-analysis from which estimates of risk reduction are taken has low to very low certainty in every case. Maybe the rather low level of certainty undermines the risk estimate impact on changing the consumption of red meat. What is the rationale behind choosing cancer despite of the low certainty evidence supporting the meta-analysis?
- I don't see clearly what is the rationale behind the assessments of the preferences on red meat consumption if the red meat target is the same for all the populations. How is this information going to be used in the analysis? Why is it important?
- The sample size of the subsample for the qualitative study is not stated. Moreover, which are the domains or the main issues in which the participants will be interviewed? If it is semi-structured, then the manuscript will require a brief description of the main questions or topics.
- I am wondering which would constitute a better outcome: i) the willingness to reduce red meat consumption or ii) the reduction of red meat consumption in the follow-up survey. In my opinion, the intervention is the initial survey and the result is the reduction of red meat consumption. Actually, we do not expect changes or at least there is not a pre and post examination after the direct-choice exercise.
- Does risk reductions from the meta-analysis consider differences in age, sex and smoking?
- Last, how the research team will address the differences between country, site and type of interview when doing the statistical analysis. My guess is that participants in face-to-face interviews will feel pushed towards a "positive" answer, while the ones taking the online survey might be free of this effect. Perhaps, a subsample of the participants could take both surveys to see if such an effect is present and the evaluations are consistent one with the other.

Minor comments

- Reference number 5 is not adequate for supporting the claim in the text. Please use a more relevant one.
- Page 3, Study population. When describing the exclusion criteria please delete the word "severe" cardiovascular disease.
- Sample size, instead of +/- 10, 0.1.

- What is the rationale for recruiting 96 in each site? From sample size calculation I would say that 96 participants in total are enough. Will the results be analysed by site or all-together? Anyway, I think the researchers choice is valid enough but some explanation would be appreciated. The definition of the main outcome and its rather high probability to occur with a quite large confidence interval might be behind this somehow small sample size for a multicenter study. On the other hand, please manifest at least some approximation to the total number of interviews for the qualitative analysis.
- Page 6, some typos, please revise.
- Revise definition of outcomes.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Partly

Are the datasets clearly presented in a useable and accessible format?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Nutrition, nutritional epidemiology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 06 May 2021

Claudia Valli, Universidad Aut3noma de Barcelona, Barcelona, Spain

Comment:

The study protocol presented by Valli et al. aims to evaluate the willingness to change their consumption of unprocessed and processed red meat in light of risk reductions in cancer incidence and mortality. The "mixed-methods" refers to the combination of quantitative and qualitative research methodologies. The qualitative research aims to study the factors behind the willingness or not to modify red meat consumption. In addition, they propose to evaluate the preferences of consumption of the participants; however, the relevance for this data is not clear in the actual version of the protocol.

Reply:

Participants' values and preferences regarding meat intake will inform us on their related

motives around their willingness or unwillingness to make any changes. We have improved the section of Outcomes in the protocol to better explain the relevance of such data.

Comment:

From a participant point of view, the tables with information of cancer incidence and mortality are more shocking than the low certainty estimates produced by the MAGICApp. Also, the figure is not of easy understanding. It does not translate in a clear message of what will happen to me if I do not reduce my red meat consumption.

Reply:

In the online survey, we will provide an explanatory video that will describe to participants how to read/interpret the data presented in the scenarios to facilitate their understanding. In addition, the online survey will provide an explicit text tailored to each scenario right below the image of the scenario. Below, we have provided the examples used with participants:

According to a recent high quality systematic review of the available scientific literature, for people like you who consume 3 servings a week of processed meat, the probability of developing cancer is 18.5%. This means that 185 people out of 1,000 may develop cancer and 815 may not. For people who consume 3 fewer servings per week of processed meat, the probability of developing cancer is 18.3%. This means that 183 people out of 1,000 may develop cancer and 817 may not. Overall, in a population of 1,000 people, 2 fewer people may develop cancer by consuming 3 fewer servings per week of processed meat compared to a population of 1,000 people who do not reduce their consumption.

In other words, a reduction of 3 servings per week of processed meat may reduce the probability of developing cancer and the certainty of this effect is very low. This means that the results we present come from studies with important limitations. Therefore, there is a possibility that a reduction in the consumption of processed meat may not result in a reduction in the risk of developing cancer.

Comment:

The meta-analysis from which estimates of risk reduction are taken has low to very low certainty in every case. Maybe the rather low level of certainty undermines the risk estimate impact on changing the consumption of red meat. What is the rationale behind choosing cancer despite of the low certainty evidence supporting the meta-analysis?

Reply:

We have decided to prioritize cancer incidence and cancer mortality because we believed these two general outcomes would be very familiar and of general interest to the public. Regarding the certainty of the evidence, for all outcomes the certainty was low- to very low because of observational design as well as issues with imprecision and/or risk of bias (Han 2019). Among the cancer outcomes, we have selected those that demonstrated the largest risk reduction effect. The certainty would be no higher had we selected cardiovascular outcomes, the other reasonable choice in terms of outcomes of most important to patients.

Comment:

I don't see clearly what is the rationale behind the assessments of the preferences on red meat consumption if the red meat target is the same for all the populations. How is this information going to be used in the analysis? Why is it important?

Reply:

Assessing the values and preferences from representative members of the population will inform us on the variability between the participants and between the countries, the objective of the study. We tailored our questions to each participant in each country depending on that average weekly intake. For instance, if participants consumed 6 servings of unprocessed red meat per week, we showed them the absolute risk reduction if they were to consume 6 fewer servings per week (stop completely), as well as 3 fewer servings in case they were unwilling to stop completely. Values and preferences from those who will actually use guideline recommendations, in this case -- members of the public -- are an important component of guideline development (Dedios 2017; Erickson 2017).

Comment:

The sample size of the subsample for the qualitative study is not stated. Moreover, which are the domains or the main issues in which the participants will be interviewed? If it is semi-structured, then the manuscript will require a brief description of the main questions or topics.

Reply:

For qualitative evaluations, it is unusual to predetermine the sample size. As stated, and referenced in the manuscript, the number of needed participants will be determined by data saturation method, that is, we will continue interviewing new participants until no additional concepts or themes emerge.

For the semi-structured interview, we have provided the draft of questionnaire as a supplementary material of the protocol. Please note, that being a semi-structured interview, questions might change and be adapted according to the conversation with the participant and to his/her responses given in the online survey.

Comment:

I am wondering which would constitute a better outcome: i) the willingness to reduce red meat consumption or ii) the reduction of red meat consumption in the follow-up survey. In my opinion, the intervention is the initial survey and the result is the reduction of red meat consumption. Actually, we do not expect changes or at least there is not a pre- and post-examination after the direct-choice exercise.

Reply:

Not totally clear to us what the reviewer means by "better". From some peoples' perspective a good outcome might be that respondents who say they are willing to reduce their meat consumption as a result of the information presented would actually do so. Our aim is to assess both outcomes, report the results and reflect on their implications.

To clarify, the outcome "willingness" will inform us about participants willingness to change only after being informed on the potential undesirable health outcomes, the first study of its kind to our knowledge. On the other hand, assessing participants' meat consumption in the follow-up will show us if participants have made any changes in their meat intake compared to what they reported to consume in the online survey and also compared to what they affirmed to be willing to do in the direct-choice exercise (3 months earlier). This will allow us to detect if participants have been made any changes.

Comment:

Do risk reductions from the meta-analysis consider differences in age, sex and smoking?

Reply:

Some of the studies included in the meta-analysis had limitations due to limited adjustment for potential confounders (Han 2019). That means that some studies took into account potential confounders such as age and sex and smoking but others did not. Lack of adequate adjustment for potential confounders (e.g., age, sex, smoking, socioeconomic status, exercise etc.) was one of the main sources of potential bias. Limitations in adjustment was an important reason for rating down the certainty of the evidence.

Comment:

Last, how the research team will address the differences between country, site and type of interview when doing the statistical analysis. My guess is that participants in face-to-face interviews will feel pushed towards a "positive" answer, while the ones taking the online survey might be free of this effect. Perhaps, a subsample of the participants could take both surveys to see if such an effect is present and the evaluations are consistent one with the other.

Reply:

Thanks for the suggestion to compare responses online versus face-to-face surveys. Due to the COVID-19 pandemic, all sites will conduct the study remotely through an online survey. The pilot study was conducted in-person since it was implemented before the start of the pandemic. Each country will run their own analysis separately resulting in four different publications.

Comment:

Reference number 5 is not adequate for supporting the claim in the text. Please use a more relevant one.

Reply:

We believe the said reference *Rabassa 2018* is appropriate since it refers to a recent study assessing the quality of nutrition guidelines with the use of the AGREE tool, an internationally recognized instrument used to evaluate the process of practice guideline development and the quality of reporting. We have added an additional reference *Blake 2018*, which is an analysis the appropriateness of methods used to synthesize evidence and grade recommendations in food-based dietary guidelines.

Comment:

Page 3, Study population. When describing the exclusion criteria please delete the word "severe" cardiovascular disease.

Reply:

Thank you, we have edited the text according to the reviewer's suggestion.

Comment:

Sample size, instead of +/- 10, 0.1.

Reply:

Thank you, we have edited the text by following the reviewers' suggestions.

Comment:

What is the rationale for recruiting 96 in each site? From sample size calculation I would say that 96 participants in total are enough. Will the results be analysed by site or all-together? Anyway, I think the researcher's choice is valid enough but some explanation would be

appreciated. The definition of the main outcome and its rather high probability to occur with a quite large confidence interval might be behind this somehow small sample size for a multicenter study. On the other hand, please manifest at least some approximation to the total number of interviews for the qualitative analysis.

Reply:

The more variable the response, the larger the sample size necessary to assess whether observed results are representative of the target population or simply reflects random variation. The sample size calculation does not take into account the multi-centred nature of the study. Since we are conducting the study in different sites/countries and considering the cultural differences, the responses of approximately 20 participants in each site/country (96 participants in total) will not give us representative results within each country. Therefore, we have used a more conservative approach by attempting to recruit at least 96 participants per site. As stated above, for qualitative evaluations, it is unusual to predetermine the sample size, rather we will sample participants until we reach data saturation, meaning that we will continue interviewing new participants until no additional concepts or themes emerge.

Comment:

Page 6, some typos, please revise.
Revise definition of outcomes.

Reply:

Thank you, we have made the corrections in the text.

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Competing Interests: No competing interests were disclosed.

Reviewer Report 21 October 2020

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Mary Dicklin

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Kevin Maki

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This paper describes a protocol for a study designed to investigate the potential impact on participants' thoughts and actions with regard to reducing or avoiding red and processed meat intake when educated about the potential effects on cancer incidence and cancer mortality. The study began in 2019 with expected completion early next year (2021).

1. The NutriRECS investigation has grouped unprocessed red meat and processed meat into a single category. It is not clear in the description of the questionnaires for this study whether these will be distinguished. Entry for the study is based on consumption of a minimum of 3 servings/week of either unprocessed red meat or processed meat. It appears that the investigators will only be asking the participants 1 question about their willingness to stop or reduce "consuming either unprocessed red meat or processed meat (whichever they are eating more of)." The "whichever they are eating more of" part of the question is confusing. I think a better approach would be to investigate their willingness to stop or reduce consumption of each of these types of meats in separate questions.
2. Does "four different sites in four countries" mean a total of 16 sites, which would be a total of 1536 participants, or 4 sites total, which would be 484 participants?
3. The participants' educational backgrounds are being analyzed, but do your questionnaires also ask the participants about their baseline knowledge of the potential relation between diet and cancer (including specific types of cancer)?
4. In the sample size section, you refer to the proportions as 0.44 (44%) and 0.5 (50%), but then indicate that a confidence interval of ± 10 is acceptable. I think this should be 0.1 for consistency.

5. Can you make the current meat consumption questionnaire available as supplemental material? Also, can you please provide more details about the question(s) that will be asked of the participants at the 3-month follow-up interview?
6. Can you provide data showing the average intake of unprocessed red meat vs. processed meat in Poland, instead of total unprocessed and processed meat that you have reported?
7. Table 1: In the 2nd bullet point, I think "other" should be "others are"; something appears to be missing in "a combination of subsequent is needed."
8. Table 2: Some of the statements about mortality seem obvious, and I am not sure how they will be interpreted by the participants, i.e., "You are dead and you do not feel any pain or breathlessness" and "You will leave everything that was important in short time span".
9. Figures 1 and 2: Although these figures will likely be understandable if described to the participants by the investigator, as stand-alone figures, the "2 fewer" and "9 fewer" may not be clear to them. I think the statement "Among a 1000 patients like you..." could be expanded to include a description of the 2 fewer (or 9 fewer) to make this clearer.
10. In a few places you refer to a "subsample" but it is not clear in the Study procedures section where you discuss asking additional questions about motives that this is the subsample.
11. Will you analyze the data separately according to countries/sites?
12. In the Quantitative analysis section you say that you will describe "willingness to reduce meat consumption in the face of undesirable cancer health risks" and "willingness to avoid meat consumption in the face of the undesirable cancer health risks." I think these should specify that the meat is red and processed meats.
13. I appreciate your desire to "not overburden participants with too much information, we prioritized two cancer outcomes" – cancer incidence and cancer mortality. However, I wonder in your interviews with the participants if you will be providing them with more information about the relation between meat intake and specific types of cancers, e.g., colorectal, breast, etc.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Partly

Are sufficient details of the methods provided to allow replication by others?

Partly

Are the datasets clearly presented in a useable and accessible format?

Not applicable

Competing Interests: Received research funding from the National Cattlemen's Beef Association/Beef Checkoff.

Reviewer Expertise: Design and conduct of clinical studies in human nutrition, metabolism, and chronic disease risk factor management.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 06 May 2021

Claudia Valli, Universidad Autónoma de Barcelona, Barcelona, Spain

Comment:

This paper describes a protocol for a study designed to investigate the potential impact on participants' thoughts and actions with regard to reducing or avoiding red and processed meat intake when educated about the potential effects on cancer incidence and cancer mortality. The study began in 2019 with expected completion early next year (2021). The NutriRECS investigation has grouped unprocessed red meat and processed meat into a single category. It is not clear in the description of the questionnaires for this study whether these will be distinguished. Entry for the study is based on consumption of a minimum of 3 servings/week of either unprocessed red meat or processed meat. It appears that the investigators will only be asking the participants 1 question about their willingness to stop or reduce "consuming either unprocessed red meat or processed meat (whichever they are eating more of)." The "whichever they are eating more of" part of the question is confusing. I think a better approach would be to investigate their willingness to stop or reduce consumption of each of these types of meats in separate questions.

Reply:

We would like to clarify that red meat and processed meat have not been considered as one category, instead they will be presented to participants as two different types of meat. Unprocessed red meat is defined as mammalian meat (e.g., beef, pork, lamb) and processed meat is defined as white or red meat preserved by smoking, curing, salting, or by the addition of preservatives (e.g., hot dogs, charcuterie, sausage, ham, and cold cut deli meats) (World Cancer Research Fund, 2007).

We will include participants consuming a minimum of 3 servings per week of either unprocessed red meat or processed meat. Each participant will be presented with one question to assess their unprocessed red meat intake and one question to assess their processed meat intake per week. That means we will determine unprocessed red meat intake and processed meat intake separately for all included participants. Based on the reported intake of unprocessed red meat and processed meat, participants will be presented with scenarios tailored to their consumption. After presenting them with the scenario, participants will be asked series of questions regarding their willingness to change their meat intake. First, participants will be presented with one question about their willingness to stop eating unprocessed red meat. If participants are unwilling to stop (≤ 4 of the Likert-scale), they will be presented with an additional question about their willingness to reduce. In case participants are willing to stop their unprocessed red meat intake (≥ 5 of the Likert-scale), the questions on reduction will be no longer relevant. Subsequently, for

those that consume processed meat, they will be presented with the scenario on processed red meat and they will be asked to answer a question about their willingness to stop eating processed meat. If participants are willing to stop processed meat, we will use the same logic for questions explained above.

That means that we will determine participants' willingness to stop eating unprocessed red meat and participants' willingness to stop eating processed meat separately. Additionally, for those participants who report being unwilling to stop, we will determine their willingness to reduce unprocessed meat and their willingness to reduce processed meat intake.

Comment:

Does "four different sites in four countries" mean a total of 16 sites, which would be a total of 1536 participants, or 4 sites total, which would be 484 participants?

Reply:

To clarify, the study is conducted in 3 different sites in total (one site in each country: Spain, Poland and Brazil). In 2019, we conducted a pilot study in Canada allowing us to obtain preliminary data to inform our sample size calculation. Based on the pilot data, we calculated a sample size of at least 96 participants per site.

Comment:

The participants' educational backgrounds are being analysed, but do your questionnaires also ask the participants about their baseline knowledge of the potential relation between diet and cancer (including specific types of cancer)?

Reply:

Although we inquired their consumption of meat related to health, we did not specifically ask participants questions about their knowledge regarding potential cancer risks associated with dietary behaviours. Instead, we asked participants if they had reduced their unprocessed red meat and processed meat intake in the past because of health reasons.

Comment:

In the sample size section, you refer to the proportions as 0.44 (44%) and 0.5 (50%), but then indicate that a confidence interval of ± 10 is acceptable. I think this should be 0.1 for consistency.

Reply:

Thank you, we have edited the text to correct this oversight.

Comment:

Can you make the current meat consumption questionnaire available as supplemental material? Also, can you please provide more details about the question(s) that will be asked of the participants at the 3-month follow-up interview?

Reply:

Due to the COVID-19 pandemic, we administered the questionnaire online and thus, we do not have the final version on paper in English. We have provided access through a link in the protocol to the Spanish version of the online survey. The only survey in English available is the one used in the pilot study in Canada and therefore, does not represent the final version used. For the 3-months follow up assessment we have provided the questionnaire as a supplementary material of the protocol.

Comment:

Can you provide data showing the average intake of unprocessed red meat vs. processed meat in Poland, instead of total unprocessed and processed meat that you have reported?

Reply:

The information on meat consumption in Poland was based on the data available at Statistics Poland <https://stat.gov.pl/en/topics/prices-trade/trade/domestic-deliveries-and-consumption-of-selected-consumer-goods-per-capita-in-2018,9,8.html>, which is the main Polish agency offering a national-wide data. Unfortunately, the available data did not report unprocessed red meat and processed meat separately.

Comment:

Table 1: In the 2nd bullet point, I think "other" should be "others are"; something appears to be missing in "a combination of subsequent is needed."

Reply:

Thank you, we have corrected Table 1 following the reviewers' suggestions.

Comment:

Table 2: Some of the statements about mortality seem obvious, and I am not sure how they will be interpreted by the participants, i.e., "You are dead and you do not feel any pain or breathlessness" and "You will leave everything that was important in short time span".

Reply:

The application of health states is commonly used in studies that elicit participants' health values and preference to help ensure a similar understanding of the presented health outcomes (Thomson 2002; Thomson 2009). Although, the cancer mortality health state seems to be obvious, the symptoms, treatments and consequences of dying of cancer are not the same as the ones for dying of other diseases, for example heart failure. Thus, we believe it is helpful to provide the descriptions of both outcomes separately.

Comment:

Figures 1 and 2: Although these figures will likely be understandable if described to the participants by the investigator, as stand-alone figures, the "2 fewer" and "9 fewer" may not be clear to them. I think the statement "Among 1000 patients like you..." could be expanded to include a description of the 2 fewer (or 9 fewer) to make this clearer.

Reply:

In the online survey, we are providing an explanatory video that will describe to participants how to read/interpret the data presented in the scenarios to facilitate their understanding. In addition, we will provide an explicit text tailored to each scenario. Below, we have provided examples:

According to a recent high quality systematic review of the available scientific literature, for people like you who consume 3 servings a week of processed meat, the probability of developing cancer is 18.5%. This means that 185 people out of 1,000 may develop cancer and 815 may not. For people who consume 3 fewer servings per week of processed meat, the probability of developing cancer is 18.3%. This means that 183 people out of 1,000 may develop cancer and 817 may not. Overall, in a population of 1,000 people, 2 fewer people may develop cancer by consuming 3 fewer servings per week of processed meat compared to a population of 1,000 people who do not reduce their consumption.

In other words, a reduction of 3 servings per week of processed meat may reduce the probability of developing cancer and the certainty of this effect is very low. This means that the results we present come from studies with important limitations. Therefore, there is a possibility that a reduction in the consumption of processed meat may not result in a reduction in the risk of developing cancer.

Comment:

In a few places you refer to a “subsample” but it is not clear in the Study procedures section where you discuss asking additional questions about motives that this is the subsample.

Reply:

We have addressed the reviewers’ comments in the protocol and removed the term subsample to avoid confusion.

Comment:

Will you analyze the data separately according to countries/sites?

Reply:

Each country will run their own analysis separately that will result in three different publications. Additionally, the pilot study methods and results will also be published in a separate publication.

Comment:

In the Quantitative analysis section, you say that you will describe “willingness to reduce meat consumption in the face of undesirable cancer health risks” and “willingness to avoid meat consumption in the face of the undesirable cancer health risks.” I think these should specify that the meat is red and processed meats.

Reply:

We have addressed and have now added “red and processed” meat in the protocol.

Comment:

I appreciate your desire to “not overburden participants with too much information, we prioritized two cancer outcomes” – cancer incidence and cancer mortality. However, I wonder in your interviews with the participants if you will be providing them with more information about the relation between meat intake and specific types of cancers, e.g., colorectal, breast, etc.

Reply:

We have decided to prioritize cancer incidence and cancer mortality because we believed these two general outcomes would be more familiar to the general population. Also, cancer mortality and cancer incidence were the two outcomes showing the largest absolute risk reduction. Being a cross-sectional study requiring participant’s involvement, we had to consider the length of the survey and time people would be willing to dedicate to the study.

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Competing Interests: No competing interests were disclosed.

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