PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Public perceptions of brain health: an international, online cross-sectional survey
AUTHORS	Budin Ljøsne , Isabelle; Mowinckel, Athanasia Monika; Friedman, Barbara; Ebmeier, Klaus; Drevon, Christian; Carver, Rebecca; Zsoldos, Enikő; Fredheim, Nanna; Sørensen, Øystein; Baaré, William Frans Christiaan; Madsen, Kathrine; Fjell, Anders; Kievit, Rogier; Ghisletta, Paolo; Bartrés-Faz, David; Nawijn, Laura; Solé-Padullés, Cristina; Walhovd, Kristine; Düzel, Sandra; Zasyekina, Larisa; Iulita, Maria Florencia; Ferretti, Maria Teresa

VERSION 1 – REVIEW

REVIEWER	Friedman, Daniela Univ S Carolina
REVIEW RETURNED	29-Oct-2021

GENERAL COMMENTS	The authors have conducted an important and timely study examining the public's perceptions about brain health. A large survey was conducted with over 27,000 individuals. This reviewer would like to see a deeper dive into the implications of this work and how such a large-scale survey initiative can potentially inform research interventions, practice, and policy. Specific comments follow: ABSTRACT: -Specify whether the results are significant. -Just because someone is highly educated, they may have limited health literacy and know less about the connection of risk factors and other diseases with brain health. INTRODUCTION -Authors present literature on previous surveys. Please describe more in depth qualitative work that has been conducted to examine diverse populations' perceptions and knowledge about brain health. How does this collection of work inform your current research? METHODS -Please define and give examples of "civil society organizations". This is mentioned in the conclusion but that is too late in the paper for this content. -Comparing country specific answers was not a goal of this current study. What do authors anticipate next steps could be looking across country, culture, etc.? This will be important for tailored interventions for example. RESULTS

	-One finding was that respondents in stable relationships were twice as likely to associate ADRD with the brain compared with those not in stable relationships. More is needed about this finding in the discussion/interpretation section. What does this mean for future work? Working with care partners, etc.? DISCUSSION -A stronger discussion of implications for future research and potentially intervention work is needed. While there is a brief section on implications for policy makers, there is much to be discussed regarding future research. I believe this will considerably strengthen this interesting paper.

REVIEWER	Bresjanac, Mara University of Ljubljana Faculty of Medicine, Institute of Pathophysiology, LNPR
REVIEW RETURNED	16-Nov-2021

GENERAL COMMENTS	The manuscript by Budin Ljøsne et al reports the outcome of an attempt to gather widest insight into public awareness of and interest in brain health by collecting responses to an online survey translated into 14 languages and distributed worldwide. The aim was to execute a first large-scale (i.e., global) investigation of public knowledge of factors influencing brain health, life periods critical to brain health, and awareness of disorders associated with the brain. It is a worthwhile effort, but it also has some significant shortcomings. Some of the shortcomings stem from the weaknesses of the research question and study design itself. At the minimum, the authors should acknowledge them in the list of limitations of their study and address them in the discussion. If they do so successfully, I would recommend publication of a revised manuscript. Starting from the title: “What is brain health?” this question had not been asked in the survey and the report does not present the respondents’ answers to the question, so the title, suggesting that the manuscript reports perceptions of the global public on what is brain health, is effectively misleading. Indeed, the introductory page to the survey already provided a definition of “brain health” (by the U.S. National Institute on Aging) to all candidate respondents. The second part of the title brings up another issue. The intended global nature of the survey could have been its real strength, but the final sample composition actually reveals the study weakness in several ways: - the sample is not representative of the public at large. The authors address this briefly but too tangentially. The sampling shortcoming is obvious not only from the demographic characteristics of the respondents (i.e. the predominance of highly educated older females), but even more so in some of the answers. For example, the percentage of self reported average or above average cognitive and mental health in the sample is high (93.9% and 86.8%, respectively). In addition, the reported perception of mental disorders having higher association with the brain than neurological conditions like Parkinson disease and stroke (Question 3, P55) is surprising and likely a consequence of the study recruitment strategy (e.g., reliance on the network of

stakeholders with a bias toward cognitive and psychological aspects of brain health). These factors clearly reveal a non-representative sample;
- the authors state that “Understanding the views of the general population on the drivers of brain health is crucial for public health and policy.” (P6, L53). Public health policies are designed and implemented at the state level, so in order to inform decision makers about the public views and needs, representative, high quality country-specific data analyses are required. A worldwide survey would be useful primarily if it enabled comparisons between representative samples for every included country, since that would allow policy makers in every state to make informed decisions about policy corrections needed (that goal is explicitly dismissed by the authors (P12, L2). In that sense, the study name promised more than it was designed to deliver - it presents information that cannot serve a useful purpose in any of the countries where the public responses to the survey had been collected. The authors should not have dismissed studies with smaller samples, done at the national level. Indeed, a recent publication of the findings of a strikingly similar online survey done in Slovenia in 2017 (Tomat et al., 2021, coauthored by this reviewer) could have been discussed (or at least mentioned) in the manuscript, as it offers an alternative way to gain insight into key questions regarding brain health for an actionable national plan and policy changes;
- the name of the Global Brain Health Survey is misleading in another way: as the data reveal the ¾ of the survey respondents reside in the UK, Netherlands and Norway, and less than 3% come from non-European countries. Would it not be less misleading to refer to the survey as European (after omitting the non-European data)? Indeed, the authors admit as much in the manuscript, where they explicate: “Thus, our results may provide insight into how Europeans view brain health.” (P25, L4). But in the next paragraph, they fail to acknowledge that the sample is not representative for Europe, either (see the first sentence of this bullet-point).

In sum, the authors have not addressed some major shortcomings among the study limitations. Indeed, the strength and limitations section of the manuscript does not deal with some of the major shortcomings.

In addition to the above major issues, the following points are worth mentioning:

- Statistical analysis: I am not a statistician, so I recommended that the manuscript be reviewed by one, but I would like to make a few comments.
- The data analysis included many tests and an indication of any correction for multiple testing would be welcome.
- The authors state (P18, L49): Men were less likely than women to associate the diseases with the brain, and this was particularly observed for AD/dementia (OR 0.46, 95% CI 0.36-0.57), ..., where the actual differences were: women 99,2% vs. men 98,2% (P21; Table 5). So, although the difference between men and women appears to be statistically significant (the estimated confidence interval for the odds ratio excludes 1), its practical importance is not convincing. The absolute difference in proportions is rather small. Because the issue here is an international survey response with only very indirect potential policy-making implications, rather

	than risk in the usual clinical sense, and because the sample is not representative of any specific population, in my view the difference should have been much larger to merit particular attention. - Finally, the authors had previously published study protocol (doi: 10.3389/fpubh.2020.00387) and might wish to address the comparison of the current report with the previously published protocol. - When dichotomising the answers from the 4-point Likert scale, factors deemed “moderately important” for brain health by the respondents were translated into “not important”. If the translation was adequate and “moderate” was the actual term used across all survey languages, it may have been interpreted by respondents as “average or tending toward the mean” (Merriam Webster), so classifying it as a negative response seems wrong; - When rating life periods critical for brain health, respondents ascribed relatively low importance to the prenatal period. The authors explain that this may be due to more than one way the survey question may have been interpreted. If so, this would be a clear weakness of the study. If there was a recognised ambiguity, the authors should have made an effort to eliminate it by reframing the question; - Figure titles are odd (e.g., P38 “Ratings of life periods to take care of one’s brain”) and should be renamed. - P39: A comment, why number of females and males differ from plot to plot is necessary. - Citation marks are not consistent (e.g., P7, L10, 14 and 23).

REVIEWER	Pope, Caitlin University of Kentucky, Health, Behavior & Society
REVIEW RETURNED	22-Nov-2021

GENERAL COMMENTS	Thank you for the opportunity to review the manuscript “What is brain health? Perceptions of 27,590 respondents to the Lifebrain Global Brain Health Survey”. While the paper is on an important public health topic and has notable strengths, there are additional points I feel need to be addressed after reviewing the manuscript and the provided supplemental documents. • I don’t find it particularly beneficial to have the number of participants in the title. While a large sample size is a benefit there are many other important factors that strengthen the rigor and reproducibility that could be highlighted. • I personally found the conciseness of the article summary to be more helpful than the results section of the abstract. Whereas all the information provided in the abstract is important, there is a lot of information presented that could be condensed to give a briefer overview of the paper. • The authors mention surveys from national samples on page 7. What countries do the majority of these surveys come from? Is there overlap with the countries that were sampled in this survey? • On page 7 in the second paragraph the authors make the statement “Due to the novelty of the concept of brain health, the

use of common definitions, measures, and instruments across studies was absent.” This thought feels unfinished. Are the authors trying to make the claim that this is still an issue or no longer an issue? More explanation/justification is needed.

- Nowhere in the paper do the authors mention missing data or how it was handled. Additionally, the authors marked N/A on this bullet point in the STROBE checklist. My thought with this being a global, anonymous survey was that there were people who started the survey and then stopped. Did the authors only use data from those who finished the survey, or did they use all available data points for the questions of interest? More detail on this was handled and how it could impact the findings would be helpful.

- Was there compensation for participating in the survey?

- The authors mention on page 11 that sensitivity analyses were conducted on the ordinal data. Given the large amount of supplementary information provided in the proof and the layout of the sensitivity analyses, it was difficult to interpret. What do the authors mean by the statement “note the similarities and differences are virtually identical”.

- It is unclear what the authors mean by the last sentence on page 11 starting with “The 10 binomial models per category were applied… rating of own mental health.”

- Given this is a global survey why was not reporting the findings stratified by the country not of priority to the authors (pg. 12, first sentence)? The fact that this survey is global seems like an important factor to its novelty and purpose.

- As shown in the results table and reported by the authors, the majority of the sample came from Europe. Given the small number of participants from countries outside of Europe, it doesn’t seem helpful to include them in the sample as this is likely, not generalizable and very dependent on the sampling strategy. Could also potentially introduce heterogeneity.

- The odds ratios and 95% confidence intervals on page 15 in the last paragraph that extends to page 16 make the text hard to follow. Given all this information is provided in table 3, the authors are encouraged to reduce redundancy in the text to improve readability.

- The authors mention on page 23 that views about brain health factors may differ in low- and middle-income countries. Were any low- and middle-income countries included in this study, and if not, should be stated more clearly.

- On page 24 the authors make the statement “Governments have given relatively little priority to the prevention of mental health disorders as compared to other diseases.” What do the authors mean by prevention, given mental health disorders such as schizophrenia and depression, to some extent, can likely not be prevented? Ideally, we would want governments to provide more resources for the reduction of preventable or modifiable mental health risk factors and stigma, early diagnosis/screening, and treatment.

REVIEWER	Wheeler, Fariya The University of Alabama at Birmingham, School of Nursing, University of Alabama at Birmingham, Birmingham, AL, United States.
REVIEW RETURNED	29-Nov-2021

GENERAL COMMENTS	This study examined descriptive and demographic correlates of a survey of perceptions of brain health among a large sample of Europeans. Strengths of this study include an important topic and very large sample and limitations include a not very diverse sample that is confounded by being largely highly educated. Another limitation is the very limited content of the survey, however that is outweighed by the brevity of the survey likely leading to the very large response rate and sample size. Suggestions for clarification and improvement are below. 1. Abstract: doesn't make it clear what aims, and analyses are. Makes it seem like this is only a descriptive study 2. Abstract: "Mental disorders such as schizophrenia (96%) and depression (95%) were more often associated with the brain than neurological disorders like stroke (88%) and Parkinson's disease (86%)." Should say "were more often considered to be"…or something like that since this is based on participant opinions. 3. Strengths and Limitations (1 page document): "Our respondents were probably more interested in, and knowledgeable about, brain health than the general population…" ..why?? Do you mean because the sample had a high education level, if so please be clear. 4. Intro: seems to be some good citations of other major studies examine this topic (e.g., Anderson et al, Glynn et al., Smith et al) 5. Intro: "Others have observed a lack of awareness of some mental disorders, such as schizophrenia11 and anxiety12 and limited interest, by respondents of such surveys, in adjusting their lifestyles to maintain a healthy brain13." This sentence is confusing and should be broken unto two to convey these different points. 6. Intro: purpose statement, as in abstract, doesn't have clear aims and does suggest this is a descriptive study only, when in fact associations with demos were examined. 7. Measures: not entirely clear how there are 28 brain health questions? I am adding up more than 28? 8. Measures: Also need a subheading before the demographic items 9. Abstract indicates interest was examined but this is not found in the measures section for the survey, or results 10. While this was conducted in Europe, a race/ethnicity question would have strengthened the study, as people of color even in Europe may have different responses/experiences. 11. Stats: A significant weakness of the stats is that multivariable models were not conducted. It would strengthen the paper to do so, as many of the demographic variables may be correlated. It would be helpful if after conducting the bivariate analyses between each demo variable and each brain health outcome, to then conduct multivariable models for each brain health outcome that includes any significant demo correlates. That would shed light on which are the driving factors and potential mediators/mechanisms. The results section is already quite long, so these could be posthoc analyses, with simply a sentence for each outcome. "e.g., When education and age were in the model, XXX remained a

	significant predictor of XX, while XX was no longer significant." Again the results are already quite long, but if this could be done in a way that didn't add much additional text, it would be interesting. If this is added, please add corresponding information to Discussion. 12. Discussion: "Disorders that are not defined as brain diseases but have an impact on the brain such as hypertension, diabetes and arthritis were associated with the brain only to a small extent." Fix wording, were "perceived to be associated with…" 13. Discussion: "Physical health was rated as highly important in our study in contrast to what previous surveys found….In our questionnaire, we did not provide any example of what physical health entails, so we do not know exactly how our respondents interpreted the question." Need to tie that into contrasting finding from prior paragraph, where hypertension for example was only believed to be important in a smaller subset of people.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Daniela Friedman, Univ S Carolina
Comments to the Author:

1. The authors have conducted an important and timely study examining the public's perceptions about brain health. A large survey was conducted with over 27,000 individuals. This reviewer would like to see a deeper dive into the implications of this work and how such a large-scale survey initiative can potentially inform research interventions, practice, and policy. Specific comments follow:

Many thanks for your positive assessment.

2. ABSTRACT:
a) -Specify whether the results are significant.
We have highlighted any significant results in the abstract. Reported results are significant at the 1% level of probability, as indicated in the manuscript.
b) -Just because someone is highly educated, they may have limited health literacy and know less about the connection of risk factors and other diseases with brain health.
We did not mean to imply a causal relationship here: high educational levels tend to be proxy for IQ, income, social class, and general health, including mortality, as well as taking part in research such as this. As a hypothesis, one can propose that increased health literacy may be associated, too. However, as no representative general population data are available, our data cannot assess this point. We have revised the abstract and this statement is now removed.
3. INTRODUCTION

a) -Authors present literature on previous surveys. Please describe more in-depth qualitative work that has been conducted to examine diverse populations' perceptions and knowledge about brain health. How does this collection of work inform your current research?

Response
We have revised the second paragraph in the introduction to include references to qualitative European studies. We primarily focused on including studies investigating perceptions of cognitive and mental health. We explain that the studies reported varying awareness of actions beneficial for

the brain and emphasized the importance of providing people with evidence-based and trustworthy information to encourage the adoption of brain-friendly behaviours.

4. METHODS
a) -Please define and give examples of "civil society organizations". This is mentioned in the conclusion but that is too late in the paper for this content.

Response
By civil society organization, we mean for instance patient organizations and charities. This is now described in the PPI and sampling sections.

b) -Comparing country specific answers was not a goal of this current study. What do authors anticipate next steps could be looking across country, culture, etc.? This will be important for tailored interventions for example.

Response
We agree that it would be interesting to compare answers between countries, however, the sample sizes vary largely among countries as well as the recruitment strategies and pathways. This makes it difficult to arrive at meaningful comparisons between countries. However, we think that an interesting next step might be to investigate whether results differ between the three countries with most responses (United Kingdom, the Netherlands, Norway), and how any difference may influence brain health promotion at national level. This is now proposed in the Conclusion as a potential activity for future research.

5. RESULTS
a) -One finding was that respondents in stable relationships were twice as likely to associate ADRD with the brain compared with those not in stable relationships. More is needed about this finding in the discussion/interpretation section. What does this mean for future work? Working with care partners, etc.?

Response
In our survey, we observed that awareness of Alzheimer’s disease was higher among our respondents living in stable relationships. In the “Implications for policymakers” section, we now discuss this finding in light of previous research showing a higher risk of dementia among unmarried as compared with married people living in stable relationships. We suggest that targeted brain health information toward single people may be needed.
6. DISCUSSION
-A stronger discussion of implications for future research and potentially intervention work is needed. While there is a brief section on implications for policy makers, there is much to be discussed regarding future research. I believe this will considerably strengthen this interesting paper.

Response
We now discuss potential intervention work in more detail in the “Implications for policymakers” section. We mention that governments should prioritize reduction of preventable or modifiable mental health risk factors, for instance by identifying individuals in early stages of disease or creating social environments that promote psychological wellbeing. We refer to a recent Lancet paper providing recommendations for the prevention of mental health disorders.
We also discuss implications for future research in more details in the conclusion.

Reviewer: 2
Dr. Mara Bresjanac, University of Ljubljana Faculty of Medicine Comments to the Author:

The manuscript by Budin Ljøsne et al reports the outcome of an attempt to gather widest insight into public awareness of and interest in brain health by collecting responses to an online survey translated into 14 languages and distributed worldwide. The aim was to execute a first large-scale (i.e., global) investigation of public knowledge of factors influencing brain health, life periods critical to brain health, and awareness of disorders associated with the brain.

It is a worthwhile effort, but it also has some significant shortcomings. Some of the shortcomings stem from the weaknesses of the research question and study design itself. At the minimum, the authors should acknowledge them in the list of limitations of their study and address them in the discussion. If they do so successfully, I would recommend publication of a revised manuscript.

Response
Thank you for your thoughtful review of the manuscript.

1. Starting from the title: "What is brain health?" this question had not been asked in the survey and the report does not present the respondents' answers to the question, so the title, suggesting that the manuscript reports perceptions of the global public on what is brain health, is effectively misleading. Indeed, the introductory page to the survey already provided a definition of "brain health" (by the U.S. National Institute on Aging) to all candidate respondents.

Response
We agree with this comment. This study investigated people's views on brain health (factors influencing brain health, life periods to take care of the brain, and diseases associated with the brain). The title has now been modified to reflect this and address the requirements of the editor. We propose the following title: "Public perceptions of brain health: an international, online cross-sectional survey".

2. The second part of the title brings up another issue. The intended global nature of the survey could have been its real strength, but the final sample composition actually reveals the study weakness in several ways:

- the sample is not representative of the public at large. The authors address this briefly but too tangentially. The sampling shortcoming is obvious not only from the demographic characteristics of the respondents (i.e. the predominance of highly educated older females), but even more so in some of the answers. For example, the percentage of self reported average or above average cognitive and mental health in the sample is high (93.9% and 86.8%, respectively). In addition, the reported perception of mental disorders having higher association with the brain than neurological conditions like Parkinson disease and stroke (Question 3, P55) is surprising and likely a consequence of the study recruitment strategy (e.g., reliance on the network of stakeholders with a bias toward cognitive and psychological aspects of brain health). These factors clearly reveal a non-representative sample;

Response
We agree that our sample is not representative of the general population. We revised the Limitations section of the paper to clearly state this. We explain that our sample was highly educated, mostly female, and self-reported good cognitive and mental health. We also explain in the second paragraph of the Discussion section that since we partly relied on our network of stakeholders working in fields of relevance for brain health to recruit survey respondents, it is likely that our sample was more interested in cognitive and psychological aspects of brain health than the general population.
3. - the authors state that "Understanding the views of the general population on the drivers of brain health is crucial for public health and policy." (P6, L53). Public health policies are designed and implemented at the state level, so in order to inform decision makers about the public views and needs, representative, high quality country-specific data analyses are required. A worldwide survey

would be useful primarily if it enabled comparisons between representative samples for every included country, since that would allow policy makers in every state to make informed decisions about policy corrections needed (that goal is explicitly dismissed by the authors (P12, L2). In that sense, the study name promised more than it was designed to deliver - it presents information that cannot serve a useful purpose in any of the countries where the public responses to the survey had been collected. The authors should not have dismissed studies with smaller samples, done at the national level. Indeed, a recent publication of the findings of a strikingly similar online survey done in Slovenia in 2017 (Tomat et al., 2021, coauthored by this reviewer) could have been discussed (or at least mentioned) in the manuscript, as it offers an alternative way to gain insight into key questions regarding brain health for an actionable national plan and policy changes;

Response
We agree with the reviewer's point and have removed this sentence. We also conducted a new search to find recent national studies that may be of relevance and included reference to the Slovenian study by Tomat et al. in the introduction. We mention that the study identified lack of time and information as potential hindrance to the purposeful adoption of behaviours beneficial for the brain.

4. - the name of the Global Brain Health Survey is misleading in another way: as the data reveal the ¾ of the survey respondents reside in the UK, Netherlands and Norway, and less than 3% come from non-European countries. Would it not be less misleading to refer to the survey as European (after omitting the non-European data)? Indeed, the authors admit as much in the manuscript, where they explicate: "Thus, our results may provide insight into how Europeans view brain health." (P25, L4). But in the next paragraph, they fail to acknowledge that the sample is not representative for Europe, either (see the first sentence of this bullet-point).
In sum, the authors have not addressed some major shortcomings among the study limitations. Indeed, the strength and limitations section of the manuscript does not deal with some of the major shortcomings.

Response
We removed the first statement mentioned by the reviewer and revised the next paragraph to explain better that our sample is not representative of the general population.
When we developed the survey, we did not have resources to use the services of market research companies and recruit a representative sample of participants. We decided that it would be interesting to collect responses from as many people as possible, irrespective of their geographical location. Thus, we made the survey freely available online to anyone above the age of 18 years and used our staff resources to translate the survey into 14 languages. We relied on help from our various stakeholders primarily located in Europe to disseminate the survey and assumed that it would also be shared by stakeholders outside of Europe, e.g., through social media. As an invitation to anyone interested in the topic to take the survey, we featured the survey as "global," as described in our study protocol paper (Budin-Ljøsne and al, 2020).
We collected 515 respondents outside geographical Europe. The 515 respondents represent 1.8% of the total number of respondents and primarily were from the USA (n=165), Turkey (n=139), Australia (n=33), and South Africa (n=28).
We discussed the reviewer's suggestion to omit responses from non-Europeans and reframe the survey as European. We believe that revising our text to better explain our strategy, and emphasize that our sample is not representative of the general population, may be preferable for several reasons:

- Excluding the non-European respondents from the sample will not make our sample more representative. Recruitment strategies differed between countries (via diverse networks), also in Europe, and we do not have a full overview of how respondents were recruited in each country since the survey was freely available online. Stakeholders may have shared our survey with specific groups without our knowledge.

- Excluding the non-European respondents from the sample will likely not make our sample more “European”. Although we have responses from several European countries, we do not have responses from all countries in Europe and the number of responses vary enormously from one country to another. Some countries such as the Netherlands and Norway are overrepresented in our sample with several thousand responses, whereas many large countries are underrepresented (e.g., France with less than a hundred responses). In some countries, we have less than 10 responses. We could in theory try to weight responses between countries, but this would inflate the importance of the smallest countries in the sample.
- We collected more responses in non-European countries such as the USA (n=165) and Turkey (n=139) than in European countries such as Ireland (n=40) or Poland (n=7). Excluding responses from the non-European countries may therefore be seen as arbitrary. The exclusion of upper-middle-income countries is often an issue in surveys. We think that excluding responses from Turkey and keeping those from European countries (with only a few responses) would be contrary to the principle of diversity.
- Although 515 non-European respondents are not much compared to the European sample, 515 people in absolute terms is still informative.
- We find it ethically challenging to exclude respondents that have given us some of their time to answer the survey.

Thus, we suggest keeping the whole sample as it is. We revised the Methods/Sampling section to describe better our recruitment strategy. We also explain in more detail in the Limitations section that our sample is not representative of the general population.

5. In addition to the above major issues, the following points are worth mentioning:

- Statistical analysis: I am not a statistician, so I recommended that the manuscript be reviewed by one, but I would like to make a few comments. The data analysis included many tests and an indication of any correction for multiple testing would be welcome.

Response

The statistical analysis was determined by several aspects that differ from smaller case-control or cohort studies:

- The very large sample size with high statistical power makes it very likely that group differences apparent on inspection of numbers will be statistically significant (e.g., using chi-square tests).
- This means that many statistically significant results may not be of practical importance, because of small effect sizes (see this Reviewer’s 6th point).
- So rather than using methods of controlling for multiple comparisons, we decided to report results only significant at the 1% level of probability (see Supplementary materials) and make a distinction between practically unimportant and probably important effects, by relying on appropriate effect size indices.

6. - The authors state (P18, L49): Men were less likely than women to associate the diseases with the brain, and this was particularly observed for AD/dementia (OR 0.46, 95% CI 0.36-0.57), ..., where the actual differences were: women 99,2% vs. men 98,2% (P21; Table 5). So, although the difference between men and women appears to be statistically significant (the estimated confidence interval for the odds ratio excludes 1), its practical importance is not convincing. The absolute difference in proportions is rather small. Because the issue here is an international survey response with only very indirect potential policy-making implications, rather than risk in the usual clinical sense, and because the sample is not representative of any specific population, in my view the difference should have been much larger to merit particular attention.

Response
We agree with the reviewer and this statement has been removed.

7. - Finally, the authors had previously published study protocol (doi: 10.3389/fpubh.2020.00387) and might wish to address the comparison of the current report with the previously published protocol.

Response
This paper is the second in a number to emerge from the study, of which we previously have published the protocol's development (doi: 10.3389/fpubh.2020.00387). A close comparison would require the introduction of many extraneous issues mentioned in the previous paper, which would not be manageable in the given format.

8. - When dichotomising the answers from the 4-point Likert scale, factors deemed "moderately important" for brain health by the respondents were translated into "not important". If the translation was adequate and "moderate" was the actual term used across all survey languages, it may have been interpreted by respondents as "average or tending toward the mean" (Merriam Webster), so classifying it as a negative response seems wrong.

Response
A 4-point Likert scale was used in the second question: "In your opinion, at what stages in life is it important to look after one's brain?" The Likert comprised the following items: very important, important, moderately important, not important. We agree with the reviewer that it is difficult to assess what the respondents meant when selecting "moderately important." We wanted to make a distinction between what the respondents saw as important vs. what they saw as less important and we assumed that when they selected "moderately important," they meant less than important. To make the distinction clearer, we now explain in the Methods/statistical analysis section that the responses of "very important" and "important" were classified as an indication that respondents considered the life period as important to take care of the brain, indicating a positive association between the question and response category, whereas responses of the remaining ("moderately important," and "not important") were classified as an indication that the respondents considered the life period as not so important or not important.

9. - When rating life periods critical for brain health, respondents ascribed relatively low importance to the prenatal period. The authors explain that this may be due to more than one way the survey question may have been interpreted. If so, this would be a clear weakness of the study. If there was a recognised ambiguity, the authors should have made an effort to eliminate it by reframing the question;

Response
The respondents were asked to rate 6 life periods of which "in the womb (before birth)" was one. By this, we meant taking care of the brain of the unborn child and we expect that most respondents understood this life period in the same way. After the survey was launched and available online, we discussed that there is a slight risk that the respondents may have interpreted the life period "in the womb (before birth)" as being one where the pregnant mother takes care of her own brain. Reframing the question after the survey was launched and data collection had started, was not possible. We have no way of knowing whether some respondents interpreted this life period as focusing on the mother's brain. We now explain in the first paragraph of the Discussion section that this item in the questionnaire aimed to describe the life period during which one can take care of the unborn child's brain during pregnancy. There is a slight risk that our respondents interpreted this life period as taking care of the mother's brain during pregnancy. However, irrespective of how this question was interpreted, taking care of the mother' brain and the unborn child's brain during pregnancy, is important and requires attention.

10. - Figure titles are odd (e.g., P38 “Ratings of life periods to take care of one’s brain”) and should be renamed.

Response
We have renamed the figures to make their meaning clearer.

11. - P39: A comment, why number of females and males differ from plot to plot is necessary.

Response
Numbers of females and males differ from plot to plot due to different response rates, i. e. the denominator changed between questions. This is now explained in the figure legend.

12. - Citation marks are not consistent (e.g., P7, L10, 14 and 23).

Response
We apologize. This has been fixed now.

Reviewer: 3
Dr. Caitlin Pope, University of Kentucky
Comments to the Author:
Thank you for the opportunity to review the manuscript “What is brain health? Perceptions of 27,590 respondents to the Lifebrain Global Brain Health Survey”. While the paper is on an important public health topic and has notable strengths, there are additional points I feel need to be addressed after reviewing the manuscript and the provided supplemental documents.

Many thanks for your positive assessment.

1. I don’t find it particularly beneficial to have the number of participants in the title. While a large sample size is a benefit there are many other important factors that strengthen the rigor and reproducibility that could be highlighted.

Response

We agree. The title has now been modified to “Public perceptions of brain health: an international, online cross-sectional survey” and the number of respondents is removed.

2. I personally found the conciseness of the article summary to be more helpful than the results section of the abstract. Whereas all the information provided in the abstract is important, there is a lot of information presented that could be condensed to give a briefer overview of the paper.

Response
We have condensed the abstract, as suggested.

3. The authors mention surveys from national samples on page 7. What countries do the majority of these surveys come from? Is there overlap with the countries that were sampled in this survey?

Response
Most of the surveys we refer to were conducted in European countries such as Ireland, the Netherlands, the United Kingdom and France. We have updated the text in the second paragraph of the Introduction to give information about the surveys’ country of origin. Our survey had respondents

in these countries so there is some overlap with other national surveys although they had a slightly different focus (e.g., cognitive health). This is now discussed in the introduction.

4. On page 7 in the second paragraph the authors make the statement “Due to the novelty of the concept of brain health, the use of common definitions, measures, and instruments across studies was absent.” This thought feels unfinished. Are the authors trying to make the claim that this is still an issue or no longer an issue? More explanation/justification is needed.

Response
The studies we have found provide useful insights into public perceptions of some aspects of brain health. However, we observed that the studies often focused on one specific aspect of brain health such as cognitive health or a mental illness, rather than explored views on brain health (encompassing both cognitive and mental health) although some studies discussed implications of their findings for brain health. Most previous studies also used different measures and instruments and did not share a common definition of brain health, making any comparison of results between studies challenging. For instance, when exploring perceptions of cognitive health, the studies focused on expectations regarding cognitive skills in aging, attitudes on early diagnostic testing for Alzheimer`s disease, or public perceptions about risk and protective factors related to dementia. The studies also used different measures and instruments (for e.g., the list/formulation of protective and risk factors investigated, age-groups/populations targeted) and did not share a common definition of brain health, making any comparison of results between studies challenging. In contrast, our study tried to operationalize the term “brain health” to cover most aspects of cognitive and mental health.

The sentence in the second paragraph is now updated to make our point clearer.

5. Nowhere in the paper do the authors mention missing data or how it was handled. Additionally, the authors marked N/A on this bullet point in the STROBE checklist. My thought with this being a global, anonymous survey was that there were people who started the survey and then stopped. Did the authors only use data from those who finished the survey, or did they use all available data points for the questions of interest? More detail on this was handled and how it could impact the findings would be helpful.

Response
In the Methods section, we now explain that anyone taking the survey had to complete at least five multiple-choice questions and the 12 demographic questions to be able to submit the questionnaire. In the Statistical analysis section, we added some text to explain that only responses from submitted questionnaires were used in the analysis. In the Results section, we provide a count of the number of respondents who responded to each of the 3 multiple-choice questions. 99.9% of respondents (n=27,552) completed the first question, 99.8% (n=27,536) completed the second question and 99.8% (n=27,530) completed the third question.

6. Was there compensation for participating in the survey?
Response
No financial compensation was provided to respondents taking the survey. This is now indicated in the Methods section. We accept that this may have skewed the respondents away from those motivated by monetary reward.

7. The authors mention on page 11 that sensitivity analyses were conducted on the ordinal data. Given the large amount of supplementary information provided in the proof and the layout of the sensitivity analyses, it was difficult to interpret. What do the authors mean by the statement “note the similarities and differences are virtually identical”.

Response
We have updated Supplementary Material 1 (Comparison of binary vs. continuous outcome models) after we discovered an error in the coding. We updated the coding and found that very few models now diverge between the binary and continuous models. By divergence we mean that results differed in terms of ‘significance’ between binary vs. continuous outcome models. This is now explained in the Statistical analysis section.

8. It is unclear what the authors mean by the last sentence on page 11 starting with “The 10 binomial models per category were applied… rating of own mental health.”

Response
The sentence reads: “The 10 binomial models per category were applied with a single demographic variable as predictor, one for each of the demographic variables of age, gender, education, relationship status, experience or education in health care, experience with illness, experience of being a caregiver for someone with a brain disease, rating of own cognitive health and rating of own mental health.” We re-phrased this to: “For each category, separate predictive models for (1) age, (2) gender, (3) education, (4) relationship status, (5) experience or education in health care, (6) experience with illness, (7) experience of being a caregiver for someone with a brain disease, (8) rating of own cognitive health, and (9) rating of own mental health as predictors were computed,” to make it more intelligible.

9. Given this is a global survey why was not reporting the findings stratified by the country not of priority to the authors (pg. 12, first sentence)? The fact that this survey is global seems like an important factor to its novelty and purpose.

Response
We agree with the reviewer that it would be interesting to compare response patterns between countries. However, the sample sizes varied largely between countries; whereas we had many respondents in some countries, such as the United Kingdom, we had only a few in other European countries, making any comparison challenging. Even if we were to compare results between the three countries where we collected most responses (United Kingdom, Netherlands, and Norway), the recruitment strategies varied between countries. Since our survey was freely available online it may also have been shared with specific groups in some countries without our knowledge. Thus, we do not have sufficient information about the characteristics of the samples in each country to be able to make some meaningful comparisons. This is now explained in the second paragraph in the Results section starting with “Table 1 provides an overview…”.

10. As shown in the results table and reported by the authors, the majority of the sample came from Europe. Given the small number of participants from countries outside of Europe, it doesn’t seem helpful to include them in the sample as this is likely, not generalizable and very dependent on the sampling strategy. Could also potentially introduce heterogeneity.

Response
As explained earlier (See comment to reviewer 2, Q4), when we developed the survey, we did not have resources to use the services of market research companies and recruit a representative sample of participants. We decided that it would be interesting to collect responses from as many people as possible, irrespective of their geographical location. Thus, we made the survey freely available online to anyone above the age of 18 years and used our staff resources to translate the survey into 14 languages. We relied on help from various stakeholders primarily located in Europe to disseminate the survey and assumed it would also be shared by stakeholders outside of Europe, e.g., through social media. As an invitation to anyone interested in the topic to take the survey, we featured the survey as “global,” as described in our study protocol paper (Budin-Ljøsne and al, 2020).

We collected 515 respondents outside of geographical Europe. The 515 respondents represent 1.8% of the total number of respondents and primarily were from the USA (n=165), Turkey (n=139), Australia (n=33), and South Africa (n=28).

We discussed the reviewer's suggestion to omit responses from non-Europeans. We think that revising our text to explain better our strategy, and emphasize that our sample is not representative of the general population, may be preferable for several reasons:

- Excluding the non-European respondents from the sample will not make our sample more representative. Recruitment strategies differed between countries (via diverse networks), also in Europe, and we do not have a full overview of how respondents were recruited in each country because the survey was freely available online. Stakeholders may have shared our survey with specific groups without our knowledge.
- Excluding the non-European respondents from the sample will probably not make our sample more "European." Although we have responses from several European countries, we do not have responses from all countries in Europe and the number of responses vary enormously from one country to another. Some countries such as the Netherlands and Norway are overrepresented in our sample with several thousand responses, whereas many large countries are underrepresented (e.g., France with less than a hundred responses). In some countries, we have less than 10 responses. We could in theory try to weight responses between countries, but this would inflate the importance of the smallest countries in the sample.
- We collected more responses in non-European countries such as the USA (n=165) and Turkey (n=139) than in European countries such as Ireland (n=40) or Poland (n=7). Thus, excluding responses from the non-European countries may be seen as arbitrary. The exclusion of upper-middle-income countries is often an issue in surveys. We think that excluding responses from Turkey and keeping those from European countries (with only a few responses) would be contrary to the principle of diversity.
- Although 515 non-European respondents are not much compared to the European sample, 515 people in absolute terms is still informative.
- We find it ethically challenging to exclude respondents that have given us some of their time to answer the survey.

Thus, we suggest keeping the whole sample as it is. We revised the Methods/Sampling section to describe better our recruitment strategy. We also explain in more detail in the Limitations section that our sample is not representative of the general population.

11. The odds ratios and 95% confidence intervals on page 15 in the last paragraph that extends to page 16 make the text hard to follow. Given all this information is provided in table 3, the authors are encouraged to reduce redundancy in the text to improve readability.

Response
The text in this paragraph has been simplified.

12. The authors mention on page 23 that views about brain health factors may differ in low- and middle-income countries. Were any low- and middle-income countries included in this study, and if not, should be stated more clearly.

Response
Most of our participants lived in high-income countries. We had 139 responses from Turkey, which is ranked as an upper-middle income country by the World Bank. We had very few respondents from low-income countries (usually 1-3 responses by country). This is now explained in more detail in the second paragraph of the "Relevance to previous research" section in the Discussion.

13. On page 24 the authors make the statement "Governments have given relatively little priority to the prevention of mental health disorders as compared to other diseases." What do the authors mean

by prevention, given mental health disorders such as schizophrenia and depression, to some extent, can likely not be prevented? Ideally, we would want governments to provide more resources for the reduction of preventable or modifiable mental health risk factors and stigma, early diagnosis/screening, and treatment.

Response
Yes, we agree. We have revised this statement to explain that governments should give more attention to the reduction of preventable or modifiable mental health risk factors, for instance by identifying individuals in early stages of disease or creating social environments promoting psychological wellbeing. We refer to a recent Lancet paper providing recommendations for the prevention of mental health disorders.

Reviewer: 4
Dr. Fariya Wheeler, The University of Alabama at Birmingham Comments to the Author:
This study examined descriptive and demographic correlates of a survey of perceptions of brain health among a large sample of Europeans. Strengths of this study include an important topic and very large sample and limitations include a not very diverse sample that is confounded by being largely highly educated. Another limitation is the very limited content of the survey, however that is outweighed by the brevity of the survey likely leading to the very large response rate and sample size. Suggestions for clarification and improvement are below.

Thank you for your thoughtful review of the manuscript.

1. Abstract: doesn’t make it clear what aims, and analyses are. Makes it seem like this is only a descriptive study

Response
We have clarified these aspects in the abstract. Although the study describes the sample examined, we have now included some analyses controlling effects for commonly measured confounding variables (see below).

2. Abstract: “Mental disorders such as schizophrenia (96%) and depression (95%) were more often associated with the brain than neurological disorders like stroke (88%) and Parkinson’s disease (86%).” Should say “were more often considered to be”…or something like that since this is based on participant opinions.

Response
The text has been updated as suggested by the reviewer.

3. Strengths and Limitations (1 page document): “Our respondents were probably more interested in, and knowledgeable about, brain health than the general population…” ..why??
Do you mean because the sample had a high education level, if so please be clear.

Response
This statement was circular in a way: as they took part in a brain health questionnaire, by definition, they were more interested and (perhaps) more knowledgeable than those who did not participate. We know they had high levels of education, and education level tends to be a proxy for IQ, income, social class, and general health, including mortality (see Reviewer 1.2.b.). We have revised the “Strengths and limitations” section to comply with requirements from the editor and this sentence has been removed.

4. Intro: seems to be some good citations of other major studies examine this topic (e.g., Anderson et al, Glynn et al., Smith et al)

Response
In addition to these references, we have also revised the introduction to include reference to qualitative studies conducted in Europe as requested by reviewer 1.

5. Intro: "Others have observed a lack of awareness of some mental disorders, such as schizophrenia11 and anxiety12 and limited interest, by respondents of such surveys, in adjusting their lifestyles to maintain a healthy brain13." This sentence is confusing and should be broken unto two to convey these different points.

Response
This paragraph has been revised and the sentence has been modified as suggested.

6. Intro: purpose statement, as in abstract, doesn't have clear aims and does suggest this is a descriptive study only, when in fact associations with demos were examined.

Response
Although the study describes the sample examined, we have now included some analyses controlling effects for commonly measured confounding variables (see below). This is now expressed in the abstract.

7. Measures: not entirely clear how there are 28 brain health questions? I am adding up more than 28?

Response
The full questionnaire included 28 questions of which 16 were multiple-choice and 12 were demographic questions. We focus on results from 3 of the 16 multiple-choice questions and use information provided in the 12 demographic questions. This is now explained in the Methods section under Measures.

8. Measures: Also need a subheading before the demographic items
Response
A subheading has now been provided.

9. Abstract indicates interest was examined but this is not found in the measures section for the survey, or results

Response
We agree. Interest was explored in some questions of the survey, but these are not used in this paper. The abstract has been updated to correct for this.

10. While this was conducted in Europe, a race/ethnicity question would have strengthened the study, as people of color even in Europe may have different responses/experiences.

Response
To our knowledge, it is not common to collect ethnicity data in most European countries, possibly except for the United Kingdom. This is mainly due to the research institutions' interpretation of European anti-discrimination laws. In some countries, such as France, collecting ethnicity data is in

principle prohibited by law, although derogations may apply (Loi No 78-17 du 6 Janvier 1978 Informatique et Libertés). Thus, we decided not to collect race/ethnicity data although we agree with the reviewer that such data would have strengthened the paper. We discuss this in the second paragraph of the Conclusion and refer to a report from the Directorate-General for Justice and Consumers of the European Commission that encourages member states to establish methods and best practices for collection of data on racial and ethnic origin. (https://ec.europa.eu/info/sites/default/files/data_collection_in_the_field_of_ethnicity.pdf).

1. Stats: A significant weakness of the stats is that multivariable models were not conducted. It would strengthen the paper to do so, as many of the demographic variables may be correlated. It would be helpful if after conducting the bivariate analyses between each demo variable and each brain health outcome, to then conduct multivariable models for each brain health outcome that includes any significant demo correlates. That would shed light on which are the driving factors and potential mediators/mechanisms. The results section is already quite long, so these could be posthoc analyses, with simply a sentence for each outcome. "e.g., When education and age were in the model, XXX remained a significant predictor of XX, while XX was no longer significant." Again the results are already quite long, but if this could be done in a way that didn't add much additional text, it would be interesting. If this is added, please add corresponding information to Discussion.

Response
We agree with the reviewer's compromise suggestion to conduct multivariable models on selected variables. We selected one finding of interest for each question and conducted multivariable models on each of them to check for consistency.

For question 1 (factors influencing brain health), we found that "Men were less likely than women to consider factors such as substance use, sleeping habits and diet as having strong or very strong influence on the brain. In contrast, men were more prone to rate profession and education as important." After controlling for educational level and age we found that these effects remained significant.

For question 2 (life periods important for the brain), we found that "men were less likely to consider life periods such as the middle age and old age as important as compared with women." After controlling for educational level and age we found that these effects remained significant.

For question 3 (diseases associated with the brain), we found that "respondents in a stable relationship were more likely to associate Alzheimer's disease with the brain as compared with respondents not in a stable relationship." We controlled for educational level and age and found that this association was no longer significant.

The implications of these results have been discussed in the Discussion section.

12. Discussion: "Disorders that are not defined as brain diseases but have an impact on the brain such as hypertension, diabetes and arthritis were associated with the brain only to a small extent." Fix wording, were "perceived to be associated with…"

Response
The text has been revised as suggested.

13. Discussion: "Physical health was rated as highly important in our study in contrast to what previous surveys found….In our questionnaire, we did not provide any example of what physical health entails, so we do not know exactly how our respondents interpreted the question." Need to tie

that into contrasting finding from prior paragraph, where hypertension for example was only believed to be important in a smaller subset of people.

Response

We have now included a sentence in this paragraph to link to the previous statement.

In closing, we would like to thank the reviewers for their insightful comments, which have helped to improve our manuscript. We hope that the changes introduced in our revised submission will meet the editorial standards expected for this publication.

VERSION 2 – REVIEW

REVIEWER	Friedman, Daniela Univ S Carolina
REVIEW RETURNED	28-Jan-2022

GENERAL COMMENTS	The authors have done a nice job addressing reviewers' comments and responding to questions in the separate document. While the authors indicate that only significant results are presented in the abstract per the findings within the manuscript, this is still unclear to readers in my opinion and the abstract should specify this clearly in the results section and ensure the flow of the abstract text is appropriate.

REVIEWER	Wheeler, Fariya The University of Alabama at Birmingham, School of Nursing, University of Alabama at Birmingham, Birmingham, AL, United States.
REVIEW RETURNED	14-Feb-2022

GENERAL COMMENTS	Overall the authors did a satisfactory job of addressing my prior comments, and those of other reviewers. I have some lingering comments, below, most important related to the analyses. 1. Strengths and limitations: “We attempted to adjust for measured confounders using multivariable analyses. The knowledge gaps observed in this sample are likely to be an issue also in a more representative sample.” Maybe reword to something like “The knowledge gaps observed in this sample of largely highly educated individuals are likely to be an issue, and perhaps even to a greater degree, in the broader population.” 2. Intro: “The survey included four overall themes: perception of some aspects of brain health, interest in undertaking brain health tests, motivations to look after one’s brain, and support needed to make lifestyle changes beneficial for the brain. In this paper, we report responses to survey questions relating to: (1) factors believed to influence brain health, (2) specific life periods considered important to look after one’s brain, and (3) diseases and disorders associated with the brain.” Should you state/or cite the papers that are examining the other survey questions? 3. Next sentence “…considering the diverse recruitment rates and sample characteristics in different countries” I am not sure what

	you mean by diverse recruitment rates? Do you just mean diverse sample characteristics? 4. “Thus, rather than using methods of controlling for multiple comparisons, we report results only significant at the 1% level of probability and make a distinction between practically unimportant and probably important effects.” How was practically important determined? 5. “If there was an obvious risk of confounding by the descriptive variables age, sex, and education, we used multivariable testing to adjust results appropriately.” Please be more specific. And don’t use words like “obvious”. Do you mean to say if a demographic factor was associated with the brain health measure, you conducted a multivariable regression? Was this a logistic regression? 6. “For each category, separate predictive models for (1) age, (2) gender, (3) education, (4) relationship status, (5) experience or education in health care, (6) experience with illness, (7) experience of being a caregiver for someone with a brain disease, (8) rating of own cognitive health, and (9) rating of own mental health as predictors were computed.” What specific statistical test was used? 7. “After controlling for educational level and age, these effects remained significant.” It is very unclear what the criteria was for the multivariable models. Just variables statistically associated with each brain health question, or just conceptually related. This point is related to comment 5 above. 8. Please confirm if Table 3 is adjusted/ multivariable or unadjusted/univariate analyses 9. Implications for policy makers: “This may suggest the need for targeted brain health information to single people.” Perhaps instead say “single people and those living alone” ?

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1 (R1)

Dr. Daniela Friedman, Univ S Carolina

Comments to the Author:

The authors have done a nice job addressing reviewers' comments and responding to questions in the separate document. While the authors indicate that only significant results are presented in the abstract per the findings within the manuscript, this is still unclear to readers in my opinion and the abstract should specify this clearly in the results section and ensure the flow of the abstract text is appropriate.

Now reads:

“Of all significant effects, the survey respondents recognized the impact of lifestyle factors on brain health but had relatively less awareness of the role that socio-economic factors might play. Most respondents rated all life periods as important for the brain (95-96%), although the prenatal period was ranked significantly lower (84%). Equally, women and highly educated respondents more often rated factors and life periods to be important for brain health. Ninety-nine percent of respondents associated Alzheimer's disease and dementia with the brain. The respondents made a clear connection between mental health and the brain, and mental disorders such as schizophrenia and depression were significantly more often considered to be associated with the brain than neurological disorders such as stroke and Parkinson's disease. Few respondents (<32%) associated cancer, hypertension, diabetes, and arthritis with the brain."

Reviewer: 4 (R4(

Dr. Fariya Wheeler, The University of Alabama at Birmingham

Comments to the Author:

Overall the authors did a satisfactory job of addressing my prior comments, and those of other reviewers. I have some lingering comments, below, most important related to the analyses.

1. Strengths and limitations: "We attempted to adjust for measured confounders using multivariable analyses. The knowledge gaps observed in this sample are likely to be an issue also in a more representative sample." Maybe reword to something like "The knowledge gaps observed in this sample of largely highly educated individuals are likely to be an issue, and perhaps even to a greater degree, in the broader population."

Point 4 of 'Strengths and limitations of this study' now reads:

"- The knowledge gaps observed in this sample of largely highly educated individuals are likely to be an issue, and perhaps even to a greater degree, in the broader population."

2. Intro: "The survey included four overall themes: perception of some aspects of brain health, interest in undertaking brain health tests, motivations to look after one's brain, and support needed to make lifestyle changes beneficial for the brain. In this paper, we report responses to survey questions relating to: (1) factors believed to influence brain health, (2) specific life periods considered important to look after one's brain, and (3) diseases and disorders associated with the brain." Should you state/or cite the papers that are examining the other survey questions?

Response:

Two reports have recently been made public, that provide information about the respondents' motivation to look after one's brain and support needed to make lifestyle changes beneficial for the brain. References to these reports have now been added. Results pertaining to the respondents' interest in undertaking brain health tests are currently being examined and are therefore not available yet.

3. Next sentence “…considering the diverse recruitment rates and sample characteristics in different countries” I am not sure what you mean by diverse recruitment rates? Do you just mean diverse sample characteristics?

Happy to replace the sentence with:

“Whereas extrapolating from responses in this convenience sample to the general population will not be feasible considering the sample characteristics in different countries, ...”

4. “Thus, rather than using methods of controlling for multiple comparisons, we report results only significant at the 1% level of probability and make a distinction between practically unimportant and probably important effects.” How was practically important determined?

This is an important theme that recurs below in points 5 and 7. We did in fact use “false-discovery-rate (FDR) correction across all models and covariates for each outcome variable”, as now stated in the methods section. We now clarify, being more specific: “We used multivariable testing with logistic regression to adjust specific results only for questions 1 and 2 adjusting the observed sex effect for age and education. Similarly, in question 3 we controlled the ‘stable relationship effect’ for age and education.”

5. “If there was an obvious risk of confounding by the descriptive variables age, sex, and education, we used multivariable testing to adjust results appropriately.” Please be more specific. And don’t use words like “obvious”. Do you mean to say if a demographic factor was associated with the brain health measure, you conducted a multivariable regression? Was this a logistic regression?

This sentence now reads, as shown under Point 4.

6. “For each category, separate predictive models for (1) age, (2) gender, (3) education, (4) relationship status, (5) experience or education in health care, (6) experience with illness, (7) experience of being a caregiver for someone with a brain disease, (8) rating of own cognitive health, and (9) rating of own mental health as predictors were computed.” What specific statistical test was used?

The sentence now reads:

“For each category, separate predictive logistic regression models for (1) age...”

7. “After controlling for educational level and age, these effects remained significant.” It is very unclear what the criteria was for the multivariable models. Just variables statistically associated with each brain health question, or just conceptually related. This point is related to comment 5 above.

This is now explained in the methods section (point 4).

8. Please confirm if Table 3 is adjusted/ multivariable or unadjusted/univariate analyses

Response:

Table 3-5 presents univariate results, and this has been made explicit in the Legend.

9. Implications for policy makers: “This may suggest the need for targeted brain health information to single people.” Perhaps instead say “single people and those living alone” ?

We have made this change:

“This may suggest the need for targeted brain health information to single people and those living alone.”