

Associations Between Plant-Based vs Animal-Based Protein Supplies and Age-Specific Mortality in Human Populations

Corresponding Author: Ms Caitlin Andrews

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)

Abstract - Adapt sentence on line 26-27 to say your data analysis (technique) found associations between increased rates of mortality and..... because this is an association study and only infers causation.

Introduction - please correct the word sustainability to read environmental sustainability (line 40) if that is what you mean here. Line 69-72 needs re-writing to mention red meat(s) rather than animal protein - which would include poultry and fish. Line 86 - add in a reference for the geometric framework for nutrition as it looks like a tool developed by your own lab for precision nutrition (doi: 10.3233/NHA-170027). This is a different approach, with an entirely different large-scale data-science approach.

Results - line 111 what is LT survivorship ? Please briefly define supply, PBP and ABP as a key feature of figures. It is not clear the source of the nutrition data - add in a sentence to guide readers (explained in full in methods). Just a note that alcohol is not mentioned as a macronutrient - how was this adjusted for in energy/calorie intake.

Discussion is well written. Was looking for mention of iron intake from plant and animal sources, as a major problem linked to deficiency anaemia. Line 287 mentions pre-clinical studies, please add a comment about limitations of mice models to infer to human health. No mention of the co-founder of PBP to contain dietary fibre as a mechanism to promote health - not the protein per se (add to limitations section ?).

(Remarks on code availability)

Reviewer #2

(Remarks to the Author)

I am having a difficult time finding out what exactly is meant by "food supply". If it just means the average amount of food and nutrients available to the population, then I'm sorry but I don't think any conclusions can be made about the biological role of proteins on the health and mortality risk of an individual. I am not saying that it is not important to know how the national food supply affects mortality but that it will tell us very little about the biology of it since there are many confounding variable such as socioeconomic status, mixing a healthy low protein diet with malnourishment, etc etc. which could lead to misleading results and interpretations. I suggest to rewrite the paper and title to make it very clear that it is not reporting on protein intake and mortality but on national supplies and mortality, with much more explanations and detail about the data used early in the manuscript. If I misunderstood, I would be happy to review a revised version that is much clearer.

(Remarks on code availability)

Reviewer #3

(Remarks to the Author)

This study examined the population-level substitution associations of plant-based protein supplies (PBS) vs. animal-based protein supplies (ABS) with all-cause mortality across various age groups. The topic is relevant given the interest in the role

of dietary protein—and protein sources—as determinants of human lifespan and healthspan. Moreover, the analysis of survival at different ages is novel and a relevant strength of the study. However, there are important methodological limitations, especially the lack of adjustment for total energy intake in the statistical analyses, which is essential to model the associations of macronutrient intake with health outcomes.

Main comments:

1. The most important limitation in the statistical analysis is that the geometric framework for nutrition (GFN) method and the GAMM models presented in Table S13 do not include adjustment for total energy intake. The inclusion of total energy intake in the statistical model is essential—especially in the study of macronutrient intake—because the caloric contributions from each macronutrient, as they replace calories from other components of the diet, are associated with survival (Reference #26, Chen et al., includes a relevant discussion in the methods section).

Secondly, individuals unconsciously control their total energy within a very narrow range unless accompanied by a substantial change in body weight or physical activity. Additionally, total energy intake is an important determinant of survival and is an important confounder in the associations presented in the study. Thus, the adjustment for total energy intake helps model the fact that increases in energy from one protein source are accompanied by decreases in energy from other protein sources or other macronutrients rather than changes in overall food and total energy intake.

The same limitation is true for the GFN framework as the relationship of macronutrient intakes relative to other nutrient intakes used an energy partition model, which does not include a coefficient for total energy intake. Because this model includes the coefficients for each macronutrient as the dietary components that contribute total energy, this is an additive model (i.e., calories from each macronutrient are added without a total energy restriction), thus removing the substitution nature of protein from animal sources for plant sources intended in the analysis.

2. The second important limitation is that dietary carbohydrates and fat are each modeled as homogeneous macronutrients, which ignores the heterogeneity within each macronutrient (refined carbohydrates, fiber, sugar, saturated fats, poly-unsaturated fats, etc.) and their effects on health. For instance, various types of fatty acids have heterogeneous associations with survival (PMID: 27379574). Thus, defining the type of fat is important when presenting results for the substitution of fats for protein and the type of carbohydrate is relevant when comparing against protein intake. The authors need to explicitly state the type of macronutrient being compared to protein intake.

3. The study design (ecological study) must be clearly stated in the abstract, and methods section. The first mention of the study design occurs in the discussion section (line 252). Moreover, an explicit mention of the ecological fallacy limitation (i.e., those who replaced ABS with PBS are not necessarily those who experienced reductions in mortality) must be included in the limitations.

Other comments:

Lines 63-65: The sentence “Protein intake appears to exhibit a non-linear relationship with all-cause mortality...” needs to clarify that this association is relative to calories from the entire diet.

Lines 69-70: the wording of the sentence “High intake of animal protein, processed and with less certainty unprocessed red meats, has been associated...” is unclear.

Lines 85-86: The introduction of the GFN methodology lacks references

Line 91: There is an extra ‘to’ after the period

Line 132: Define the acronym LT

Line 242: The words ‘adding energy from any protein source’ suggest an additive effect, which is consistent with the statistical models. However, this is inconsistent with the intended substitution effects presented in the rationale of the study. Figure 5. The mention of total energy intake for males and females makes it unclear whether the models were adjusted for total energy intake. This is important for the reasons stated above and also to account for decreasing total energy intakes with age (PMID: 33838032).

(Remarks on code availability)

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)

The reviewers have fully addressed the comments.

(Remarks on code availability)

Reviewer #2

(Remarks to the Author)

I'm fine with most of the changes made but I think the authors should make it clearer that national food supplied can only

give us ideas about the biological effects of any level of type of nutrient on survival

(Remarks on code availability)

Reviewer #3

(Remarks to the Author)

I thank the authors for addressing most of the points raised during the initial review. I am including additional comments on points that were incompletely addressed and a list of additional notes on the revised content.

Main comments:

1. In response to the authors (text included here):

- a. I did not find the isolines for 3023, 3120, and 3228 kcal per capita per day in Figure 2 as mentioned above. The figure shows the adjustment for NPE, not total calories. Please clarify this point.
- b. Please provide the results for the models adjusted for total energy intake in a summary table or figure. The claim that these are identical to the main results is difficult to evaluate in the absence of data.

We agree with the reviewer that total energy supply is incredibly important, and in many places, we emphasise the importance of total energy and its interactions with protein supply, as evidenced by our analyses (for example, see results and discussion at lines 164-170, and 208-210).

For reference, the following text has been added to the results section at lines 164-170:

"The grey dashed isolines on Figure 2 at 400 kcal/capita/day total protein supplies, show the effects of isocalorically substituting ABP for PBP (and vice versa) while holding total energy supplies constant at 3023, 3120 and 3228 kcal/capita/day (Figures 2A and 2 D, Figures 2 B and 2 E, and Figures 2C and 2 F, respectively). Moving in the direction of the isolines illustrates improvements in *l_s* associated with the substitution of ABP from PBP without changing the amounts of total protein and total energy supplies. *l_s* also demonstrated positive association with total fat supplies."

Lines 208-210 (previously 193-195) read:

"Higher ABP supplies were associated with enhanced survivorship during infancy and early childhood, independent of total calorie supplies, while PBP-rich environments were associated with improved survivorship in later life and overall life expectancy at birth."

Before responding in detail, we want to summarise that: 1) the GAMM models do not assume the nutrients are additive, but models their interactions; 2) consequently the model does already account for the distinction between total energy from macronutrients; 3) illustrating this, we have re-run the models using total energy as a covariate as suggested and the results are identical to those presented in the main text.

2. Figure 2 presents survivorship to age 5. Are the calorie intakes and the respective calories from protein and NPE assessed at age 5? The intakes do not match the averages for those ages. Could you please describe the method used to assess calories for survival to age 5?

Other comments:

1. Please include a brief description of 'food systems' in the introduction. The concept is introduced in line 33 and referred to subsequently, but it is not clear.
2. Line 23: The year range should read: "from 1961 to 2018" or "ranging 1961-2018"
3. Line 56: The term "its relationship to carbohydrate" is unclear. Please define.
4. Lines 62 and 74: Please replace "effects" with "associations" as the references cited (16, 17, and 23) are observational studies.
5. Lines 91 and 92. Please specify the age ranges for which the dietary data is available.
6. Lines 111, 119, 123, 148, 205: "Daily per caput" should read "daily per capita".
7. Line 177: Please replace "effects" with "associations". Same in lines 180/181, and 192
8. Lines 339 and 341: Please replace "impact" and "effect" with associational language, perhaps "unfavorably associated".

(Remarks on code availability)

Version 2:

Reviewer comments:

Reviewer #3

(Remarks to the Author)
No additional comments

(Remarks on code availability)
N/A

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RESPONSES TO REVIEWER COMMENTS

Please note all line references in this document correspond to the final version of the manuscript, where all edits have been accepted and any markup has been removed.

COMMENTS

Reviewer #1 (Remarks to the Author):

☒ *Abstract - Adapt sentence on line 26-27 to say your data analysis (technique) found associations between increased rates of mortality and..... because this is an association study and only infers causation.*

Adjusted as suggested to specify that we found associations between mortality and low protein supplies. See lines 23-25.

Previously read:

“Following corrections for time, population size and economic factors, our findings reveal increased rates of mortality across all age groups to be consistently associated with low total protein supplies.”

Now reads:

“After adjusting for time, population size, and economic factors, we found associations between low total protein supplies and higher mortality rates across all age groups.”

Introduction

☒ *please correct the word sustainability to read environmental sustainability (line 40) if that is what you mean here.*

Adjusted as suggested. See line 32.

Previously read:

“In an era marked by the pressing need for decarbonization and sustainability, global food systems, which contribute a third of all greenhouse gas emissions...”

Now reads:

“In an era marked by the pressing need for decarbonization and **environmental** sustainability, global food systems, which contribute a third of all greenhouse gas emissions...”

☒ ***Line 69-72 needs re-writing to mention red meat(s) rather than animal protein - which would include poultry and fish.***

Sentence adjusted as suggested. See lines 63-65.

Previously read:

“High intake of animal protein, processed and with less certainty unprocessed red meats, has been linked to an increased risk of certain chronic diseases, including cardiovascular disease, type 2 diabetes, and some types of cancer”

Now reads:

“In particular, high intake of processed meats and – with less certainty – unprocessed red meats, has been linked to an increased risk of certain chronic diseases, including cardiovascular disease, type 2 diabetes, and some types of cancer”

☒ ***Line 86 - add in a reference for the geometric framework for nutrition as it looks like a tool developed by your own lab for precision nutrition (doi: 10.3233/NHA-170027). This is a different approach, with an entirely different large-scale data-science approach.***

References added. See line 79.

Results

☒ ***Line 111 what is LT survivorship?***

LT survivorship stood for life-table survivorship. The LT acronym has been removed from the paper, and this specific sentence has also been adjusted for clarity (now at line 108). We also added information to the introduction and results to make clear the datatypes we are working with. See lines 98-99 and 109-110.

Lines 98-99 previously read (previously 102-103):

“We used macronutrient supply data from food balance sheets (FBS) compiled by the Food and Agriculture Organisation of the United Nations (FAO), sex-specific mortality data within life tables (LTs) from the Human Mortality Database, and economic statistics from...”

Lines 98-99 now read:

“This FBS supply data was combined with sex-specific mortality data (specifically, the proportion of individuals within a cohort that survive to each age) from life tables provided at the Human Mortality Database, economic statistics from...”

Lines 109-110 previously read (previously line 111):

“The collated data comprised complete entries for macronutrient supplies, LT survivorship, and...”

Now reads:

“The collated data comprised complete entries for macronutrient supplies from national food balance sheets (FBSs), survivorship at ages 5 and 60 (l_5 and l_{60} , i.e., the proportion of a cohort still alive at ages 5 and 60) from national life tables, and...”

☒ ***Please briefly define supply, PBP and ABP as a key feature of figures.***

To address this comment and others around clarity of the datatypes, the final paragraph of the introduction has been adjusted (lines 92-97). These adjustments have been made to clarify the lifetable data being used and the guide readers to the methods section for greater detail on the FBS nutrition data.

Previously read:

“We used macronutrient supply data from food balance sheets (FBS) compiled by the Food and Agriculture Organisation of the United Nations (FAO)...”

Now reads:

“We used data on macronutrient supply quantities available for human consumption from food balance sheets (FBS; see methods for full explanation) compiled by the Food and Agriculture Organisation of the United Nations (FAO). Specifically, these data reflect the average availability of food and nutrients at the national level which are crucial for understanding the nutritional environment’s ability to support the population’s health.”

☒ ***It is not clear the source of the nutrition data - add in a sentence to guide readers (explained in full in methods).***

The start of the results section has been updated to add clarity around the type of nutrition data we are working with (food-balance sheets). See lines 92-97 (detailed above) and 111-121.

The following text has been added at lines 111-121:

“Briefly, per caput food supply data provided by FBSs refers to the average amount of food available for consumption per person within a nation for a given year, a foundational element of the nutritional environments contributing to health outcomes across different populations. Quantities of food items available for consumption are calculated based on the total quantities produced and imported, adjusting for any changes in stocks including exports. FBSs also give daily supplies daily per capita supplies in terms of total energy, and specific energy sources, based on composition factors¹. Here we have analysed daily per capita protein supplies

from animal and vegetal sources (i.e., animal-based protein and plant-based protein; ABP and PBP), as well as daily per caput supplies of total fat supplies and carbohydrate (note carbohydrate was estimated as total available energy less energy from alcohol, ABP, PBP and fat).”

☒ ***Just a note that alcohol is not mentioned as a macronutrient - how was this adjusted for in energy/calorie intake.***

Here we are dealing with energy from all sources other than alcohol. Total calories were adjusted for alcohol. Food balance sheets report the total energy available per capita per person from alcohol. Thus, alcohol supply was adjusted by subtracting alcohol from total energy to yield energy from macronutrients. This aligns with population, experimental and mechanistic applications of Nutritional Geometry framework, in which macronutrient interactions have been the focus. We have tried to make this clear in the *Results* section and in the Methods section under Data. See lines 120 and 418.

The following note has been added at line 120, for clarity:

“...as well as daily per caput supplies of total fat supplies and carbohydrate (note carbohydrate was estimated as total available energy less energy from alcohol, ABP, PBP and fat)”

The same detail has been reiterated in the methods section at lines 418-422:

“Protein, fat, and alcohol supply quantities were subtracted from the reported total food supplies per capita, given in terms of caloric value (kcal/person/day) for each (country, year) population. The difference was used to represent the average per capita nutritional contribution of energy from carbohydrate, for the specified (country, year) combination.”

☒ ***Discussion is well written. Was looking for mention of iron intake from plant and animal sources, as a major problem linked to deficiency anaemia.***

We have added an additional discussion of iron and iron supplies, particularly around their effects on child-hood mortality. See lines 259 to 266 in the discussion.

The following text has been added at lines 259-266:

“For example, growth and development increase the demand for iron in pregnant and lactating women, and children, putting them at higher risk of rapidly developing iron deficiency anaemia and increasing the risk of child mortality². Noting that iron deficiency has been reported to be less frequent in countries where meat constitutes a significant part of the diet³, it is possible that the increased content and bioavailability of micronutrients, particularly iron, present in ABP may contribute to the stronger association between improved early life survivorship and increased ABP supplies, compared to PBP supplies⁴.”

☒ ***Line 287 mentions pre-clinical studies, please add a comment about limitations of mice models to infer to human health.***

We have caveated inferences drawn from the results of animal-model studies and how they map on to human data. See lines 325 to 328.

Previously read:

“Several pre-clinical studies have suggested that reducing the ratio of total protein to carbohydrate in the diet may extend longevity⁵⁻⁹.”

Now reads:

“Several pre-clinical studies have suggested that reducing the ratio of total protein to carbohydrate in the diet may extend longevity⁵⁻⁷. It is important to note that findings from animal models may not always directly translate to human health outcomes, especially at the population/ecological level.”

☒ ***No mention of the co-founder of PBP to contain dietary fibre as a mechanism to promote health - not the protein per se (add to limitations section ?).***

Indeed, fibre is just one many such nutrients. In the revised version we have mentioned fibre explicitly as an example of such a nutrient, which has been linked with improved health and give the example of a clinical trial which has this exact same issue of the PBO and Fibre covariance. Within the limitations we have mentioned that we are not able to control out any potential effects of other nutrients that covary ABP and PBP. We have mentioned fibre explicitly as an example of such a nutrient, which has been linked with improved health and give the example of a clinical trial which has this exact same issue of the PBP and fibre covariance. See lines 361-364, 379 to 383 and 389 to 393.

The following text has been added at lines 361-364:

“Additionally, to maintain the interpretability of our models, our analyses do not account for the heterogeneity within the carbohydrate and fat supplies, such as the differences between refined carbohydrates, fibre, and sugar, as well as between saturated and polyunsaturated fats.”

The following text has been added to the limitations section of the discussion at lines 379-383:

“Our analyses incorporated statistical adjustments for total fat and carbohydrate supplies. However, limitations in the data prevented us from further separating out the effects of different fat and carbohydrate types, as well as other nutrients such as fibre. It is important to note such nutritional covariances represent potential confounders.”

The following example of a clinical trial with this same issue has been included at the end of the discussion at lines 389-393:

“One 12 week clinical trial in healthy Finnish adults replacing ABP with PBP sources resulted in improved plasma lipoprotein levels¹⁰. However, the dietary transition was also associated with improved overall dietary fat quality and increased intake of dietary fibre and complex carbohydrates¹⁰. All of these dietary dimensions have been linked, variably, to decreased risks of chronic diseases and mortality from all causes, cardiovascular diseases, and cancer in the general human population^{5,11,12}, making it hard to pin-point if any one individual dietary change was causal.”

Reviewer #2 (Remarks to the Author):

☒ *I am having a difficult time finding out what exactly is meant by “food supply”. If it just means the average amount of food and nutrients available to the population, then I’m sorry but I don’t think any conclusions can be made about the biological role of proteins on the health and mortality risk of an individual. I am not saying that it is not important to know how the national food supply affects mortality but that it will tell us very little about the biology of it since there are many confounding variable such as socioeconomic status, mixing a healthy low protein diet with malnourishment, etc etc. which could lead to misleading results and interpretations. I suggest to rewrite the paper and title to make it very clear that it is not reporting on protein intake and mortality but on national supplies and mortality, with much more explanations and detail about the data used early in the manuscript. If I misunderstood, I would be happy to review a revised version that is much clearer.*

Our manuscript adopts FAO terminology, where “food supply” refers to the average amount of food and nutrients available for consumption, per person, in a national population, based on national food balance sheets. This includes macronutrient distributions such as protein and fat, which are crucial for understanding the nutritional environment at a national level. We agree with the reviewer that understanding how these supplies affect mortality is not unimportant; this was the main aim of our analysis. Our approach captures the association between the nutritional landscape (type, quantity, and source of nutrients available for consumption) and population health outcomes, as clarified in our manuscript at lines 41-43, 52-54 and 95-97.

Lines 41-43 (previously 49-51) read:

“In general, the nutritional environment, encompassing factors such as the quality, quantity, and source of nutrients available for consumption, has been identified as a critical determinant of health and survivorship at different ages¹³.”

Lines 52-54 (previously 60-61) read:

“The availability of macronutrients, and particularly protein, at the national level is of interest when considering how nutritional environments affect health and survivorship as a function of age.”

The following text has been added to the end of the introduction, at lines 95-97:

“Specifically, these data reflect the average availability of food and nutrients at the national level which are crucial for understanding the nutritional environment’s ability to support the population’s health.”

We also agree that food supply data cannot directly tell us how nutrient intake affects individual biology and mortality risk. Our aim was not to draw conclusions about biological effects but to provide valuable insights into potential population-level impacts. The observed associations between protein supplies and mortality align with and might be explained by existing epidemiological literature on dietary intake and health, even if they do not directly elucidate individual biological mechanisms.

We agree that socioeconomic status, dietary patterns and other confounding variables can influence health outcomes. Our statistical models adjust for economic factors, temporal trends and population size to mitigate these effects, helping to isolate the associations between macronutrient supplies and age-specific mortality. In our discussion we acknowledge the risk of residual confounding that will always exist in these types of ecological studies and emphasize that our findings highlight associations rather than causations.

In this revised manuscript, we have:

- 1) Clarified that we are testing the effects of national nutritional supplies, not food intake, by:
 - a. Adjusting the title.
 - b. Referring to ‘supply’ explicitly as ‘daily per capita supply’.
 - c. Adding a detailed description of the food-balance sheets in the results.
 - d. clearly distinguishing between literature on food intake vs nutrient supply.
- 2) Clarified the relationship between supply and dietary intake, and what existing literature says about that, early in the Discussion. Specifically, the following lines have been added to the discussion at lines 221-240 (please note lines 222- 232 have been moved from the end of the discussion, previously at lines 306-315):

“This method offers a complementary, but different, perspective relative to assessments of individual dietary habits and nutrient intake. Firstly, FBS data facilitate extensive temporal and trans-national comparisons of food availability and consumption patterns, which can reveal long-term trends and regional differences; such extensive coverage is not currently available for intra-national data on diet pattern. Secondly, the FBS data capture the nutritional environment, which is likely to

be highly responsive to policy interventions (e.g., agricultural, trade, and environmental policies affecting food systems), where individual diets can prove hard to affect.

Food and nutrient supplies, as captured by FBSs, are an upstream and key determinant of individual diet, and population-wide dietary patterns; the food supply influences the accessibility, affordability, and distribution of various food groups and nutrients, as well as setting a hard upper limit on average intake¹⁴. Indeed, several studies have shown that at the level of nutrient composition and food patterns, average national diet is correlated with nutrient supply^{15,16}. Despite these correlations nutrient supply cannot be considered a direct surrogate for intake, the latter being influenced by myriad intervening factors including inefficiencies in the food system such as food waste. Hence, our results should not be interpreted as evidence for the effects of nutrient intake on health. We can however look to the literature on dietary intake and health to provide potential nutritional explanations for the differential associations between ABP and PBP supplies and mortality that we have observed.”

- 3) Emphasised that references to dietary intake literature are to triangulate evidence, and not to assert causation.
- 4) Thoroughly acknowledged confounding factors and nuances of ecological studies in the Limitations section.
- 5) Included comprehensive explanations and detailed descriptions of data sources, methodologies, and statistical analyses early in the manuscript to ensure clarity and transparency.

Reviewer #3 (Remarks to the Author):

This study examined the population-level substitution associations of plant-based protein supplies (PBS) vs. animal-based protein supplies (ABS) with all-cause mortality across various age groups. The topic is relevant given the interest in the role of dietary protein—and protein sources—as determinants of human lifespan and healthspan. Moreover, the analysis of survival at different ages is novel and a relevant strength of the study. However, there are important methodological limitations, especially the lack of adjustment for total energy intake in the statistical analyses, which is essential to model the associations of macronutrient intake with health outcomes.

Main comments:

☒ **1. The most important limitation in the statistical analysis is that the geometric framework for nutrition (GFN) method and the GAMM models presented in Table S13 do not include adjustment for total energy intake. The inclusion of total energy intake in the statistical model is essential—especially in the study of macronutrient intake— because the caloric contributions from each macronutrient, as they replace calories from other components of the diet, are associated with survival (Reference #26, Chen et al., includes a**

relevant discussion in the methods section).

Secondly, individuals unconsciously control their total energy within a very narrow range unless accompanied by a substantial change in body weight or physical activity.

Additionally, total energy intake is an important determinant of survival and is an important confounder in the associations presented in the study. Thus, the adjustment for total energy intake helps model the fact that increases in energy from one protein source are accompanied by decreases in energy from other protein sources or other macronutrients rather than changes in overall food and total energy intake.

The same limitation is true for the GFN framework as the relationship of macronutrient intakes relative to other nutrient intakes used an energy partition model, which does not include a coefficient for total energy intake. Because this model includes the coefficients for each macronutrient as the dietary components that contribute total energy, this is an additive model (i.e., calories from each macronutrient are added without a total energy restriction), thus removing the substitution nature of protein from animal sources for plant sources intended in the analysis.

We agree with the reviewer that total energy supply is incredibly important, and in many places, we emphasise the importance of total energy and its interactions with protein supply, as evidenced by our analyses (for example, see results and discussion at lines 164-170, and 208-210).

For reference, the following text has been added to the results section at lines 164-170:

“The grey dashed isolines on Figure 2 at 400 kcal/capita/day total protein supplies, show the effects of isocalorically substituting ABP for PBP (and vice versa) while holding total energy supplies constant at 3023, 3120 and 3228 kcal/capita/day (Figures 2A and 2D, Figures 2B and 2E, and Figures 2C and 2F, respectively). Moving in the direction of the isolines illustrates improvements in l_5 associated with the substitution of ABP from PBP without changing the amounts of total protein and total energy supplies. l_5 also demonstrated positive association with total fat supplies.”

Lines 208-210 (previously 193-195) read:

“Higher ABP supplies were associated with enhanced survivorship during infancy and early childhood, independent of total calorie supplies, while PBP-rich environments were associated with improved survivorship in later life and overall life expectancy at birth.”

Before responding in detail, we want to summarise that: 1) the GAMM models do not assume the nutrients are additive, but model their interactions; 2) consequently the model does already account for the distinction between total energy from macronutrients; 3)

illustrating this, we have re-run the models using total energy as a covariate as suggested and the results are identical to those presented in the main text.

First, the GAMMs do not assume additive effects of the macronutrients, but model their interactions using a multi-dimensional spline, which received the best statistical support based on AIC. Therefore, the effect of one nutrient can't be added without altering the effects of others; increasing total energy by adding different sources, can change the individual effects of ABP or PBP.

Second, the current model, and the GFN in general, aim to separate the effects of total energy from its sources by modelling the energy sources in absolute terms. Our analysis accounts for energy from protein, carbohydrates and fat in kcal/capita/day, representing total energy supply from macronutrients. This differs from 'controlling' for total energy and examining individual nutrients in isolation.

After modelling the total energy supply from macronutrients, the effects/associations of total supply and individual nutrients can be interpreted from the surface plots. These plots allow readers to see the impact of increasing protein levels while holding other nutrients constant or substituting them isocalcorically. On each surface, carbohydrate and fat are fixed, while energy from animal and plant protein is shown on the x and y axes. Each point represents a total energy supply from different macronutrient combinations. Following along vectors from the surface origin shows the effects of adding protein energy, while holding non-protein energy constant (thus increasing total energy only via protein). For example, at (ABP, PBP) = (150, 150) illustrated below on Figure 1B, total energy (Fat + Carb + Protein = 1148 + 1572 + 300) is 3019kcal/capita/day. Increasing both ABP and PBP by 50 (to (200, 200)) raises total energy to 3119kcal/capita/day, reflecting the protein increase. Fat and carbohydrate energy remain constant at both points. Comparing across surfaces, the only difference is the fat supply, meaning a combination of ABP and PBP on a higher fat surface

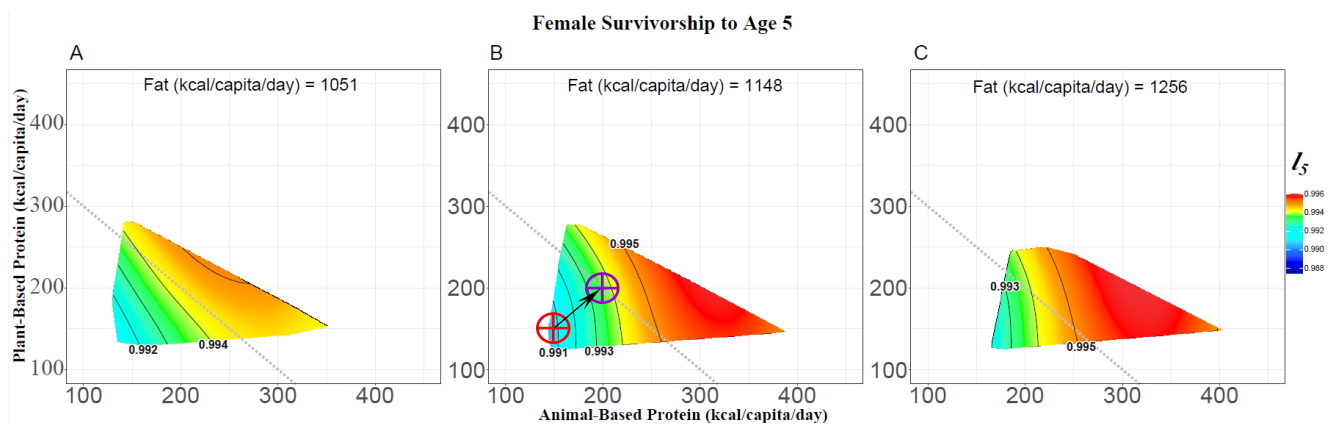


Figure 1: Figure 2A-C taken from final manuscript with annotations added to surface (B) to illustrate increasing total protein energy while holding total non-protein energy constant, supporting the example provided in the above written response to reviewer #3. The red cross is marked at (ABP, PBP) = (150, 150). The purple cross marks the point (200, 200). The black arrow is a vector representing a total protein energy increase of 100 kcal/capita/day from (150, 150) to (200, 200).

contributes to a smaller percentage of total energy than the same combination on a lower fat surface.

An energy-controlled substitution analysis, as suggested by the reviewer (and Chen et al.), can be interpreted from the existing surfaces by reading across diagonal isolines on the surfaces. Doing so holds energy from all macronutrients constant while substituting PBP for ABP, and vice versa. We have now updated the surfaces in figures 2 to 4 with isolines. Specifically, a line at $ABP + PBP = 400$ kcal/capita/day is included on each surface, based on the 2017 median protein supply. Reading along this line keeps total protein energy constant, merely substituting between animal and plant-based proteins. Since fat and carbohydrate are held constant on each surface, total energy along these lines is the sum of protein, fat and carbohydrate. For example, the isolines in figure 1A-C (copied below) indicate total energies of 3026, 3120 and 3224 kcal/capita/day, respectively. This has been clarified in the manuscript figure legends.

Finally, a common question in GFN analyses is whether it is appropriate or necessary to include total energy as a covariate after modelling all macronutrients individually. Each point on a surface shows the combined total energy of the macronutrients. Since carbohydrate and fat are held constant across a surface, total energy changes only with protein, based on the (ABP, PBP) coordinates. Further controlling for total energy would mean holding total energy constant while simultaneously varying protein, which is illogical since fat and carbohydrate are fixed. Therefore, including total energy as a covariate contradicts the surface interpretation and is unnecessary. For illustration, we re-ran our models with total energy included, as suggested, and found no change in results, reinforcing that controlling for total energy is not meaningful in the context of our GFN analyses. The resulting 'energy-controlled' surfaces for female survivorship are shown below, with a purple gradient to distinguish them from the rainbow gradient surfaces discussed in our manuscript.

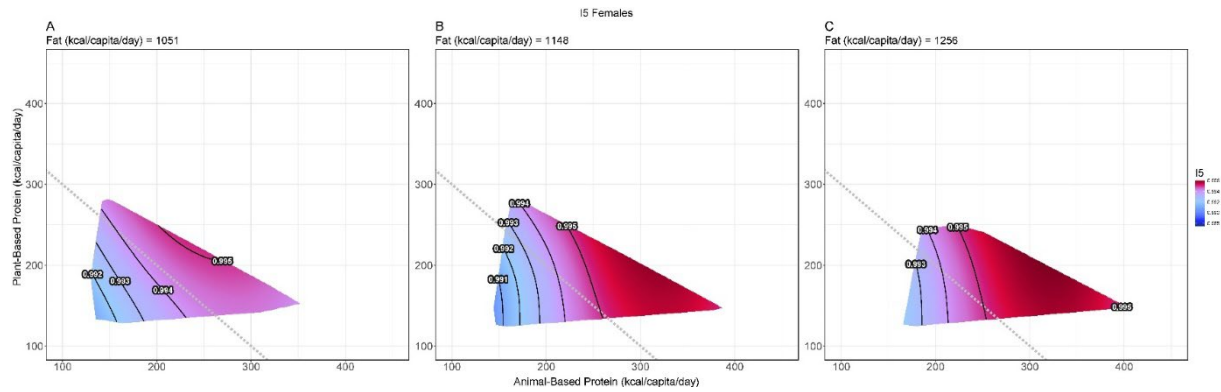


Figure 2. Surfaces for female survivorship to age 5, based on the ‘energy-controlled’ models, as described in the above response to reviewer #3

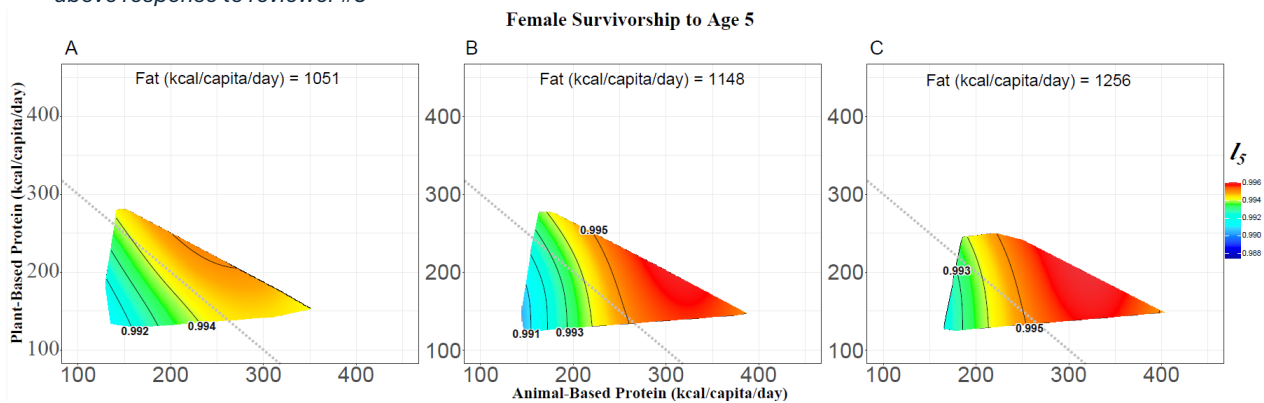


Figure 3. Surfaces for female survivorship to age 5, based on the models described in our manuscript. (Figures 2A-C in final manuscript)

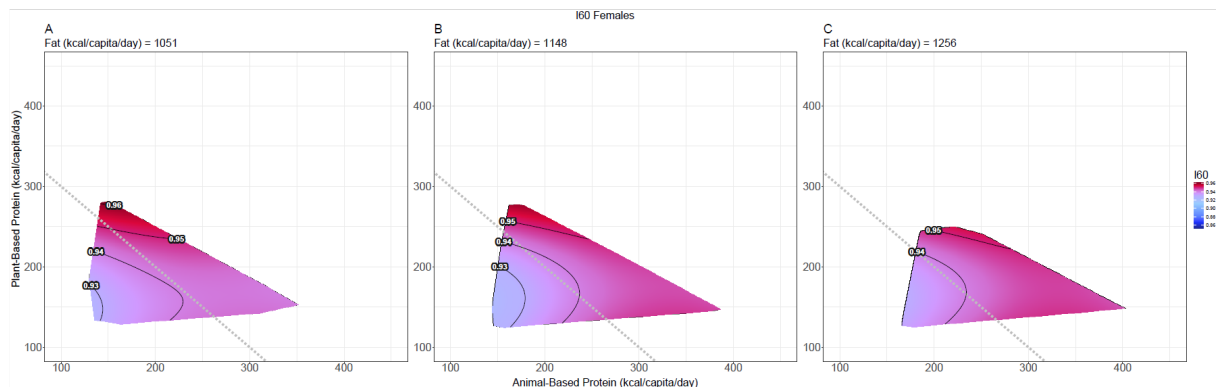


Figure 4. Surfaces for female survivorship to age 60, based on the ‘energy-controlled’ models, as described in the above response to reviewer #3.

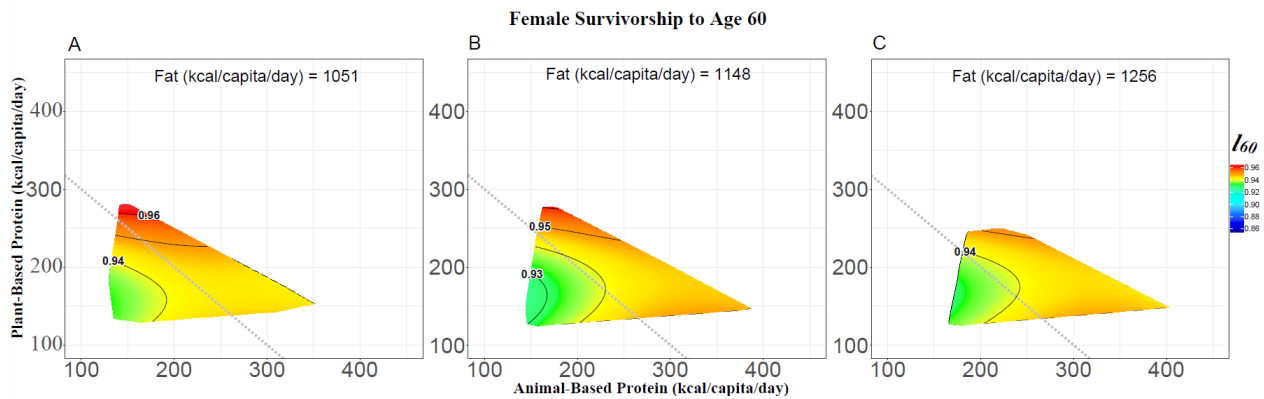


Figure 5. Surfaces for female survivorship to age 5, based on the models described in our manuscript. (Figures 3A-C in final manuscript)

☒ **2. The second important limitation is that dietary carbohydrates and fat are each modeled as homogeneous macronutrients, which ignores the heterogeneity within each macronutrient (refined carbohydrates, fiber, sugar, saturated fats, poly-unsaturated fats, etc.) and their effects on health. For instance, various types of fatty acids have heterogeneous associations with survival (PMID: 27379574). Thus, defining the type of fat is important when presenting results for the substitution of fats for protein and the type of carbohydrate is relevant when comparing against protein intake. The authors need to explicitly state the type of macronutrient being compared to protein intake.**

The reviewer is correct that this is a limitation of the analyses and data. We acknowledge that different types of fatty acids have varying associations with health outcomes, as noted in the referenced paper (PMID: 27379574). Our data only measures overall nutrient supply available for human consumption and distinguishes between food sources of macronutrients (e.g. plant vs. animal) but not subtypes of macronutrients such as saturated vs. polyunsaturated fats and refined vs. unrefined carbs.

Supplies of these nutrient subtypes may well co-vary with availability of animal- and/or plant-based proteins; ABP sources often come with more saturated fats, while PBP sources are typically associated with unsaturated fats^{17–20}. This correlation makes it challenging to separate the effects of protein from associated fat types.

However, this issue is not unique to our analysis. For example, the referenced study (PMID: 27379574) examines dietary fat while accounting for total protein without distinguishing protein source. Similarly, we cannot differentiate between fat types in our protein analysis. This highlights a common challenge in nutritional epidemiology regarding covariances among dietary components.

We have explicitly stated these limitations in our discussion (lines 360-367) and updated line 383-384 with references to provide clearer context.

Lines 358 – 370 previously read (previously lines 329-332):

“...as extensively detailed elsewhere²¹, there can be discrepancies between foods supplies and habitual diet. While these issues make assigning the effect of the nutritional environment directly to diet difficult, our findings still emphasise the potential side effects of shifts to more sustainable food systems on population survivorship.”

Lines 358-370 now read:

“As detailed elsewhere and above²¹, discrepancies can arise between foods supplies and habitual diets due to factors such as food wastage, processing losses and variations in individual consumption patterns. Additionally, to maintain the interpretability of our models, our analyses do not account for the heterogeneity within the carbohydrate and fat supplies, such as the differences between refined carbohydrates, fibre, and sugar, as well as between saturated and polyunsaturated fats. The current analyses

focus on the impacts of protein sources. Specifically, we examine the potential effects of reduced animal-based food production, resulting in the substitution of ABP for PBP and/or a reduction in total protein supplies on age-specific mortality. It should therefore be noted that our results may not fully capture the true impact of variations in carbohydrate and fat supplies on mortality outcomes. While these issues make assigning the effect of the nutritional environment directly to diet a vexed issue, our findings emphasise the potential side effects of shifts to more sustainable food systems on population survivorship.”

☒ ***3. The study design (ecological study) must be clearly stated in the abstract, and methods section. The first mention of the study design occurs in the discussion section (line 252). Moreover, an explicit mention of the ecological fallacy limitation (i.e., those who replaced ABS with PBS are not necessarily those who experienced reductions in mortality) must be included in the limitations.***

In this revised version we have made clear that our study is ecological. This includes adjustments in the abstract, discussion and methods. See lines 20-21, 345, and 408-409.

For reference, lines 20-21 now read:

“To explore how this transition may relate to demographic patterns, we undertook an ecological analysis of global associations between age-specific mortality, total national macronutrient distributions, and protein substitution.”

Lines 345-349 previously read (previously lines 322-323):

“As an ecological study our findings overlook intra-population variations in dietary patterns, and the possibility of unaccounted for confounding variables should be considered.”

Lines 345-349 now read:

“As an ecological study our findings overlook intra-population variations in both the nutritional environment and dietary patterns and are based on national food supply data rather than individual dietary intake. This distinction is important as it highlights the broader availability of nutrients rather than specific consumption behaviours, and the possibility of unaccounted for confounding variables should be considered.”

The first sentence of Methods previously read (previously line 367):

“To build our dataset we combined data from several sources.”

The sentence now reads (now at lines 408-409):

“To build our dataset we combined data from several sources, incorporating ecological design principles to ensure a comprehensive analysis of the environmental impacts of dietary shifts.”

Other comments:

☒ ***Lines 63-65: The sentence “Protein intake appears to exhibit a non-linear relationship with all-cause mortality...” needs to clarify that this association is relative to calories from the entire diet.***

Sentence adjusted as suggested. See lines 57-59.

Previously read:

“Protein intake appears to exhibit a non-linear relationship with all-cause mortality, with both low and high protein intakes associated with increased mortality risk^{5,22-27}.”

Now reads:

“At the level of individual intakes, protein appears to exhibit a non-linear relationship with all-cause mortality, relative to total caloric intake in the diet, with both low and high protein intakes associated with increased mortality risk^{23,27}.”

☒ ***Lines 69-70; the wording of the sentence “High intake of animal protein, processed and with less certainty unprocessed red meats, has been associated...” is unclear.***

Sentence adjusted for clarity. See lines 63-66.

Previously read:

“High intake of animal protein, processed and with less certainty unprocessed red meats, has been linked to an increased risk of certain chronic diseases, including cardiovascular disease, type 2 diabetes, and some types of cancer”

Now reads:

“In particular, high intake of processed meats and – with less certainty – unprocessed red meats, has been linked to an increased risk of certain chronic diseases, including cardiovascular disease, type 2 diabetes, and some types of cancer”

☒ ***Lines 85-86: The introduction of the GFN methodology lacks references***

References added. See line 80.

☒ ***Line 91: There is an extra ‘to’ after the period***

Resolved. See line 85.

☒ ***Line 132: Define the acronym LT***

LT acronym removed from paper.

☒ ***Line 242: The words ‘adding energy from any protein source’ suggest an additive effect, which is consistent with the statistical models. However, this is inconsistent with the intended substitution effects presented in the rationale of the study.***

As discussed above, the aim of the GFN is to partition effects of absolute supply and substitution in an isocaloric setting. Additionally, lines 35-37 in the introduction set up rationale of study to consider the effects of both substitution and total reduction.

“Reduced production of animal-based foods is likely to result in a substitution of animal-based protein (ABP) for plant-based protein (PBP) and/or a reduction in total protein supplies within food systems²⁸.”

The referenced line (now at line 278):

“While our findings reinforce the benefits of ABP for early life survivorship, it is crucial to acknowledge the potential role of PBP, particularly in resource-constrained environments. In these settings – specifically, regions with limited ABP and fat supplies – **our results indicated that adding energy from any protein source, plant or otherwise, was beneficial.** This supports the idea that our findings do not refute the advantage of incorporating PBP in a malnourished environment^{29,30}.”

refers to the increase in early life survivorship that can be seen when starting from low ABP on any low-fat surface and increasing protein supplies in any direction (i.e. any increase in total protein, regardless of the ratio of ABP:PBP is associated with increased early life survivorship, when starting from a low fat and low ABP environment.)

☒ ***Figure 5. The mention of total energy intake for males and females makes it unclear whether the models were adjusted for total energy intake. This is important for the reasons stated above and also to account for decreasing total energy intakes with age (PMID: 33838032).***

The analyses in figure 5 convey the relative effects of two (ABP- vs PBP-dominated) nutritional environments in each sex, held constant (incl. total energy) across all ages. The exact values for males are females are given in the figure legend, and we have edited the figure legend to try and make clearer what is shown.

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REVIEWER COMMENTS

Reviewer #1 (Remarks to the Author):

☒ The reviewers have fully addressed the comments.

Reviewer #2 (Remarks to the Author):

☒ I'm fine with most of the changes made but I think the authors should make it clearer that national food supplies can only give us ideas about the biological effects of any level of type of nutrient on survival.

The discussion makes clear in several places that the power for our analysis to pinpoint how these associations arise is limited. In addition, the following text (shown in bold) has now been added to the conclusions (at lines 406-409) to clarify this point:

*“Our analysis of historical associations between protein supplies and age-specific mortality patterns predicts the potential impact of transitioning from ABP to PBP. Our results indicate that low overall protein supplies negatively associate with survivorship across all age intervals. In the context of energy sufficiency, higher proportions of ABP supplies associate with greater improvement in early life survivorship, while nutritional environments richer in PBP maximise later life survivorship and overall life expectancy. We also note, similarly, high fat supplies may be beneficial in early life, but detrimental later throughout life. **However, it is important to note that while national food supplies can highlight potential trends and associations, they are not definitive in establishing the direct biological effects of specific nutrient levels on survival. Although** we cannot establish causality, these patterns align with existing literature linking diet and healthspan in humans, particularly the long-term advantages of consuming a plant-based diet. In the context of advocating for decarbonisation of food systems, especially the shift from animal-based to plant-based products, our findings stress the importance age-specific considerations.”*

Reviewer #3 (Remarks to the Author):

I thank the authors for addressing most of the points raised during the initial review. I am including additional comments on points that were incompletely addressed and a list of additional notes on the revised content.

Main comments:

1. In response to the authors (text included here):

☒ a. I did not find the isolines for 3023, 3120, and 3228 kcal per capita per day in Figure 2 as mentioned above. The figure shows the adjustment for NPE, not total calories. Please clarify this point.

For clarity, the word ‘isoline’ has been added to the label pointing to the grey, dashed isolines in Figures 2A, 3A and 4A. We have also included breakdowns of NPE + PE in brackets next to the total energy supplies listed at line 167-172.

Lines 167-172 previously read:

“The grey dashed isolines on Figure 2 at 400 kcal/capita/day total protein energy (PE) supplies, show the effects of isocalcorically substituting ABP for PBP (and vice versa) while holding total energy supplies constant at 3023, 3120 and 3228 kcal/capita/day (Figures 2A and 2D, Figures 2B and 2E, and Figures 2C and 2F, respectively).”

Lines 167-172 now read:

“The grey dashed isolines on Figure 2 at 400 kcal/capita/day total protein energy (PE) supplies, show the effects of isocalcorically substituting ABP for PBP (and vice versa) while holding total energy supplies constant at 3023 (non-protein energy (NPE) + PE = 2623 + 400), 3120 (NPE + PE = 2720 + 400) and 3228 (NPE + PE = 2828 + 400) kcal/capita/day (Figures 2A and 2D, Figures 2B and 2E, and Figures 2C and 2F, respectively).”

The figure at the top of the panel shows the adjustment for non-protein energy (NPE) on the surface, while the isolines indicate the points on each surface at which total protein energy (i.e., ABP + PBP) is equal to 400kcal/capita/day. Hence, along this isoline both NPE and protein energy (PE) are held constant, yielding a constant total energy for macronutrient energy. As such, total energy is held constant along these diagonal lines,

with the only difference being the fraction of the 400kcal protein coming from ABP vs PBP.

☒ b. Please provide the results for the models adjusted for total energy intake in a summary table or figure. The claim that these are identical to the main results is difficult to evaluate in the absence of data.

We re-ran our models with the inclusion of total macronutrient energy as a covariate, as suggested by reviewer #3 in the first round of revision. We found no change in results, reinforcing that controlling for total energy is not meaningful in the context of our GFN analyses. To illustrate the concordance of results for the reviewer, here we have included (1) a comparison of surfaces between total energy adjusted models, and the unadjusted models in the main text, (2) a tabulation of the comparable terms from the adjusted and unadjusted models, and (3) the 2D projection of the predicted change across our isolines indicating the substitution of PBP for ABP from the adjusted and unadjusted models.

First, we have included the resulting surfaces for male and female survivorship at ages 5 and 60 from adjusted and unadjusted models, based on the 'total macronutrient energy' adjusted models. Figure R1 vs R2 show survivorship for females at age-5 in adjusted and unadjusted modes. Figure R3 vs Figure R4 show survivorship for females at age-60 in adjusted and unadjusted modes. Figure R5 vs R6 show survivorship for males at age-5 in adjusted and unadjusted modes. Figure R7 vs Figure R8 show survivorship for males at age-60 in adjusted and unadjusted modes. In all instances the surfaces for adjusted and unadjusted models show the same association.

Second, in table R1 below is the statistical output for comparable terms from the total energy adjusted and unadjusted GAMMs. In all instances the terms have identical statistical interpretation.

Finally, have also included an additional figure R9 below that shows the changes in survivorship along the 400 kcal/capita/data protein energy supply isolines, while holding total macronutrients energy supply at 3120 ($NPE + PE = 2720 + 400$). This is effectively the predicted effects of PBP for ABP substitution as predicted by the unadjusted models in the manuscript (black-dashed lines) vs the energy adjusted models (red lines) are shown. In all cases the sign and shape the predicted effect of substitution is identical.

We want to reiterate our position that we do not believe it is appropriate or necessary to include total macronutrient energy as a covariate. After modelling all macronutrients individually, each point on the surfaces in our manuscript already shows the total energy of the combined macronutrient supplies. Across a single surface both carbohydrate and fat are held constant. However, total energy will vary across a single surface. This is because total energy at any point on the surface will differ based on

energy from protein supplies. We have implemented the energy-adjusted models shown here for the reviewer, so that they can see including total energy as a covariate does not alter the results of our analyses.

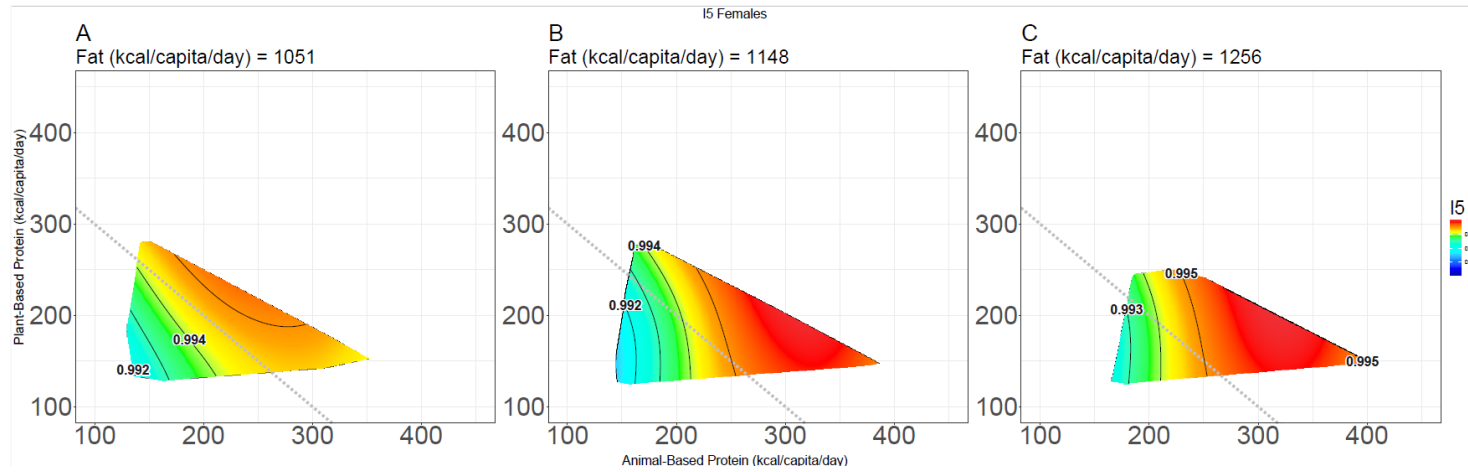


Figure R1. Surfaces for female survivorship to age 5, based on the 'energy adjusted' models requested.

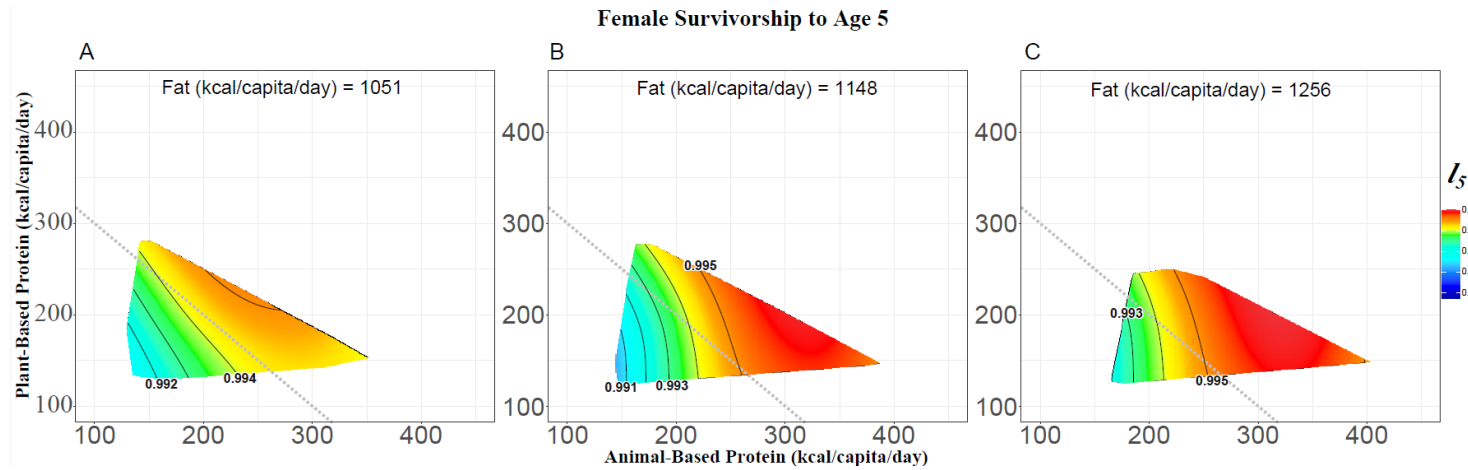


Figure R2. Surfaces for female survivorship to age 5, based on the 'unadjusted' models described in our manuscript.
(Figures 2A-C in manuscript)

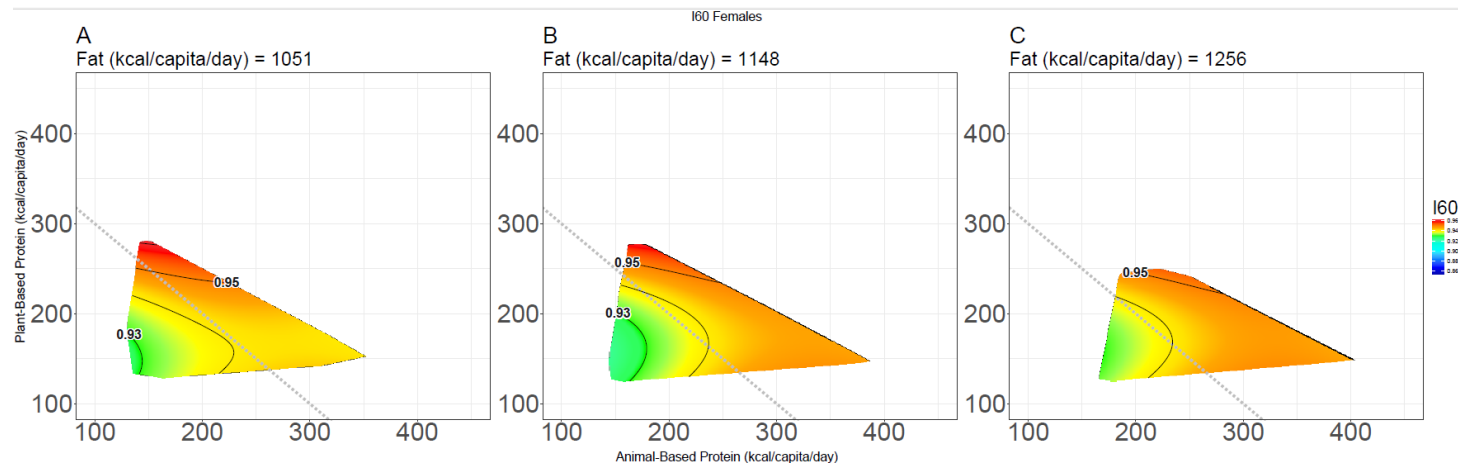


Figure R3. Surfaces for female survivorship to age 60, based on the 'energy adjusted' models requested.

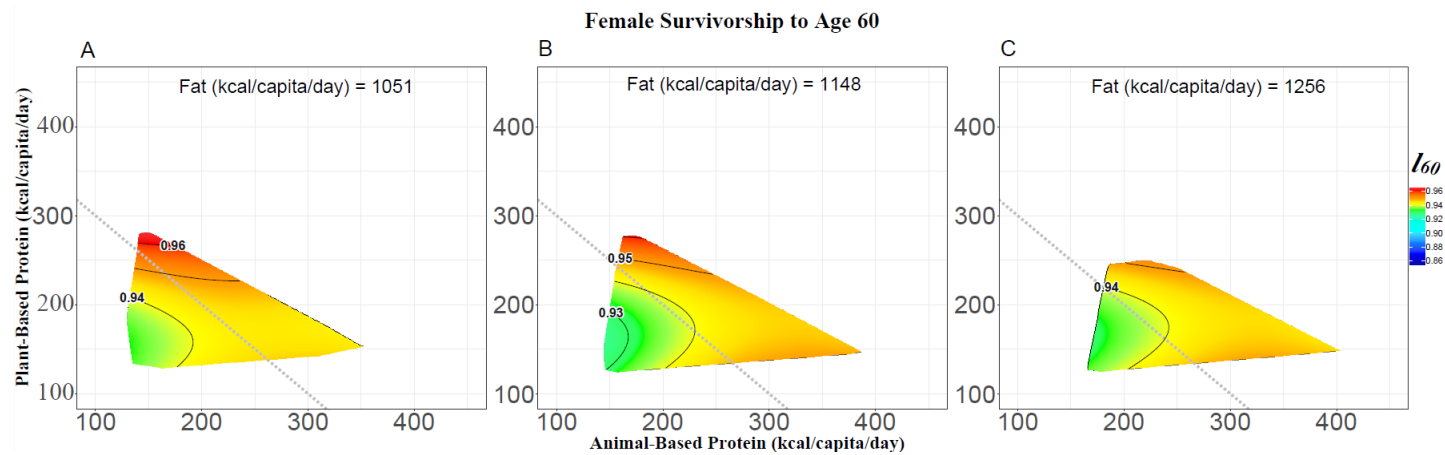


Figure R4. Surfaces for female survivorship to age 60, based on the 'unadjusted' models described in our manuscript. (Figures 3A-C in manuscript)

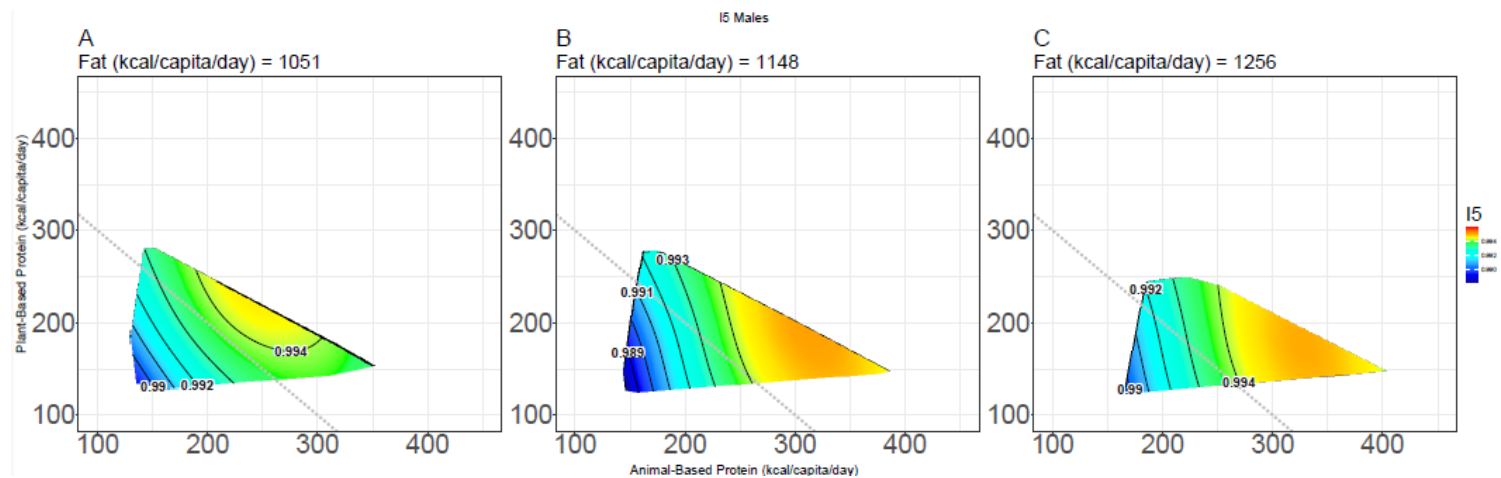


Figure R5. Surfaces for male survivorship to age 5, based on the ‘energy adjusted’ models requested.

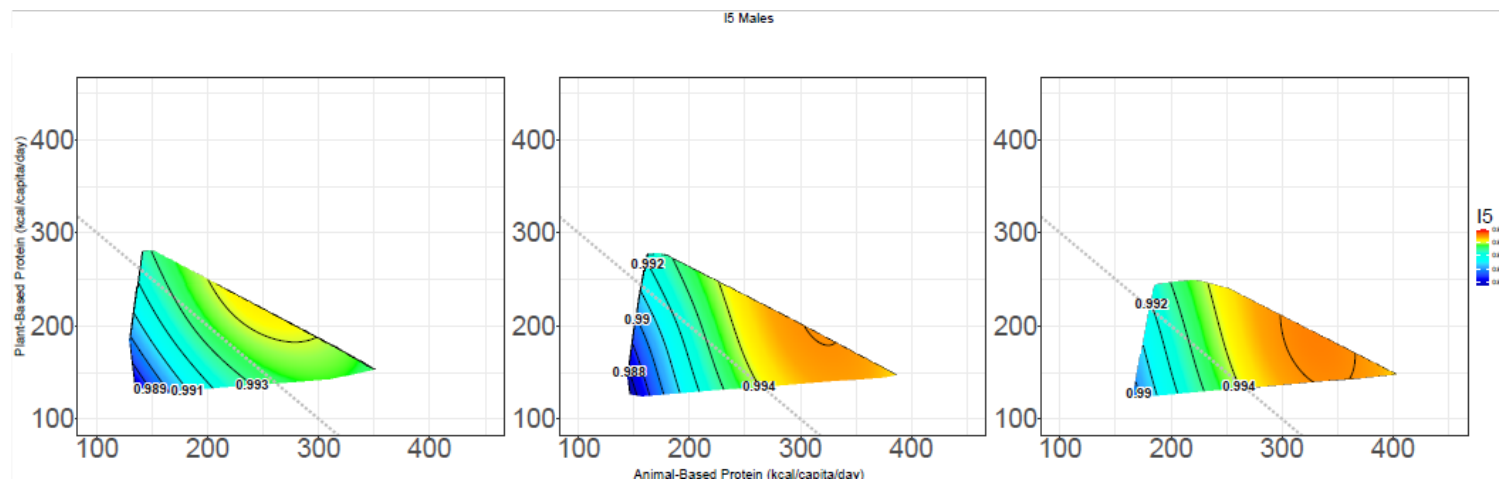


Figure R6. Surfaces for male survivorship to age 5, based on the ‘unadjusted’ models described in our manuscript. (Figures 2D-F in manuscript)

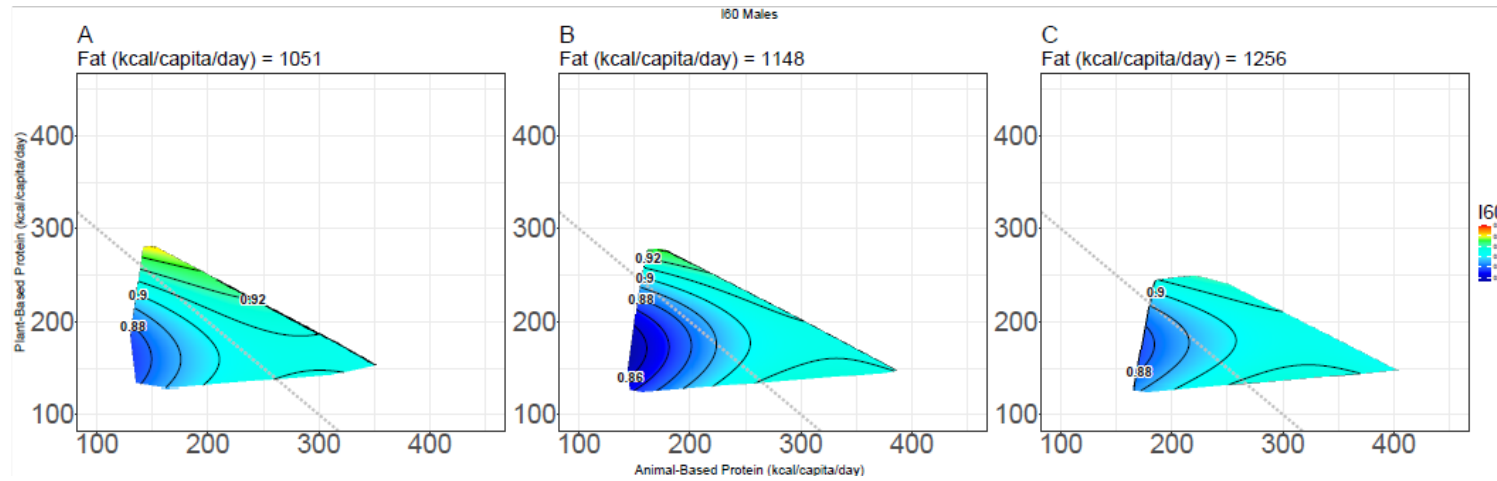


Figure R7. Surfaces for male survivorship to age 60, based on the 'energy adjusted' models requested.

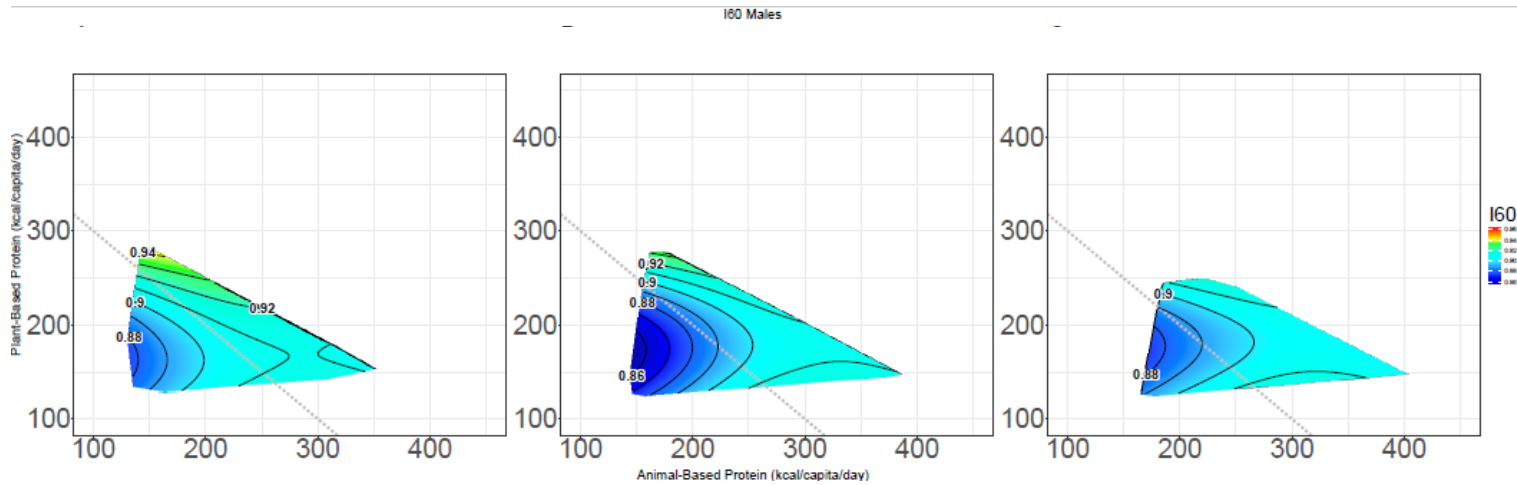


Figure R8. Surfaces for male survivorship to age 60, based on the 'unadjusted' models described in our manuscript. (Figures 3D-F in manuscript)

Table R1. Equivalent output from GAMMs, including total macronutrient energy as an adjustment, and without.

Males Age 5		‘Energy Adjusted’ Model				‘Unadjusted’ Model - Main Text			
Parametric Coef.		Estimate	Std. Error	z value	p-value	Estimate	Std. Error	z value	p-value
(Intercept) l_5		3.93562	0.03193	123.3	<0.001	3.94	0.03	123.30	<0.001
Non-Parametric Coef.		edf	Ref.df	Chi.sq	p-value	edf	Ref.df	Chi.sq	p-value
te(ABP.kcal, PBP.kcal, Fat.kcal, Year)		73.612	94.217	1077.438	<0.001	73.61	94.22	1319.41	<0.001
te(Carb.kcal, Year)		10.641	12.920	77.864	<0.001	11.64	13.92	78.15	<0.001
s(GDP_perCapita, Year)		14.203	94.000	2648.909	<0.001	14.20	94.00	2681.56	<0.001
s(Country)		92.700	100.000	10319.824	<0.001	92.70	100.00	10325.42	<0.001
Deviance explained		98.8%				98.8%			
Females Age 5									
Parametric Coef.		Estimate	Std. Error	z value	p-value	Estimate	Std. Error	z value	p-value
(Intercept) l_5		4.13969	0.03334	124.2	<0.001	4.14	0.03	124.60	<0.001
Non-Parametric Coef.		edf	Ref.df	Chi.sq	p-value	edf	Ref.df	Chi.sq	p-value
te(ABP.kcal, PBP.kcal, Fat.kcal, Year)		72.507	93.086	1322.838	<0.001	72.08	92.28	1366.70	<0.001
te(Carb.kcal, Year)		11.427	13.808	90.892	<0.001	12.24	14.56	109.40	<0.001
s(GDP_perCapita, Year)		5.550	92.000	2659.605	<0.001	12.56	94.00	2877.60	<0.001
s(Country)		92.536	100.000	9820.111	<0.001	92.44	100.00	9756.30	<0.001
Deviance explained		98.8%				98.8%			

Males Age 60								
Parametric Coef.	Estimate	Std. Error	z value	p-value	Estimate	Std. Error	z value	p-value
(Intercept) l_{60}	1.42961	0.02239	63.86	<0.001	1.43	0.02	64.38	<0.001
Non-Parametric Coef.	edf	Ref.df	Chi.sq	p-value	edf	Ref.df	Chi.sq	p-value
te(ABP.kcal, PBP.kcal, Fat.kcal, Year)	73.831	94.677	2168.20	<0.001	74.92	96.10	2397.2	<0.001
te(Carb.kcal, Year)	6.090	6.965	57.05	<0.001	7.15	8.022	76.4	<0.001
s(GDP_perCapita, Year)	16.497	94.000	4233.48	<0.001	17.72	94.00	4665.3	<0.001
s(Country)	90.499	100.000	11305.74	<0.001	90.43	100.00	11305.5	<0.001
Deviance explained	98.1%				98.1%			

Females Age 60								
Parametric Coef.	Estimate	Std. Error	z value	p-value	Estimate	Std. Error	z value	p-value
(Intercept) l_{60}	2.05820	0.02136	96.38	<0.001	2.06	0.02	97.12	<0.001
Non-Parametric Coef.	edf	Ref.df	Chi.sq	p-value	edf	Ref.df	Chi.sq	p-value
te(ABP.kcal, PBP.kcal, Fat.kcal, Year)	71.039	91.210	2582.08	<0.001	71.544	91.80	3147.60	<0.001
te(Carb.kcal, Year)	6.437	7.238	85.99	<0.001	7.58	8.35	126.90	<0.001
s(GDP_perCapita, Year)	6.036	91.000	2518.62	<0.001	6.495	92.00	3030.10	<0.001
s(Country)	91.173	100.000	10133.04	<0.001	91.10	100.00	10371.00	<0.001
Deviance explained	98.7%				98.7%			

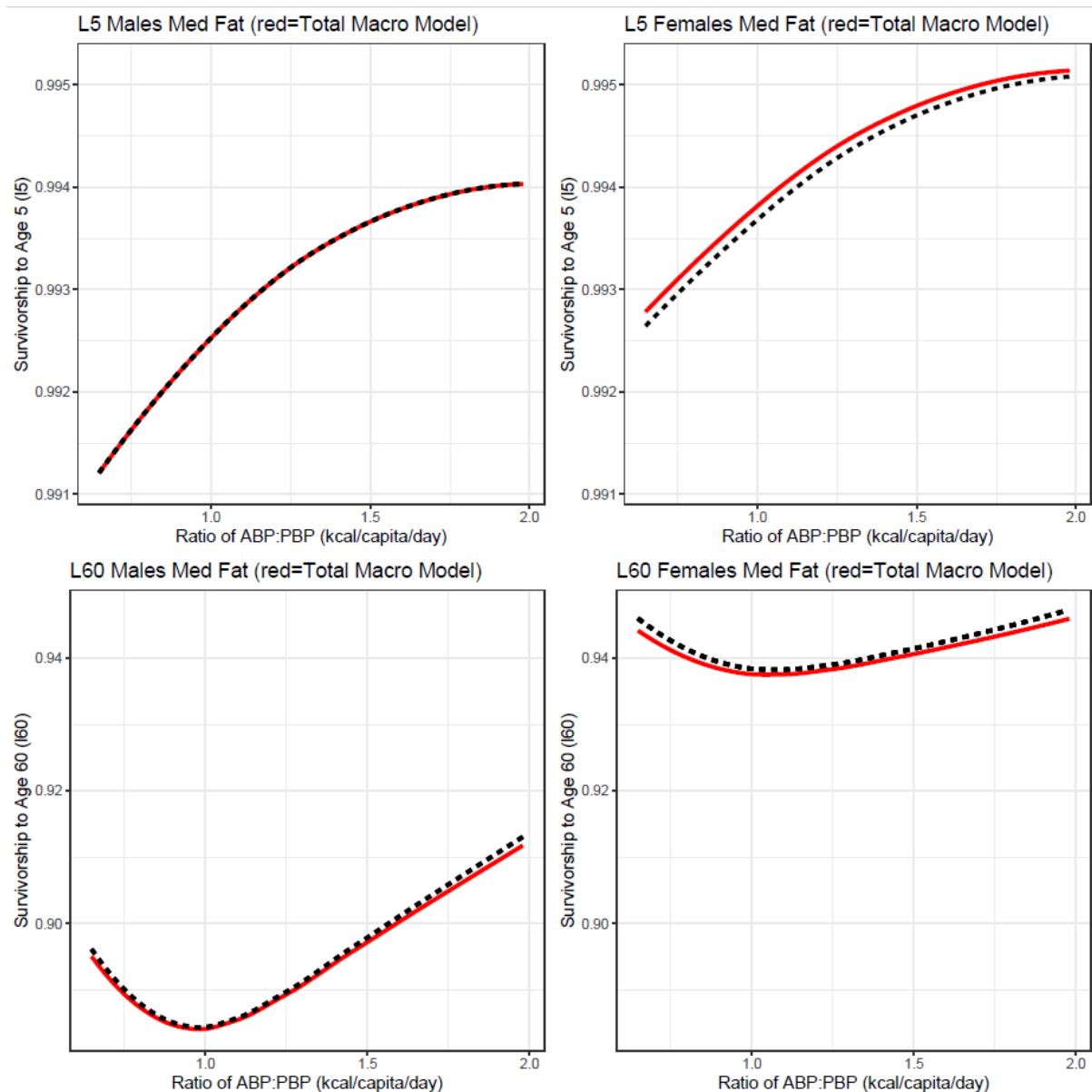


Figure R9. Change in survivorship as a function of changing the ratio of ABP to PBP along the 400kcal/capita/day protein energy isolines shown in Figures 2 and 3 of the manuscript. The black-dashed line shows survivorship outcomes based on the models described in the manuscript. The red lines show survivorship outcomes based on the 'total macronutrient energy' adjusted models that were run for illustration purposes in response to reviewer #3.

☒2. Figure 2 presents survivorship to age 5. Are the calorie intakes and the respective calories from protein and NPE assessed at age 5? The intakes do not match the averages for those ages. Could you please describe the method used to assess calories for survival to age 5?

Our analysis does not test for effects/associations between average age-specific intakes and survivorship at any point. We have analysed the associations between kcal of macronutrient per capita and survivorship. Our nutritional data are based on food balance sheets, which are the total nutrient supplies of a nation (production – export + import) divided by the population size. This number is a national per capita statistic and is not age-specific (e.g., just as GDP per capita is the same for all people in a country).

In the previous revision of the manuscript, we added an extensive description of where our nutritional data came from (lines 98-100; 114-124; 419-430), that supply-level analysis provides a different and complementary perspective to an intake-based analysis (lines 226-238). We have double checked all aspects of the paper to ensure we do not inadvertently refer to our analyses as being an intake-based analysis; we can find not instance of this.

Other comments:

☒ 1. Please include a brief description of ‘food systems’ in the introduction. The concept is introduced in line 33 and referred to subsequently, but it is not clear.

We have included a definition of food systems based on the published literature. The following text (shown in bold) has been added to the introduction at lines 34-35:

*“In an era marked by the pressing need for decarbonization and environmental sustainability, global food systems, which contribute a third of all greenhouse gas emissions, are under increasing scrutiny¹. **Food systems are complex social-ecological networks that encompass all processes and infrastructure involved in feeding a population². Many have argued that a reduction in the production of animal-based foods is key to achieving more sustainable food systems³.**”*

☒ 2. Line 23: The year range should read: “from 1961 to 2018” or “ranging 1961-2018”

Adjusted as suggested. Lines 22-23 now read:

“Our dataset includes per capita daily food supply and demographic data for 101 countries from 1961 to 2018.”

☒ 3. Line 56: The term “its relationship to carbohydrate” is unclear. Please define.

Line 56 (now lines 57-59) previously read:

“At the level of diet composition, recent reviews^{10,11} suggest that protein content, and, particularly, its relationship to carbohydrate, plays a vital role in shaping age-related health outcomes.”

Lines 57-59 now read:

“At the level of diet composition, recent reviews^{10,11} suggest that protein content, and, particularly, its amounts relative to the quantity of carbohydrate, plays a vital role in shaping age-related health outcomes.”

☒4. Lines 62 and 74: Please replace “effects” with “associations” as the references cited (16, 17, and 23) are observational studies.

Line 62 (now at lines 65-67) previously read:

“At the dietary level, the of protein on mortality also appear to vary depending on the source, with ABP potentially having a greater impact on mortality than PBP sources^{16,17}. ”

Lines 65-67 now read:

“At the dietary level, the associations between protein and mortality also appear to vary depending on the source, with ABP potentially having a greater impact on mortality than PBP sources^{16,17}. ”

Line74 (now at lines 76-78) previously read:

“The differential effects of protein sources have been attributed to various dietary factors, such as nutrient composition and bioactive compounds²³. ”

Lines 76-78 now read:

“The differential associations of protein sources have been attributed to various dietary factors, such as nutrient composition and bioactive compounds²³.”

☒5. Lines 91 and 92. Please specify the age ranges for which the dietary data is available.

See response to main comment 2 above.

☒6. Lines 111, 119, 123, 148, 205: “Daily per caput” should read “daily per capita”.

All instances now read “*daily per capita*”

☒7. Line 177: Please replace “effects” with “associations”. Same in lines 180/181, and 192

Line 177 (now at lines 181-183) previously read:

“Here we see beneficial effects of elevating average daily protein supplies in the animal or plant-based dimension...”

Lines 181-183 now read:

*“Here we see **beneficial associations** when elevating average daily protein supplies in the animal or plant-based dimension...”*

Lines 180-181 (now at lines 185-187) previously read:

“While there was a positive effect of fat on l_5 , this effect appeared to reverse at older age with l_{60} peaking at low fat (Figures 2A – 2F vs Figures 3A – 3F).”

Lines 185-187 now read:

*“While there were **positive associations** between fat and l_s , this appeared to reverse at older age with l_{60} peaking at low fat (Figures 2A – 2F vs Figures 3A – 3F).”*

Line 192 (now at lines 197-199) previously read:

“A beneficial effect of PBP was seen with low to moderate ABP and fat supplies (Figures 4A-4B and Figures 4D-4E), such that e_0 was maximised where PBP is high and ABP and fat supplies were low.”

Lines 197-199 now read:

“A beneficial association between PBP and e_0 was seen with low to moderate ABP and fat supplies (Figures 4A-4B and Figures 4D-4E), such that e_0 is maximised where PBP is high and ABP and fat supplies are low.”

☒ 8. Lines 339 and 341: Please replace “impact” and “effect” with associational language, perhaps “unfavorably associated”.

Lines 339-341 (now at 344-348) previously read:

“Additionally, we observed a negative impact of higher fat in later life, potentially explained by overnutrition resulting from the higher energy density of dietary fat compared to carbohydrate and protein⁶⁷. This detrimental effect was particularly pronounced when combined with ABP consumption, indicating a synergistic negative influence.”

Lines 344-348 now read:

*“Additionally, we observed **unfavourable associations** between higher fat and survivorship in later life, potentially explained by overnutrition resulting from the higher energy density of dietary fat compared to carbohydrate and protein⁶⁷. This **detrimental***

***relationship** was particularly pronounced when combined with ABP consumption, indicating a synergistic negative influence.”*

1. Crippa, M. *et al.* Food systems are responsible for a third of global anthropogenic GHG emissions. *Nat Food* **2**, 198–209 (2021).
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4. Willett, W. *et al.* Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *Lancet* **393**, 447–492 (2019).
5. Vermeulen, S. J., Campbell, B. M. & Ingram, J. S. I. Climate change and food systems. *Annu. Rev. Environ. Resour.* **37**, 195–222 (2012).
6. Allen, T. & Prosperi, P. Modeling sustainable food systems. *Environ. Manage.* **57**, 956–975 (2016).
7. Béné, C. *et al.* When food systems meet sustainability – Current narratives and implications for actions. *World Dev.* **113**, 116–130 (2019).