# **Legume consumption and risk of metabolic dysfunction-associated steatotic liver disease in the UK Biobank Study**

## Background

To reduce climate impacts of our diets the EAT-Lancet reference diet was introduced in 2019 as a globally sustainable and healthy diet with a large emphasis on plant-based proteins instead of animal-based proteins, e.g., with a recommendation of 100 g legumes daily (1-3). Legumes are the pods and fruits from the Leguminosae or Fabaceae plant families (4). The climate impact of legumes is undoubtedly low (4-7), however the scientific evidence to support that 100 g of legumes/day improves health is sparse. Legumes are good sources of protein, low in saturated fat and energy density, and rich in dietary fibre; all components associated with a healthy diet (8, 9).

**Animal** studies imply that legume consumption **minimizes the risk of metabolic dysfunction-associated steatotic liver disease (MASLD) by reducing build-up of fats in the liver** (10-14)**.** MASLD is the most prevalent chronic liver disease in the Western countries with a prevalence of 15-45 % (15, 16). MASLD is caused by Western diet high in red meat, fats, and sugars, obesity, physical inactivity, and smoking (15-18), and even children can develop the disease (19). MASLD is the liver manifestation of Metabolic Syndrome with shared causes and comorbidities such as abdominal adiposity, increased blood glucose levels, hypertension, and generally associated with increased risk of cardiovascular diseases (20, 21). MASLD was previously known as non-alcoholic fatty liver disease (NAFLD), but the definition was changed in 2023 to shift focus towards the metabolic factors underlying the disease and not merely the lack of alcohol consumption and to aid the prevention and early diagnoses of MASLD (22). Consumption of legume-rich compared to Western diets has been associated with overall better diet quality and greater health (23-33). Most evidence is derived from studies of dietary patterns including higher legume consumption, such as vegetarian diets. Thus, the evidence of an association is indirect and **limited (9).**

**As legumes are a source of both carbohydrates and proteins, research frequently compare legumes with other carbohydrate sources (9, 34-37).** When individuals limit intake of certain food groups, they will most often increase the intake of certain other food groups, in an otherwise stable diet (38, 39). **Replacing protein from animal sources with protein from plant sources has previously been associated with a substantially lower mortality rate (40).** An Asian study substituting a whole serving of animal-based foods with a whole serving of plant-based foods has shown to be beneficial against MASLD (11). The key question remains, how the replacement of different amounts of meats, poultry, or fish with legumes impacts the risk of MASLD. Consumption of legumes in the Western countries has been negligible to date and the impact of markedly increasing intakes of legumes on hepatobiliary and other diseases is understudied. Therefore, this study aims to investigate the effect of replacing meats, poultry, or fish with legumes and the risk of metabolic dysfunction-associated steatohepatitis (MASH) or MASLD contingent on potential confounding factors. As it might be more feasible for Western populations to include legumes and substituting dietary components that are not meats, this study will also aim to investigate the association between total consumption of legumes and MASLF and MASH.

**Hypotheses**

* Replacing meats and poultry intakes with legumes is associated with a lower risk of MASLD and MASH.
* Replacing fish intake with legumes is not associated with a lower risk of MASLD and MASH.

## Methods

**Study population and setting**

The initial recruitment of participants for the UK Biobank started in 2006 and ran until June 2010. Of 9.2 million people identified from the National Health Service registers and invited to participate in the study, 5.5% participated, approximately 500,000 participants, aged 37-73 years at baseline. The study protocol and more information are available elsewhere (41, 42). At baseline, participants provided detailed information on several sociodemographic, physical, lifestyle, and health-related characteristics via self-completed touch-screen questionnaires and a computer assisted personal interview (43). Professionally trained staff did physical, anthropometric, and biomedical measures following standardized procedures (41). Diet was assessed through a touchscreen questionnaire at baseline and a 24-hour dietary assessment tool designed for the UK Biobank study. 210,965 individuals completed one or more 24-hour dietary assessments (44). All participants gave written, informed consent prior to baseline, and the study was approved by the National Information Governance Board for Health and Social Care and the National Health Service North West Multicentre Research Ethics Committee (reference number 06/MRE08/65).

For the current study, only participants with two or more 24 h dietary assessments will be included in the analyses, while missing information on covariates will be filled in by statistical imputations where applicable.

**Assessment of diet**

The Oxford WebQ was designed as an internet based 24-hour dietary assessment tool for measuring diet on repeated occasions. The questionnaire is a short set of food frequency questions on commonly eaten food groups in the British population on the day before. The questionnaire aims to measure the type and quantity of food and beverages consumed in the last 24 hours and estimate nutrients from the entered information through the UK Nutrient Databank Food Composition Tables (45, 46). The Oxford WebQ was compared with interviewer administered 24-hour dietary recalls and validated for macronutrients and total energy intake using recovery biomarkers and comparing with a single food frequency questionnaire (45, 47, 48). Recently, the Oxford WebQ nutrient calculation was updated to provide more detailed information on nutrient intakes and to incorporate new dietary variables (46).

Participants recruited between April 2009 and September 2010 completed the Oxford WebQ at baseline (n=70,747). The Oxford WebQ was not available until April 2009 and participants recruited before that date who provided a valid email address were invited to complete the four subsequent 24-hour dietary assessments online (49).

**Legumes**

Legume consumption will be estimated based on participants reported diets from the self-administered online 24-hour dietary assessments, the Oxford WebQ. Consumption of legumes and pulses will be based on total weight by food group intakes estimated from participants’ responses in the Oxford WebQ. Despite the high detail level of the Oxford WebQ, a single 24-hour dietary assessment cannot capture habitual intake of legumes in a UK-setting (50). Therefore, this study will include varying numbers of 24-hour dietary assessments to ensure that we capture usual intake of legumes.

**Meat, poultry, and fish**

Consumption of red and processed meats, poultry, and fish will be based on total weight by food group intakes estimated from participants’ responses to the Oxford WebQs.

Red and processed meat will be defined as beef, pork, lamb, and other meats including offal, and processed meat including sausages, bacon, ham, and liver paté. Poultry will be defined as poultry with or without skin, and fried poultry with batter or breadcrumbs. Fish will be defined as oily fish, white fish and tinned tuna, fried fish with batter or breadcrumbs, and shellfish.

**Metabolic dysfunction-associated steatotic liver disease**

Incident cases of MASH and MAFLD will be assessed through linkage to the National Health Service registers where diagnosis after hospital admission or primary care visits are coded according to the International Classification of Diseases and Related Health Problems (ICD-10) (51). Due to a recent change in the definition of MASLD, incident cases of MASLD are diagnosed based on ICD-10-code for NAFLD, K76.0, at first admission to hospital, while incident cases of MASH are diagnosed based on ICD-10-code for NASH, K75.8 (52).

**Covariates**

The directed acyclic graph presented below (Figure 1) illustrates the potential and known association between covariates of the association between legume consumption and development of MASLD and NASH.

Information on covariates will include information on all other dietary components based on total weight by food group intakes as g/day and kcal/day retrieved from the Oxford WebQ (fruits, vegetables, cereal products, dairy products, egg products, nuts, mixed dishes, condiments, added sugar and sweets, non-alcoholic beverages, and alcoholic beverages), sex (male, female), age (years), alcohol consumption (g ethanol/day as restricted cubic splines), ethnic group (white, mixed background, Asian, black, other, and unknown), socioeconomic status (Townsend deprivation score [quintiles], educational level), geographical region of recruitment (ten UK regions), lives with a wife or partner (yes, no), anthropometry (BMI [kg/m2]), physical activity (low [0-9.9 METs/week], moderate [10-49.9 METs/week], and high [≥50 METs/week], unknown), smoking status (never, former, current 1-15 cigarettes per day, current ≥15 cigarettes per day, current but number of cigarettes per day unknown, and smoking status unknown); history of metabolic diseases (ICD-codes [E10-E14, E78, I10-I15], and self-reported [yes, no, unknown] own or family members’ diagnoses of diabetes, hypertension, high cholesterol).

A network of lines and dots

Description automatically generated

Figure 1. Directed Acyclic Graph representing the association between replacement of animal foods with legumes and risk of non-alcoholic fatty liver and the assumed relationship with covariates. \*Own or family history with diabetes, hypertension, or high cholesterol, obesity, previous liver disease. \*\* Physical activity, smoking, alcohol consumption.

**Statistical analyses**

Standard summary statistics will be performed to describe the distribution of total legume consumption as an average g/day based on participants’ 24-h WebQ responses and across baseline characteristics of participants in the study.

Multi-variable adjusted Cox Proportional Hazards regression models will be used to estimate the hazard ratios for each of the outcomes based on replacing meats, poultry, or fish with legumes.

* Replacing red and processed meats, poultry, or fish with legumes (e.g., per 30 g/day)
* Replacing red and processed meats, poultry, or fish with legumes (e.g., per 40 kcal/day)

Age will be used as the underlying time scale in the analyses. Follow-up time will begin with participants’ last completed Oxford WebQ. As participants in UKB are still followed-up today, participants will be right censored at the date of the most recent registry update of full follow-up for the outcomes. Otherwise, censoring will occur at the event of death, loss to follow-up from the study, or date of diagnosis of MASLD or MASH, whichever comes first.

The substitution analyses will be conducted with different adjustment levels. Model 1 will be minimally adjusted for strata of age at recruitment (<45, 45-49, 50-54, 55-59, 60-64, ≤65 years) and geographical region of recruitment (ten UK regions), sex, and intake of all other dietary components apart from the substitute components (red and processed meats; poultry; fish). When substituting g legumes/day, the unit for all dietary components will be g/day and the analyses will be adjusted for total amount of consumed foods in g/day. When substituting calories of legumes, the unit for all dietary components will be calories/day and the analyses will be adjusted for total amount of consumed calories/day. Model 2 will be further adjusted for alcohol consumption, ethnic group, socioeconomic status, living with a wife or partner, physical activity, smoking status, and history of metabolic diseases. As obesity may either confound or mediate the association between replacing red and processed meats, poultry, or fish with legumes and risk of MASLD, model 3 will further adjust for anthropometry (BMI [kg/m2]).

**Secondary and sensitivity analyses**

To evaluate the association between overall legume intake and hepatobiliary disease risk, quintiles of legume intake (g/day) will be evaluated with adjustment levels similar to the substitution models.

Peas are increasingly used as a plant-based meat alternative in the food industry (53). Despite this, peas are also included in the NHS 5 A Day recommendations for fruits and vegetables consumption in the UK (54). Therefore, in sensitivity analyses consumption of legumes will include participants self-reported intake of legumes and pulses together with consumed peas. The amount of peas consumed will be estimated based on participants’ reported daily portions consumed with a portion size of peas weighing 80 g (55).

To evaluate the robustness of the main analyses, sensitivity analyses will include varying numbers of Oxford WebQ returns, imputations of missing information, and removal of participants with increased serum levels of alanine-aminotransferase (>45 U/L for women and >70 U/L for men) and aspartate-aminotransferase (>35 U/L for women and >45 U/L for men). Sensitivity analyses will further include removal of participants with alcoholic liver disease and removal of those with previous diseases of the liver, although not necessarily MASLD, as they may be predisposed for developing further liver diseases. All analyses will be conducted in R with a significance level of 5%.

**References**

1. Loken B, DeClerck, F. Diets for a better future. Oslo: The EAT-Lancet Commission on Food, Planet, Health, 2020.

2. Springmann M, Spajic L, Clark MA, Poore J, Herforth A, Webb P, et al. The healthiness and sustainability of national and global food based dietary guidelines: modelling study. BMJ. 2020;370:m2322. doi: <https://doi.org/10.1136/bmj.m2322>.

3. Willett W, Rockström J, Loken B, Springmann M, Lang T, Vermeulen S, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. Lancet. 2019;393(10170):447-92 Epub 2019/01/21. doi: <https://doi.org/10.1016/s0140-6736(18)31788-4>. PubMed PMID: 30660336.

4. Food and Agriculture Organization of the United Nations. What are pulses? : FAO; 2015 [cited 2022 23 November]. Available from: <https://www.fao.org/pulses-2016/news/news-detail/en/c/337107/>.

5. Stehfest E, Bouwman L, van Vuuren DP, den Elzen MGJ, Eickhout B, Kabat P. Climate benefits of changing diet. Climatic Change. 2009;95(1):83-102. doi: 10.1007/s10584-008-9534-6.

6. Garnett T. Livestock-related greenhouse gas emissions: impacts and options for policy makers. Environmental Science & Policy. 2009;12(4):491-503. doi: <https://doi.org/10.1016/j.envsci.2009.01.006>.

7. Weber CL, Matthews HS. Food-Miles and the Relative Climate Impacts of Food Choices in the United States. Environmental Science & Technology. 2008;42(10):3508-13. doi: 10.1021/es702969f.

8. Rebello CJ, Greenway FL, Finley JW. A review of the nutritional value of legumes and their effects on obesity and its related co-morbidities. Obes Rev. 2014;15(5):392-407. Epub 2014/01/18. doi: 10.1111/obr.12144. PubMed PMID: 24433379.

9. Lee YP, Puddey IB, Hodgson JM. Protein, fibre and blood pressure: potential benefit of legumes. Clin Exp Pharmacol Physiol. 2008;35(4):473-6. Epub 2008/03/01. doi: 10.1111/j.1440-1681.2008.04899.x. PubMed PMID: 18307744.

10. Hong J, Kim S, Kim H-S. Hepatoprotective Effects of Soybean Embryo by Enhancing Adiponectin-Mediated AMP-Activated Protein Kinase α Pathway in High-Fat and High-Cholesterol Diet-Induced Nonalcoholic Fatty Liver Disease. Journal of Medicinal Food. 2016;19:549-59. doi: 10.1089/jmf.2015.3604.

11. Zhang S, Yan Y, Meng G, Zhang Q, Liu L, Wu H, et al. Protein foods from animal sources and risk of nonalcoholic fatty liver disease in representative cohorts from North and South China. J Intern Med. 2022. Epub 20221126. doi: 10.1111/joim.13586. PubMed PMID: 36433820.

12. Bouchenak M, Lamri-Senhadji M. Nutritional quality of legumes, and their role in cardiometabolic risk prevention: a review. J Med Food. 2013;16(3):185-98. Epub 2013/02/13. doi: 10.1089/jmf.2011.0238. PubMed PMID: 23398387.

13. Son Y, Jang MK, Jung MH. Vigna nakashimae extract prevents hepatic steatosis in obese mice fed high-fat diets. J Med Food. 2014;17(12):1322-31. Epub 2014/10/31. doi: 10.1089/jmf.2014.3194. PubMed PMID: 25357150.

14. Rigotti A, Marzolo M-P, Ulloa N, González O, Nervi F. Effect of bean intake on biliary lipid secretion and on hepatic cholesterol metabolism in the rat. J Lipid Res. 1989;30:1041-8. doi: 10.1016/S0022-2275(20)38291-2.

15. Benedict M, Zhang X. Non-alcoholic fatty liver disease: An expanded review. World J Hepatol. 2017;9(16):715-32. doi: 10.4254/wjh.v9.i16.715. PubMed PMID: 28652891; PubMed Central PMCID: PMC5468341.

16. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73-84. Epub 20160222. doi: 10.1002/hep.28431. PubMed PMID: 26707365.

17. Younossi ZM, Loomba R, Rinella ME, Bugianesi E, Marchesini G, Neuschwander-Tetri BA, et al. Current and future therapeutic regimens for nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Hepatology. 2018;68(1):361-71. Epub 2017/12/10. doi: 10.1002/hep.29724. PubMed PMID: 29222911; PubMed Central PMCID: PMC6508084.

18. Al-Dayyat HM, Rayyan YM, Tayyem RF. Non-alcoholic fatty liver disease and associated dietary and lifestyle risk factors. Diabetes Metab Syndr. 2018;12(4):569-75. Epub 2018/03/25. doi: 10.1016/j.dsx.2018.03.016. PubMed PMID: 29571977.

19. Grønbæk H, Lange A, Birkebæk NH, Holland-Fischer P, Solvig J, Hørlyck A, et al. Effect of a 10-week weight loss camp on fatty liver disease and insulin sensitivity in obese Danish children. J Pediatr Gastroenterol Nutr. 2012;54(2):223-8. Epub 2011/07/16. doi: 10.1097/MPG.0b013e31822cdedf. PubMed PMID: 21760546.

20. Angulo P. GI epidemiology: nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2007;25(8):883-9. doi: 10.1111/j.1365-2036.2007.03246.x. PubMed PMID: 17402991.

21. Akter S. Non-alcoholic Fatty Liver Disease and Steatohepatitis: Risk Factors and Pathophysiology. Middle East J Dig Dis. 2022;14(2):167-81. Epub 20220430. doi: 10.34172/mejdd.2022.270. PubMed PMID: 36619154; PubMed Central PMCID: PMC9489315.

22. Thornton J. Associations rename fatty liver disease to reduce stigma. BMJ. 2023;382:p1587. doi: 10.1136/bmj.p1587.

23. Papanikolaou Y, Fulgoni VL, 3rd. Bean consumption is associated with greater nutrient intake, reduced systolic blood pressure, lower body weight, and a smaller waist circumference in adults: results from the National Health and Nutrition Examination Survey 1999-2002. J Am Coll Nutr. 2008;27(5):569-76. Epub 2008/10/11. doi: 10.1080/07315724.2008.10719740. PubMed PMID: 18845707.

24. Dinu M, Abbate R, Gensini GF, Casini A, Sofi F. Vegetarian, vegan diets and multiple health outcomes: A systematic review with meta-analysis of observational studies. Critical Reviews in Food Science and Nutrition. 2017;57(17):3640-9. doi: 10.1080/10408398.2016.1138447.

25. Becerra-Tomás N, Papandreou C, Salas-Salvadó J. Legume Consumption and Cardiometabolic Health. Adv Nutr. 2019;10(Suppl\_4):S437-s50. Epub 2019/11/16. doi: 10.1093/advances/nmz003. PubMed PMID: 31728491; PubMed Central PMCID: PMC6855964.

26. Mollard RC, Luhovyy BL, Panahi S, Nunez M, Hanley A, Anderson GH. Regular consumption of pulses for 8 weeks reduces metabolic syndrome risk factors in overweight and obese adults. Br J Nutr. 2012;108 Suppl 1:S111-22. Epub 2012/08/25. doi: 10.1017/s0007114512000712. PubMed PMID: 22916807.

27. Appleby PN, Key TJ. The long-term health of vegetarians and vegans. Proc Nutr Soc. 2016;75(3):287-93. Epub 2015/12/29. doi: 10.1017/s0029665115004334. PubMed PMID: 26707634.

28. Miller V, Mente A, Dehghan M, Rangarajan S, Zhang X, Swaminathan S, et al. Fruit, vegetable, and legume intake, and cardiovascular disease and deaths in 18 countries (PURE): a prospective cohort study. Lancet. 2017;390(10107):2037-49. Epub 2017/09/03. doi: 10.1016/s0140-6736(17)32253-5. PubMed PMID: 28864331.

29. Mitchell DC, Lawrence FR, Hartman TJ, Curran JM. Consumption of dry beans, peas, and lentils could improve diet quality in the US population. J Am Diet Assoc. 2009;109(5):909-13. Epub 2009/04/28. doi: 10.1016/j.jada.2009.02.029. PubMed PMID: 19394480.

30. Mudryj AN, Yu N, Hartman TJ, Mitchell DC, Lawrence FR, Aukema HM. Pulse consumption in Canadian adults influences nutrient intakes. Br J Nutr. 2012;108 Suppl 1:S27-36. doi: 10.1017/s0007114512000724. PubMed PMID: 22916812.

31. Bazzano LA, He J, Ogden LG, Loria C, Vupputuri S, Myers L, et al. Legume consumption and risk of coronary heart disease in US men and women: NHANES I Epidemiologic Follow-up Study. Arch Intern Med. 2001;161(21):2573-8. Epub 2001/12/26. doi: 10.1001/archinte.161.21.2573. PubMed PMID: 11718588.

32. Knuppel A, Papier K, Key TJ, Travis RC. EAT-Lancet score and major health outcomes: the EPIC-Oxford study. Lancet. 2019;394(10194):213-4 Epub 2019/06/27. doi: <https://doi.org/10.1016/s0140-6736(19)31236-x>. PubMed PMID: 31235280.

33. Kushi LH, Meyer KA, Jacobs DR, Jr. Cereals, legumes, and chronic disease risk reduction: evidence from epidemiologic studies. Am J Clin Nutr. 1999;70(3 Suppl):451s-8s. Epub 1999/09/09. doi: 10.1093/ajcn/70.3.451s. PubMed PMID: 10479217.

34. Sievenpiper JL, Kendall CW, Esfahani A, Wong JM, Carleton AJ, Jiang HY, et al. Effect of non-oil-seed pulses on glycaemic control: a systematic review and meta-analysis of randomised controlled experimental trials in people with and without diabetes. Diabetologia. 2009;52(8):1479-95. Epub 2009/06/16. doi: 10.1007/s00125-009-1395-7. PubMed PMID: 19526214.

35. Jayalath VH, de Souza RJ, Sievenpiper JL, Ha V, Chiavaroli L, Mirrahimi A, et al. Effect of dietary pulses on blood pressure: a systematic review and meta-analysis of controlled feeding trials. Am J Hypertens. 2014;27(1):56-64. Epub 2013/09/10. doi: 10.1093/ajh/hpt155. PubMed PMID: 24014659; PubMed Central PMCID: PMC5391775.

36. Belski R, Mori TA, Puddey IB, Sipsas S, Woodman RJ, Ackland TR, et al. Effects of lupin-enriched foods on body composition and cardiovascular disease risk factors: a 12-month randomized controlled weight loss trial. Int J Obes (Lond). 2011;35(6):810-9. Epub 2010/10/13. doi: 10.1038/ijo.2010.213. PubMed PMID: 20938438.

37. Linlawan S, Patcharatrakul T, Somlaw N, Gonlachanvit S. Effect of Rice, Wheat, and Mung Bean Ingestion on Intestinal Gas Production and Postprandial Gastrointestinal Symptoms in Non-Constipation Irritable Bowel Syndrome Patients. Nutrients. 2019;11(9). Epub 2019/09/06. doi: 10.3390/nu11092061. PubMed PMID: 31484315; PubMed Central PMCID: PMC6771122.

38. Ibsen DB, Laursen ASD, Würtz AML, Dahm CC, Rimm EB, Parner ET, et al. Food substitution models for nutritional epidemiology. The American Journal of Clinical Nutrition. 2020;113(2):294-303. doi: 10.1093/ajcn/nqaa315.

39. Ibsen DB, Dahm CC. Food substitutions revisited. The American Journal of Clinical Nutrition. 2022;116(5):1195-8. doi: 10.1093/ajcn/nqac222.

40. Song M, Fung TT, Hu FB, Willett WC, Longo VD, Chan AT, et al. Association of Animal and Plant Protein Intake With All-Cause and Cause-Specific Mortality. JAMA Internal Medicine. 2016;176(10):1453-63. doi: 10.1001/jamainternmed.2016.4182.

41. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med. 2015;12(3):e1001779. Epub 2015/04/01. doi: 10.1371/journal.pmed.1001779. PubMed PMID: 25826379; PubMed Central PMCID: PMC4380465 steering committee, or of one of UK Biobank’s working groups. PM is a part-time employee and holder of stock and options in GlaxoSmithKline and has received attendance fees and contributed to panels convened by the Medical Research Council, a public funder of UK Biobank. JD has received research funding from The Wellcome Trust, British Heart Foundation, UK Medical Research Council, BUPA Foundation, Denka, diaDexus, European Research Council, European Union, Evelyn Trust, Fogarty International Centre, GlaxoSmithKline, Merck, National Heart, Lung and Blood Institute, National Health Service Blood and Transplant, National Institute for Health Research, National Institute of Neurological Disorders and Stroke, Novartis, Pfizer, Roche, UK Biobank. RC is the CEO and PI of UK Biobank, which is a charity set up by the MRC and Wellcome Trust to establish this prospective cohort as a resource for researchers from around the world. RC is a member of the Editorial Board of PLOS Medicine. All other authors have declared that no competing interests exist.

42. UK Biobank. UK Biobank: Protocol for a large-scale prospective epidemiological resource Cheshire: UK Biobank Coordinating Centre; 2007 [cited 2021 3 December]. Available from: <https://www.ukbiobank.ac.uk/media/gnkeyh2q/study-rationale.pdf>.

43. Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, et al. Comparison of Sociodemographic and Health-Related Characteristics of UK Biobank Participants With Those of the General Population. Am J Epidemiol. 2017;186(9):1026-34. doi: 10.1093/aje/kwx246. PubMed PMID: 28641372; PubMed Central PMCID: PMC5860371.

44. UK Biobank. Data-Field 105010 2021. Available from: <https://biobank.ndph.ox.ac.uk/crystal/field.cgi?id=105010>

45. Liu B, Young H, Crowe FL, Benson VS, Spencer EA, Key TJ, et al. Development and evaluation of the Oxford WebQ, a low-cost, web-based method for assessment of previous 24 h dietary intakes in large-scale prospective studies. Public Health Nutr. 2011;14(11):1998-2005. Epub 2011/07/07. doi: 10.1017/s1368980011000942. PubMed PMID: 21729481.

46. Perez-Cornago A, Pollard Z, Young H, van Uden M, Andrews C, Piernas C, et al. Description of the updated nutrition calculation of the Oxford WebQ questionnaire and comparison with the previous version among 207,144 participants in UK Biobank. Eur J Nutr. 2021;60(7):4019-30. Epub 20210506. doi: 10.1007/s00394-021-02558-4. PubMed PMID: 33956230; PubMed Central PMCID: PMC8437868.

47. Greenwood DC, Hardie LJ, Frost GS, Alwan NA, Bradbury KE, Carter M, et al. Validation of the Oxford WebQ Online 24-Hour Dietary Questionnaire Using Biomarkers. Am J Epidemiol. 2019;188(10):1858-67. doi: 10.1093/aje/kwz165. PubMed PMID: 31318012; PubMed Central PMCID: PMC7254925.

48. Carter JL, Lewington S, Piernas C, Bradbury K, Key TJ, Jebb SA, et al. Reproducibility of dietary intakes of macronutrients, specific food groups, and dietary patterns in 211 050 adults in the UK Biobank study. J Nutr Sci. 2019;8:e34. Epub 2019/11/15. doi: 10.1017/jns.2019.31. PubMed PMID: 31723428; PubMed Central PMCID: PMC6842574.

49. Kelly RK, Watling CZ, Tong TYN, Piernas C, Carter JL, Papier K, et al. Associations Between Macronutrients From Different Dietary Sources and Serum Lipids in 24 639 UK Biobank Study Participants. Arterioscler Thromb Vasc Biol. 2021;41(7):2190-200. Epub 20210527. doi: 10.1161/atvbaha.120.315628. PubMed PMID: 34039019; PubMed Central PMCID: PMC8216602.

50. FAO. Dietary Assessment: A resource guide to method selection and application in low ressource settings. Rome: Food and Agriculture Organiszation of the United Nations, 2018.

51. NHS Digital. NHS Data Model and Dictionary International Classification of Diseases (ICD): The National Health Service,; 2021 [cited 2021 14 October]. Available from: <https://datadictionary.nhs.uk/supporting_information/international_classification_of_diseases__icd_.html>.

52. UK Biobank. Hospital inpatient data. UK Biobank, 2020.

53. Maningat CC, Jeradechachai T, Buttshaw MR. Textured wheat and pea proteins for meat alternative applications. Cereal Chemistry. 2022;99(1):37-66. doi: <https://doi.org/10.1002/cche.10503>.

54. UK National Health Services. 5 A Day portion sizes: UK NHS; 2022 [updated 19 July; cited 2022 16 December ]. Available from: <https://www.nhs.uk/live-well/eat-well/5-a-day/portion-sizes/>.

55. UK National Health Services. 5 A Day: what counts? : UK NHS; 2021 [updated 8 October cited 2022 16 December ]. Available from: <https://www.nhs.uk/live-well/eat-well/5-a-day/5-a-day-what-counts/>.