DIETS AND COMPOSITIONS FOR IMPROVING OR MAINTAINING CARDIOVASCULAR HEALTH

FIELD OF THE INVENTION

The present invention relates to diets and compositions for improving or maintaining cardiovascular health. The present invention also relates to methods of determining a diet or a composition for improving or maintaining cardiovascular health.

BACKGROUND TO THE INVENTION

A healthy diet plays a crucial role in preventing and managing cardiovascular diseases such as hypertension, heart disease, and stroke (see e.g. Casas, R., Castro-Barquero, S., Estruch, R. and Sacanella, E., 2018. Nutrition and cardiovascular health. International journal of molecular sciences, 19(12), p.3988).

Certain dietary patterns, such as the Mediterranean diet, ketogenic diet or the DASH diet, can be used to prevent or manage cardiovascular diseases. These diets primarily emphasize the consumption of nutritious foods, including fruits, vegetables, whole grains, lean proteins, and healthy fats, while limiting the intake of processed foods, sugary beverages, and saturated fats (see e.g. Nestel, P.J. and Mori, T.A., 2022. Reviews in Cardiovascular Medicine, 23(1), p.17; Chiavaroli, L., et al., 2019. Nutrients, 11(2), p.338; and Sanches Machado d'Almeida, K., et al., 2018. Nutrients, 10(1), p.58).

Furthermore, studies have also highlighted the importance of specific nutrients in improving cardiovascular health. For instance, a high intake of dietary fibre has been associated with a reduced risk of heart disease (see e.g. Kaczmarczyk, M.M., et al., 2012. Metabolism, 61(8), pp.1058-1066). Similarly, omega-3 fatty acids have shown diverse benefits for cardiovascular health (see e.g. Chaddha, A. and Eagle, K.A., 2015. Circulation, 132(22), pp.e350-e352; and Fernandes, G. and Venkatraman, J.T., 1993. Nutrition research, 13, pp.S19-S45).

The "single nutrient" approach is widely employed in nutrition research. In this methodology, studies are designed to focus on the impact of a single nutrient on the health outcome. However, we do not consume nutrients in isolation. The foods and meals that comprise our diets are complex mixtures of micro- and macro-nutrients. These nutrients interact with each other to affect biological processes. A low-fat diet can be a low-fat, high-carb, low-protein diet or a low-fat, low-carb, high-protein diet or a low-fat, medium-carb, medium-protein diet. Single nutrient-focused studies therefore often lead to contradictory conclusions about the dietary determinants of metabolic disease. For example, the role of carbohydrates in the obesity epidemic (see e.g. Wali, J.A., et al., 2021. Cardiovascular research, 117(2), pp.386-401).

Thus, there is a demand for new nutritional interventions to improve or maintain cardiovascular health, which use a holistic assessment of the relationship between dietary nutrients and biological parameters to gain comprehension of the connections between various variables.

SUMMARY OF THE INVENTION

The present inventors have used Nutritional Geometry (NG), a multidimensional framework that models the complex relationships between nutrients and biological parameters, to identify and develop new nutritional interventions to improve or maintain cardiovascular health.

The present inventors have surprisingly found that diets containing low-medium protein, low fat and high carbohydrate are associated with improvements in biomarkers of cardiovascular health. In particular, the present inventors have surprisingly found that diets comprising about 10-35 E% protein, about 8-22 E% fat, and about 55-80 E% carbohydrate are associated with improved cholesterol metrics (e.g. lower LDL/HDL ratio) and improved lipoprotein metrics (e.g. lower apolipoprotein B/apolipoprotein A ratio).

In one aspect, the present invention provides a diet for use in improving and/or maintaining cardiovascular health in a subject, wherein the diet comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

In another aspect, the present invention provides a nutritional composition or supplement for use in improving and/or maintaining cardiovascular health in a subject, wherein the nutritional composition or supplement is administered to the subject such that the subject's diet comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

In another aspect, the present invention provides a method of improving and/or maintaining cardiovascular health in a subject, the method comprising administering a diet to said subject, wherein the diet comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

In another aspect, the present invention provides a method of improving and/or maintaining cardiovascular health in a subject, the method comprising administering a nutritional composition or supplement to said subject, wherein the nutritional composition or supplement is administered to the subject such that the subject's diet comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

In another aspect, the present invention provides a method of determining a diet for improving and/or maintaining cardiovascular health in a subject, the method comprising: (a) providing

macronutrient requirements for protein, fat, and carbohydrate, wherein the macronutrient requirements are from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate; and (b) determining a diet that meets said macronutrient requirements. The method may be a computer-implemented method.

In another aspect, the present invention provides a method of determining a diet for a subject, the method comprising: (a) determining whether the subject has or is at risk of poor cardiovascular health; and (b) determining a diet for the subject, wherein if the subject has or is at risk of poor cardiovascular health the diet comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate. The method may be a computer-implemented method.

In another aspect, the present invention provides a diet determined by a method of the present invention.

The diet may comprise protein in any suitable amount. In some embodiments, the diet comprises protein in an amount of at least 11 E%, at least 12 E%, at least 13 E%, at least 14 E%, or at least 15 E%. In some embodiments, the diet comprises protein in an amount of 34 E% or less, 33 E% or less, 32 E% or less, 31 E% or less, 30 E% or less, 29 E% or less, 28 E% or less, 27 E% or less, 26 E% or less, or 25 E% or less. In some embodiments, the diet comprises protein in an amount of from 10 E% to 34 E%, from 10 E% to 33 E%, from 10 E% to 32 E%, from 10 E% to 31 E%, from 10 E% to 30 E%, from 11 E% to 29 E%, or from 11 E% to 28 E%.

The diet may comprise fat in any suitable amount. In some embodiments, the diet comprises fat in an amount of at least 9 E%, at least 10 E%, at least 11 E%, or at least 12 E%. In some embodiments, the diet comprises fat in an amount of 21 E% or less, 20 E% or less, 19 E% or less, 18 E% or less, 17 E% or less, 16 E% or less, 15 E% or less, 14 E% or less, or 13 E% or less. In some embodiments, the diet comprises fat in an amount of from 8 E% to 21 E%, from 8 E% to 20 E%, from 8 E% to 19 E%, from 8 E% to 18 E%, from 9 E% to 18 E%, from 10 E% to 18 E%, from 10 E% to 17 E%, from 10 E% to 16 E%, from 10 E% to 15 E%, from 10 E% to 14 E%, or from 10 E% to 13 E%.

The diet may comprise carbohydrate in any suitable amount. In some embodiments, the diet comprises carbohydrate in an amount of at least 56 E%, at least 57 E%, at least 58 E%, at least 59 E%, at least 60 E%, at least 61 E%, at least 62 E%, at least 63 E%, at least 64 E%, or at least 65 E%. In some embodiments, the diet comprises carbohydrate in an amount of 79 E% or less, 78 E% or less, 77 E% or less, 76 E% or less, or 75 E% or less. In some

embodiments, the diet comprises carbohydrate in an amount of from 60 E% to 80 E%, from 60 E% to 79 E%, from 61 E% to 79 E%, or from 62 E% to 79 E%.

The diet may comprise any suitable combination of protein, fat, and carbohydrate. In some embodiments, the diet comprises from 11 E% to 28 E% protein, from 10 E% to 13 E% fat, and from 62 E% to 79 E% carbohydrate.

The nutritional composition or supplement may comprise any suitable amounts of protein, fat, and carbohydrate. In some embodiments, the nutritional composition or supplement comprises carbohydrate in an amount of 70 E% or more, 75 E% or more, 80 E% or more, 85 E% or more, 90 E% or more, or 95 E% or more. In some embodiments, the nutritional composition or supplement comprises fat in an amount of 15 E% or less, 10 E% or less, or 5 E% or less. In some embodiments, the nutritional composition or supplement comprises protein in an amount of 20 E% or less, 15 E% or less, 10 E% or less, or 5 E% or less. In some embodiments, the nutritional composition or supplement comprises protein in an amount of 15 E% or less, fat in amount of 10 E% or less, and carbohydrate in an amount of 75 E% or more.

The diet may provide any suitable energy intake. In some embodiments, the diet comprises a total energy intake of 16.0 MJ/day or less, 15.5 MJ/day or less, 15.0 MJ/day or less, 14.5 MJ/day or less, 14.0 MJ/day or less, 13.5 MJ/day or less, 13.0 MJ/day or less, 12.5 MJ/day or less, 12.0 MJ/day or less, 11.5 MJ/day or less, 11.0 MJ/day or less, 10.5 MJ/day or less, or 10.0 MJ/day or less. In some embodiments, the diet comprises a total energy intake of 7.0 MJ/day or more, 7.5 MJ/day or more, or 8.0 MJ/day or more. In some embodiments, the diet comprises a total energy intake of from 7.0 MJ/day to 16.0 MJ/day.

In yet another aspect, the present invention provides a nutritional composition or supplement (e.g., a single nutritional composition or supplement, that is one of a plurality of components of a diet) for use in improving and/or maintaining cardiovascular health in a subject, wherein the nutritional composition or supplement comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

In another aspect, the present invention provides a nutritional composition or supplement (e.g., a single nutritional composition or supplement, that is one of a plurality of components of a diet) for use in improving and/or maintaining cardiovascular health in a subject who is consuming an initial diet, wherein the nutritional composition or supplement is administered to the subject such that the subject's modified diet (i.e., the initial diet combined with the nutritional composition or supplement) comprises, or is closer to, one or more of 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

In another aspect, the present invention provides a method of improving and/or maintaining cardiovascular health in a subject, the method comprising administering a nutritional composition or supplement (e.g., a single nutritional composition or supplement, that is one of a plurality of components of a diet) to said subject, wherein the nutritional composition or supplement comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

In another aspect, the present invention provides a method of improving and/or maintaining cardiovascular health in a subject who is consuming an initial diet, the method comprising administering a nutritional composition or supplement (e.g., a single nutritional composition or supplement, that is one of a plurality of components of a diet) to said subject, wherein the nutritional composition or supplement is administered to the subject such that the subject's modified diet (i.e., the initial diet combined with the nutritional composition or supplement) comprises, or is closer to, one or more of 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

In another aspect, the present invention provides a method of determining a nutritional composition or supplement (e.g., a single nutritional composition or supplement, that is one of a plurality of components of a diet) for improving and/or maintaining cardiovascular health in a subject, the method comprising: (a) providing macronutrient requirements for protein, fat, and carbohydrate, wherein the macronutrient requirements are from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate; and (b) determining a nutritional composition or supplement that meets said macronutrient requirements. The method may be a computer-implemented method.

In another aspect, the present invention provides a method of determining a nutritional composition or supplement (e.g., a single nutritional composition or supplement, that is one of a plurality of components of a diet) for a subject, the method comprising: (a) determining whether the subject has or is at risk of poor cardiovascular health; and (b) determining a nutritional composition or supplement for the subject, wherein if the subject has or is at risk of poor cardiovascular health, the nutritional composition or supplement comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate. The method may be a computer-implemented method.

In another aspect, the present invention provides a nutritional composition or supplement (e.g., a single nutritional composition or supplement, that is one of a plurality of components of a diet) determined by a method of the present invention.

The nutritional composition or supplement (e.g., a single nutritional composition or supplement, that is one of a plurality of components of a diet) may comprise protein in any suitable amount. In some embodiments, the nutritional composition or supplement comprises protein in an amount of at least 11 E%, at least 12 E%, at least 13 E%, at least 14 E%, or at least 15 E%. In some embodiments, the nutritional composition or supplement comprises protein in an amount of 34 E% or less, 33 E% or less, 32 E% or less, 31 E% or less, 30 E% or less, 29 E% or less, 28 E% or less, 27 E% or less, 26 E% or less, or 25 E% or less. In some embodiments, the nutritional composition or supplement comprises protein in an amount of from 10 E% to 34 E%, from 10 E% to 33 E%, from 10 E% to 32 E%, from 10 E% to 31 E%, from 10 E% to 30 E%, from 11 E% to 29 E%, or from 11 E% to 28 E%.

The nutritional composition or supplement (e.g., a single nutritional composition or supplement, that is one of a plurality of components of a diet) may comprise fat in any suitable amount. In some embodiments, the nutritional composition or supplement comprises fat in an amount of at least 9 E%, at least 10 E%, at least 11 E%, or at least 12 E%. In some embodiments, the nutritional composition or supplement comprises fat in an amount of 21 E% or less, 20 E% or less, 19 E% or less, 18 E% or less, 17 E% or less, 16 E% or less, 15 E% or less, 14 E% or less, or 13 E% or less. In some embodiments, the nutritional composition or supplement comprises fat in an amount of from 8 E% to 21 E%, from 8 E% to 20 E%, from 8 E% to 19 E%, from 8 E% to 18 E%, from 9 E% to 18 E%, from 10 E% to 18 E%, from 10 E% to 17 E%, from 10 E% to 16 E%, from 10 E% to 15 E%, from 10 E% to 14 E%, or from 10 E% to 13 E%.

The nutritional composition or supplement may comprise carbohydrate in any suitable amount. In some embodiments, the nutritional composition or supplement comprises carbohydrate in an amount of at least 56 E%, at least 57 E%, at least 58 E%, at least 59 E%, at least 60 E%, at least 61 E%, at least 62 E%, at least 63 E%, at least 64 E%, or at least 65 E%. In some embodiments, the nutritional composition or supplement comprises carbohydrate in an amount of 79 E% or less, 78 E% or less, 77 E% or less, 76 E% or less, or 75 E% or less. In some embodiments, the nutritional composition or supplement comprises carbohydrate in an amount of from 60 E% to 80 E%, from 60 E% to 79 E%, from 61 E% to 79 E%, or from 62 E% to 79 E%.

The nutritional composition or supplement may comprise any suitable combination of protein, fat, and carbohydrate. In some embodiments, the nutritional composition or supplement comprises from 11 E% to 28 E% protein, from 10 E% to 13 E% fat, and from 62 E% to 79 E% carbohydrate.

The diet, nutritional composition, or supplement may be administered to the subject for any suitable duration. In some embodiments, the diet, nutritional composition, or supplement is administered for at least one week, at least two weeks, at least three weeks, or at least four weeks. In some embodiments, the diet, nutritional composition, or supplement is administered for at least one month, at least two months, at least three months, at least six months, at least nine months, or at least twelve months. In some embodiments, the diet, nutritional composition, or supplement is administered for at least one year, at least two years, at least three years, at least four years, or at least five years.

The diet may comprise all nutrients required to support the subject's physiologic needs. In some embodiments, the diet comprises at least 4 food groups per day, at least 5 food groups per day, at least 6 food groups per day, or at least 7 food groups per day. In some embodiments, the diet comprises dietary fibre in an amount of from 10 g/1000 kcal to 16 g/1000 kcal, from 11 g/1000 kcal to 15 g/1000 kcal, or from 12 g/1000 kcal to 14 g/1000 kcal.

The subject may be any human subject in need thereof. In some embodiments, the subject is an adult. In some embodiments, the subject is at least 40 years of age.

The subject may have or may be at risk of poor cardiovascular health. In some embodiments, the subject has or is at risk of dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity. In some embodiments, the subject has or is at risk of cardiovascular disease. In some embodiments, the subject has or is at risk of atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease. In some embodiments, the subject has one or more selected from the following: (i) a plasma LDL/HDL cholesterol ratio of 2.5 or higher, 2.6 or higher, 2.7 or higher, 2.8 or higher, 2.9 or higher, or 3.0 or higher; (ii) a plasma total cholesterol of 5.0 mmol/L or higher, 5.1 mmol/L or higher, 5.2 mmol/L or higher, 5.3 mmol/L or higher, 5.4 mmol/L or higher, 5.5 mmol/L or higher, 5.6 mmol/L or higher, 5.7 mmol/L or higher, 5.8 mmol/L or higher, 5.9 mmol/L or higher, or 6.0 mmol/L or higher; (iii) a plasma LDL cholesterol of 3.0 mmol/L or higher, 3.1 mmol/L or higher, 3.2 mmol/L or higher, 3.3 mmol/L or higher, 3.4 mmol/L or higher, 3.5 mmol/L or higher, 3.6 mmol/L or higher, 3.7 mmol/L or higher, 3.8 mmol/L or higher, 3.9 mmol/L or higher, or 4.0 mmol/L or higher; (iv) a plasma apolipoprotein B/apolipoprotein A ratio of 0.70 or higher, 0.80 or higher, or 0.90 or higher; and (v) a plasma apolipoprotein B of 1.0 g/L or more, 1.1 g/L or more, 1.2 g/L or more, or 1.3 g/L or more.

The diet, nutritional composition, or supplement may improve one or more lipid biomarkers. In some embodiments, the subject's plasma LDL/HDL cholesterol ratio is reduced, optionally wherein the subject's plasma LDL/HDL cholesterol ratio is reduced by at least 0.1, at least 0.2,

at least 0.3, at least 0.4, or at least 0.5. In some embodiments, the subject's plasma total cholesterol is reduced, optionally wherein the subject's plasma total cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L. In some embodiments, the subject's plasma LDL cholesterol is reduced, optionally wherein the subject's plasma LDL cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L. In some embodiments, the subject's plasma apolipoprotein B/apolipoprotein A ratio is reduced, optionally wherein the subject's plasma apolipoprotein B/apolipoprotein A ratio is reduced by at least 0.05, at least 0.10, at least 0.15, or at least 0.20. In some embodiments, the subject's plasma apolipoprotein B is reduced, optionally wherein the subject's plasma apolipoprotein B is reduced by at least 0.05 g/L, at least 0.10 g/L, at least 0.15 g/L, or at least 0.20 g/L.

The diet, nutritional composition, or supplement may be administered to a subject to treat or prevent dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity. In some embodiments, the dyslipidaemia-related comorbidity is xanthomas, carotid bruits, femoral bruits, xanthelasmas, or corneal arcus.

The diet, nutritional composition, or supplement may be administered to a subject to treat or prevent cardiovascular disease. In some embodiments, the cardiovascular disease is atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease.

In another aspect, the present invention provides computer program comprising instructions which, when the program is executed by a computer, cause the computer to carry out a method of the present invention.

In another aspect, the present invention provides a computer-readable data carrier having stored thereon the computer program of the present invention.

In another aspect, the present invention provides a computer-readable medium comprising instructions which, when executed by a computer, cause the computer to carry out a method of the present invention.

DESCRIPTION OF DRAWINGS

Figure 1 - Example of Right-Angled Mixture Triangle (RMT)

% protein in the diet is shown along the x-axis, % carbohydrate is shown along the y-axis and % fat is shown along the implicit z-axis. At any point in this nutritional landscape, the sum of energy from protein, fat and carbohydrate is 100%. For example, the dot shown in the figure

represents a diet containing 25% protein, 50% carbohydrate and 25% fat, with their sum being 100%. Data for health outcomes is superimposed on the dietary data and shaded to generate heatmaps or response surfaces. In these heatmaps, red colour represents the maximum magnitude of the health marker and blue colour represents the lowest magnitude. The lines of the surfaces are called “isolines” and the value of the health outcome remains constant along these lines.

Figure 2 - Validation of a GAM applied to the UK Biobank dataset

Dietary macronutrient composition and daily energy intake data (kCal) analysed using the Generalized Additive Model (GAM) applied to the UK Biobank dataset are projected onto an RMT plot. The patterns of the relationship between macronutrient balance and ad-libitum energy intake are consistent with those reported in Raubenheimer, D., et al., 2015. British Journal of Nutrition, 113(S1), pp.S26-S39.

Figure 3 - Contribution of macronutrient composition to blood cholesterol profile

RMT plots for: (**A**) total cholesterol; (**B**) LDL cholesterol; and (**C**) LDL/HDL cholesterol ratio. For each cholesterol metric, the contribution of macronutrient composition was modelled with a GAM and projected onto an RMT plot. *Macronutrient ranges associated with lower LDL/HDL cholesterol ratio were identified from visual inspection of the heatmaps. Wilcoxon testing was then conducted to confirm that these macronutrient ranges were associated with significantly lower ratios of LDL/HDL cholesterol.*

Figure 4 - Contribution of macronutrient composition to blood lipoprotein profile

RMT plots for: (**A**) apolipoprotein B; and (**B**) apolipoprotein B/apolipoprotein A ratio. For each lipoprotein metric, the contribution of macronutrient composition was modelled with a GAM and projected onto an RMT plot. *Macronutrient ranges associated with lower apolipoprotein-B/apolipoprotein-A ratio were identified from visual inspection of the heatmaps. Wilcoxon testing was then conducted to confirm that these macronutrient ranges were associated with significantly lower ratios of apolipoprotein-B/apolipoprotein-A.*

DETAILED DESCRIPTION

Various preferred features and embodiments of the present invention will now be described by way of non-limiting examples. The skilled person will understand that they can combine all features of the invention disclosed herein without departing from the scope of the invention as disclosed.

Any reference to prior art documents in this specification is not to be considered an admission that such prior art is widely known or forms part of the common general knowledge in the field. All publications mentioned in the specification are herein incorporated by reference.

As used in this specification, the words “comprises”, “comprising”, and similar words, are not to be interpreted in an exclusive or exhaustive sense. In other words, they are intended to mean “including, but not limited to”. The terms “comprises”, “comprising”, and similar words also include the term “consisting of”.

The practice of the present invention will employ, unless otherwise indicated, conventional techniques which are within the capabilities of one of ordinary skill in the art. Such techniques are explained in the literature. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art.

Numeric ranges are inclusive of the numbers defining the range. As used herein the term “about” means approximately, in the region of, roughly, or around. When the term “about” is used in conjunction with a numerical value or range, it modifies that value or range by extending the boundaries above and below the numerical value(s) set forth. In general, the terms “about” and “approximately” are used herein to modify a numerical value(s) above and below the stated value(s) by 10%.

The percentages of protein, fat, and carbohydrate disclosed herein are expressed as a percentage of total dietary energy intake (i.e. E%), unless stated otherwise. The percentages of other components disclosed herein are expressed on a w/w basis, unless stated otherwise.

Diets

The present invention provides a diet for use in improving and/or maintaining cardiovascular health in a subject.

As used herein, the term “diet” or “predetermined diet” may refer to the sum of food consumed by a subject. A diet may provide macronutrients in appropriate proportions to support the energetic and physiologic needs of a subject without excess intake, while also providing sufficient micronutrients and hydration to meet the physiologic needs of the subject (see e.g. Cena, H. and Calder, P.C., 2020. Nutrients, 12(2), p.334).

The term “diet” may refer to one or more compositions (e.g. nutritional compositions or supplements) which are administered to a subject and provide the sum of food consumed by a subject. In some embodiments, the present invention provides one or more compositions for use in improving and/or maintaining cardiovascular health in a subject, wherein the one or

more compositions are each administered to the subject, such that the subject's diet is according to the present invention.

The diet may be administered to the subject for an extended duration.

Suitably, the diet is administered for at least about one week, at least about two weeks, at least about three weeks, at least about four weeks, at least about five weeks, at least about six weeks, at least about seven weeks, at least about eight weeks, at least about nine weeks, at least about ten weeks, at least about eleven weeks, or at least about twelve weeks.

Suitably, the diet is administered for at least about one month, at least about two months, at least about three months, at least about four months, at least about five months, at least about six months, at least about seven months, at least about eight months, at least about nine months, at least about ten months, at least about eleven months, or at least about twelve months.

Suitably, the diet is administered for at least about one year, at least about two years, at least about three years, at least about four years, at least about five years, at least about six years, at least about seven years, at least about eight years, at least about nine years, or at least about ten years.

The diet may comprise a plurality of menus. A "menu" may comprise a plurality of meals. Menu or meal planning may refer to the process of deciding what you will eat for each meal, including main dishes, side dishes, and desserts (see e.g. Ngo, H.C., et al., 2016. J. Comput. Sci., 12(12), pp.582-596). Suitably, the diet comprises at least 1 daily menus, at least 2 daily menus, at least 3 daily menus, at least 4 daily menus, or at least 5 daily menus.

The diet may comprise a plurality of meals. The term "meal" may refer to eating occasions or eating events and may be classified based on the food items consumed (see e.g. Leech, R.M., Worsley, A., et al., 2015. Nutrition research reviews, 28(1), pp.1-21). Suitably, the diet comprises at least 2 meals per day, at least 3 meals per day, or at least 4 meals per day.

The diet may comprise a plurality of food items. The term "food item" may refer to any substance consumed to provide nutritional support for the body. Suitably, the diet comprises at least 5 food items per day, or at least 10 food items per day, or at least 15 food items per day.

The diet may comprise a plurality of food groups. The term "food group" may refer to a collection of food items that share similar nutritional properties or biological classifications. Nutrition guides typically divide foods into food groups. Exemplary food groups include fruits;

vegetables; pulses, nuts or seeds; meats; starches or grains; dairy; and oils and fats. Suitably, the diet comprises at least 4 food groups per day, at least 5 food groups per day, at least 6 food groups per day, or at least 7 food groups per day. Suitably, the diet comprises a plurality of food groups comprising at least: fruits; vegetables; pulses, nuts or seeds; starches or grains; and oils and fats.

Macronutrients

The diet of the present invention comprises a specific ratio of macronutrients. Macronutrients (i.e., proteins, fats, and carbohydrates) provide the energy necessary for the cellular processes required for daily functioning. The amounts of protein, fat, and carbohydrate comprised in the diet may sum to 100 E%.

In some embodiments, the diet comprises from about 10 E% to about 35 E% protein, from about 8 E% to about 22 E% fat, and from about 55 E% to about 80 E% carbohydrate.

In some embodiments, the diet comprises protein in an amount of about 10 E%, about 11 E%, about 12 E%, about 13 E%, about 14 E%, about 15 E%, about 16 E%, about 17 E%, about 18 E%, about 19 E%, about 20 E%, about 21 E%, about 22 E%, about 23 E%, about 24 E%, about 25 E%, about 26 E%, about 27 E%, about 28 E%, about 29 E%, about 30 E%, about 31 E%, about 32 E%, about 33 E%, about 34 E%, or about 35 E%.

In some embodiments, the diet comprises protein in an amount of at least about 11 E%, at least about 12 E%, at least about 13 E%, at least about 14 E%, or at least about 15 E%. In some embodiments, the diet comprises protein in an amount of at least about 11 E%.

In some embodiments, the diet comprises protein in an amount of about 34 E% or less, about 33 E% or less, about 32 E% or less, about 31 E% or less, about 30 E% or less, about 29 E% or less, about 28 E% or less, about 27 E% or less, about 26 E% or less, or about 25 E% or less. In some embodiments, the diet comprises protein in an amount of about 28 E% or less.

In some embodiments, the diet comprises protein in an amount of from about 10 E% to about 34 E%, from about 10 E% to about 33 E%, from about 10 E% to about 32 E%, from about 10 E% to about 31 E%, from about 10 E% to about 30 E%, from about 11 E% to about 29 E%, or from about 11 E% to about 28 E%. In some embodiments, the diet comprises protein in an amount of from about 11 E% to about 28 E%.

In some embodiments, the diet comprises fat in an amount of about 8 E%, about 9 E%, about 10 E%, about 11 E%, about 12 E%, about 13 E%, about 14 E%, about 15 E%, about 16 E%, about 17 E%, about 18 E%, about 19 E%, about 20 E%, about 21 E%, or about 22 E%.

In some embodiments, the diet comprises fat in an amount of at least about 9 E%, at least about 10 E%, at least about 11 E%, or at least about 12 E%. In some embodiments, the diet comprises fat in an amount of at least about 10 E%.

In some embodiments, the diet comprises fat in an amount of about 21 E% or less, about 20 E% or less, about 19 E% or less, about 18 E% or less, about 17 E% or less, about 16 E% or less, about 15 E% or less, about 14 E% or less, or about 13 E% or less. In some embodiments, the diet comprises fat in an amount of about 13 E% or less.

In some embodiments, the diet comprises fat in an amount of from about 8 E% to about 21 E%, from about 8 E% to about 20 E%, from about 8 E% to about 19 E%, from about 8 E% to about 18 E%, from about 9 E% to about 18 E%, from about 10 E% to about 18 E%, from about 10 E% to about 17 E%, from about 10 E% to about 16 E%, from about 10 E% to about 15 E%, from about 10 E% to about 14 E%, or from about 10 E% to about 13 E%. In some embodiments, the diet comprises fat in an amount of from about 10 E% to about 13 E%.

In some embodiments, the diet comprises carbohydrate in an amount of about 55 E%, about 56 E%, about 57 E%, about 58 E%, about 59 E%, about 60 E%, about 61 E%, about 62 E%, about 63 E%, about 64 E%, about 65 E%, about 66 E%, about 67 E%, about 68 E%, about 69 E%, about 70 E%, about 71 E%, about 72 E%, about 73 E%, about 74 E%, about 75 E%, about 76 E%, about 77 E%, about 78 E%, about 79 E%, or about 80 E%.

In some embodiments, the diet comprises carbohydrate in an amount of at least about 56 E%, at least about 57 E%, at least about 58 E%, at least about 59 E%, at least about 60 E%, at least about 61 E%, at least about 62 E%, at least about 63 E%, at least about 64 E%, or at least about 65 E%. In some embodiments, the diet comprises carbohydrate in an amount of at least about 62 E%.

In some embodiments, the diet comprises carbohydrate in an amount of about 79 E% or less, about 78 E% or less, about 77 E% or less, about 76 E% or less, or about 75 E% or less. In some embodiments, the diet comprises carbohydrate in an amount of about 79 E% or less.

In some embodiments, the diet comprises carbohydrate in an amount of from about 60 E% to about 80 E%, from about 60 E% to about 79 E%, from about 60 E% to about 78 E%, from about 60 E% to about 77 E%, from about 60 E% to about 76 E%, or from about 60 E% to about 75 E%. In some embodiments, the diet comprises carbohydrate in an amount of from about 61 E% to about 80 E%, from about 61 E% to about 79 E%, from about 61 E% to about 78 E%, from about 61 E% to about 77 E%, from about 61 E% to about 76 E%, or from about 61 E% to about 75 E%. In some embodiments, the diet comprises carbohydrate in an amount

of from about 62 E% to about 80 E%, from about 62 E% to about 79 E%, from about 62 E% to about 78 E%, from about 62 E% to about 77 E%, from about 62 E% to about 76 E%, or from about 62 E% to about 75 E%. In some embodiments, the diet comprises carbohydrate in an amount of from about 62 E% to about 79 E%.

In some embodiments, the diet comprises:

(a) protein in an amount of from about 10 E% to about 34 E%, from about 10 E% to about 33 E%, from about 10 E% to about 32 E%, from about 10 E% to about 31 E%, from about 10 E% to about 30 E%, from about 11 E% to about 29 E%, or from about 11 E% to about 28 E%;

(b) fat in an amount of from about 8 E% to about 21 E%, from about 8 E% to about 20 E%, from about 8 E% to about 19 E%, from about 8 E% to about 18 E%, from about 9 E% to about 18 E%, from about 10 E% to about 18 E%, from about 10 E% to about 17 E%, from about 10 E% to about 16 E%, from about 10 E% to about 15 E%, from about 10 E% to about 14 E%, or from about 10 E% to about 13 E%; and

(c) carbohydrate in an amount of from 62 E% to 80 E%, from 61 E% to 80 E%, from about 60 E% to about 80 E%, from about 60 E% to about 79 E%, from about 60 E% to about 78 E%, from about 60 E% to about 77 E%, from about 60 E% to about 76 E%, or from about 62 E% to 79 E%.

In some embodiments, the diet comprises from about 11 E% to about 28 E% protein, from about 10 E% to about 13 E% fat, and from about 62 E% to about 79 E% carbohydrate.

Energy intake

The diet of the present invention may fulfil the energy requirements of the subject.

As used herein, the “energy requirements” of a subject may refer to a level of energy intake which will balance energy expenditure when the subject has a body size and composition, and level of physical activity, consistent with long-term good health. Recommended energy allowances may be expressed as kilocalories (kcal) or megajoules (MJ) per day.

The energy requirements of a subject may be determined based on published energy requirements. For example, the energy requirements of the subject may be based on WHO guidelines, EFSA guidelines (see e.g. Agostoni, C., et al., 2013. EFSA Journal, 11(1), pp.1-112), and/or USDA guidelines.

In some embodiments, the diet of the present invention is an isocaloric diet. An “isocaloric diet” may refer to a diet having the same or similar energy intake as the subject’s present diet.

In some embodiments, the diet of the present invention is not a hypercaloric diet. A “hypercaloric diet” may refer to a diet in which a subject’s energy consumption exceeds their energy expenditure.

In some embodiments, the diet of the present invention is not a hypocaloric diet. A “hypercaloric diet” may refer to a diet in which a subject’s energy expenditure exceeds their energy consumption.

Suitably, the diet comprises a total energy intake of about 16.0 MJ/day or less, about 15.5 MJ/day or less, about 15.0 MJ/day or less, about 14.5 MJ/day or less, about 14.0 MJ/day or less, about 13.5 MJ/day or less, about 13.0 MJ/day or less, about 12.5 MJ/day or less, about 12.0 MJ/day or less, about 11.5 MJ/day or less, about 11.0 MJ/day or less, about 10.5 MJ/day or less, or about 10.0 MJ/day or less. In some embodiments, the diet comprises a total energy intake of about 12.0 MJ/day or less.

Suitably, the diet comprises a total energy intake of about 5.0 MJ/day or more, about 5.5 MJ/day or more, about 6.0 MJ/day or more, about 6.5 MJ/day or more, about 7.0 MJ/day or more, about 7.5 MJ/day or more, about 8.0 MJ/day or more, about 8.5 MJ/day or more, about 9.0 MJ/day or more, about 9.5 MJ/day or more, or about 10.0 MJ/day or more. In some embodiments, the diet comprises a total energy intake of about 7.0 MJ/day or more, about 7.5 MJ/day or more, or about 8.0 MJ/day or more.

Suitably, the diet comprises a total energy intake of from about 5.0 MJ/day to about 15.0 MJ/day, from about 5.5 MJ/day to about 14.5 MJ/day, from about 6.0 MJ/day to about 14.0 MJ/day, from about 6.5 MJ/day to about 13.5 MJ/day, from about 7.0 MJ/day to about 13.0 MJ/day, from about 7.5 MJ/day to about 12.5 MJ/day, or from about 8.0 MJ/day to about 12.0 MJ/day. In some embodiments, the diet comprises a total energy intake of from about 8.0 MJ/day to about 12.0 MJ/day.

In some embodiments, the diet comprises from about 5.0 MJ/day to about 15.0 MJ/day, from about 5.5 MJ/day to about 14.5 MJ/day, from about 6.0 MJ/day to about 14.0 MJ/day, from about 6.5 MJ/day to about 13.5 MJ/day, from about 7.0 MJ/day to about 13.0 MJ/day, from about 7.5 MJ/day to about 12.5 MJ/day, or from about 8.0 MJ/day to about 12.0 MJ/day, and:

(a) protein in an amount of from about 10 E% to about 34 E%, from about 10 E% to about 33 E%, from about 10 E% to about 32 E%, from about 10 E% to about 31 E%,

from about 10 E% to about 30 E%, from about 11 E% to about 29 E%, or from about 11 E% to about 28 E%;

(b) fat in an amount of from about 8 E% to about 21 E%, from about 8 E% to about 20 E%, from about 8 E% to about 19 E%, from about 8 E% to about 18 E%, from about 9 E% to about 18 E%, from about 10 E% to about 18 E%, from about 10 E% to about 17 E%, from about 10 E% to about 16 E%, from about 10 E% to about 15 E%, from about 10 E% to about 14 E%, or from about 10 E% to about 13 E%; and

(c) carbohydrate in an amount of from 62 E% to 80 E%, from 61 E% to 80 E%, from about 60 E% to about 80 E%, from about 60 E% to about 79 E%, from about 60 E% to about 78 E%, from about 60 E% to about 77 E%, from about 60 E% to about 76 E%, or from about 62 E% to about 79 E%.

In some embodiments, the diet comprises from about 8.0 MJ/day to about 12.0 MJ/day, from about 11 E% to about 28 E% protein, from about 10 E% to about 13 E% fat, and from about 62 E% to about 79 E% carbohydrate.

Other nutrients

The diet may further comprise any other nutrients required to support the subject's physiologic needs.

The diet may fulfil the micronutrient requirements of the subject. Micronutrients (i.e., vitamins and minerals) are required in comparatively small amounts for normal growth, development, metabolism, and physiologic functioning. Exemplary micronutrients include vitamins (including vitamin A, vitamin D, vitamin C, folate, vitamin B6, vitamin B12, and vitamin E) and minerals (including sodium, potassium, calcium, iron, zinc, magnesium, and phosphorus).

Examples of minerals, vitamins and other micronutrients optionally present in the diet include vitamin A, vitamin B1, vitamin B2, vitamin B6, vitamin B12, vitamin E, vitamin K, vitamin C, vitamin D, folic acid, inositol, niacin, biotin, pantothenic acid, choline, calcium, phosphorous, iodine, iron, magnesium, copper, zinc, manganese, chlorine, potassium, sodium, selenium, chromium, molybdenum, taurine, and L-carnitine.

Suitably, the diet comprises micronutrients in an amount sufficient to meet the subject's micronutrient requirements. The micronutrient requirements of a subject may be determined based on published micronutrient requirements and minimum requirements have been established for certain vitamins and minerals. For example, the micronutrient requirements of the subject may be based on WHO guidelines (see e.g. World Health Organization, 2004.

Vitamin and mineral requirements in human nutrition), EFSA guidelines, and/or USDA Dietary Reference Intakes.

The diet may fulfil the dietary fibre requirements of the subject. Dietary fibre may refer to the part of plant material in the diet which is resistant to enzymatic digestion and may include cellulose, noncellulosic polysaccharides such as hemicellulose, pectic substances, gums, mucilages and a non-carbohydrate component lignin.

Suitably, the diet comprises dietary fibre in an amount sufficient to meet the subject's dietary fibre requirements. The dietary fibre requirements of a subject may be determined based on published dietary fibre requirements.

Suitably, the diet comprises dietary fibre in an amount of from about 10 g/1000 kcal to about 16 g/1000 kcal, from about 11 g/1000 kcal to about 15 g/1000 kcal, or from about 12 g/1000 kcal to about 14 g/1000 kcal.

Suitably, the diet comprises dietary fibre in an amount of at least about 20 g/day, at least about 25 g/day, or at least about 30 g/day.

Compositions

The present invention provides one or more compositions for use in improving and/or maintaining cardiovascular health in a subject.

The composition can be any type of composition which can form part of the subject's diet, such as a composition in the form of a food or beverage product, a supplement, or a pharmaceutical composition. The composition may be in solid (e.g. powder), liquid or semi-liquid form.

In some embodiments, the composition is a nutritional composition or a supplement.

In some embodiments, the composition is a nutritional composition. As used herein, a "nutritional composition" may mean a composition which nourishes a subject. This nutritional composition is usually to be taken orally or intravenously, and typically includes a lipid or fat source and a protein source. Suitable nutritional compositions include breakfast cereals, breakfast drinks, frozen meals, etc.

In some embodiments, the composition is a supplement. As used herein, a "supplement" or "dietary supplement" may be used to complement the nutrition of a subject (it is typically used as such but it might also be added to any kind of compositions intended to be ingested by the

subject). When the composition is a supplement, it can be provided in the form of unit doses. Supplements are typically present in the form of a liquid, a gel, a powder, a tablet or capsule.

Any suitable sources of protein, fat, and carbohydrate may be used. For example, the protein source can be animal protein (e.g. meat and/or dairy) or plant protein, the fat source can be plant and vegetable oils or animal fat, and/or the carbohydrate source can be starch (e.g. cereals and grains derived including baked items, porridges, pasta and breads, etc.) or sugar (e.g. fruits, drinks, beverages, honey, etc).

The compositions of the present invention may comprise protein, fat, and carbohydrate in any suitable amounts, such that when the one or more compositions are administered to a subject, the subject's diet is adjusted to the diet of the present invention.

Suitably, the composition comprises carbohydrate in an amount of about 60 E% or more, about 65 E% or more, about 70 E% or more, about 75 E% or more, about 80 E% or more, about 85 E% or more, about 90 E% or more, or about 95 E% or more. Suitably, the composition comprises carbohydrate in an amount of about 100 E% or less.

Suitably, the composition comprises protein in an amount of about 25 E% or less, about 20 E% or less, about 15 E% or less, about 15 E% or less, about 10 E% or less, or about 5 E% or less. Suitably, the composition comprises protein in an amount of about 0 E% or more.

Suitably, the composition comprises fat in an amount of about 20 E% or less, about 15 E% or less, about 15 E% or less, about 10 E% or less, or about 5 E% or less. Suitably, the composition comprises fat in an amount of about 0 E% or more.

Suitably, the composition comprises:

(a) protein in an amount of about 25 E% or less, about 20 E% or less, about 15 E% or less, about 15 E% or less, about 10 E% or less, or about 5 E% or less;

(b) fat in an amount of about 20 E% or less, about 15 E% or less, about 15 E% or less, about 10 E% or less, or about 5 E% or less; and

(c) carbohydrate in an amount of about 60 E% or more, about 65 E% or more, about 70 E% or more, about 75 E% or more, about 80 E% or more, about 85 E% or more, about 90 E% or more, or about 95 E% or more.

In some embodiments, the composition comprises protein in an amount of about 20 E% or less, fat in an amount of about 15 E% or less, and carbohydrate in an amount of about 70 E% or more.

In some embodiments, the composition comprises protein in an amount of about 15 E% or less, fat in an amount of about 10 E% or less, and carbohydrate in an amount of about 75 E% or more.

In some embodiments, the composition comprises protein in an amount of about 15 E% or less, fat in an amount of about 10 E% or less, and carbohydrate in an amount of about 80 E% or more.

The composition may further comprise any other nutrients required to support the subject's physiologic needs. Suitably, the composition further comprises micronutrients and dietary fibre.

In an aspect of the present invention, a nutritional composition or supplement (e.g., a single nutritional composition or supplement that is one of a plurality of components of a diet) conforms to the parameters of the diet disclosed herein, and thus the nutritional composition or supplement beneficially improves or maintains cardiovascular health in a subject when consumed or administered with the diet disclosed herein or even with a diet having one or more parameters outside those of the diet disclosed herein. In this regard, the preferred diet disclosed herein comprises 10 E% to 35 E% protein, 8 E% to 22 E% fat, and 55 E% to 80 E% carbohydrate; and thus some embodiments of the nutritional composition or supplement comprise 10 E% to 35 E% protein, 8 E% to 22 E% fat, and 55 E% to 80 E% carbohydrate. This nutritional composition or supplement may be used in any of the methods disclosed herein and administered to any of the subjects disclosed herein.

These embodiments of the nutritional composition or supplement beneficially improve or maintain cardiovascular health in a subject, even when consumed or administered with a diet having one or more parameters outside those of the diet disclosed herein, by adjusting these one or more parameters to be closer to (or within) those of the diet disclosed herein. The nutritional composition or supplement may replace one or more of the components of the initial diet having one or more parameters outside those of the diet disclosed herein, and/or the nutritional composition or supplement may be consumed additionally to the components of the initial diet having one or more parameters outside those of the diet disclosed herein. The subject may consume an increasing number of the nutritional composition or supplement (e.g., one, then two, then three, and so on) to bring the parameters of the modified diet even closer to the target ranges disclosed herein.

For example, a subject consuming an initial diet in which the overall protein is less than 10 E% or greater than 35 E% of the diet may consume an embodiment of the nutritional composition or supplement which comprises about 10 E% to about 35 E% protein, from about

8 E% to about 22 E% fat, and from about 55 E% to about 80 E% carbohydrate, to thereby adjust the overall protein of the diet closer to (or within) the target range of 10 E% to 35 E% protein. This adjustment in the protein portion of the diet may improve or maintain cardiovascular health.

As another example, a subject consuming an initial diet in which the overall fat is less than 8 E% or greater than 22 E% of the diet may consume an embodiment of the nutritional composition or supplement which comprises about 10 E% to about 35 E% protein, from about 8 E% to about 22 E% fat, and from about 55 E% to about 80 E% carbohydrate, to thereby adjust the overall fat of the diet closer to (or within) the target range of 8 E% to 22 E% fat. This adjustment in the fat portion of the diet may improve or maintain cardiovascular health.

As yet another example, a subject consuming an initial diet in which the overall carbohydrate is less than 55 E% or greater than 80 E% of the diet may consume an embodiment of the nutritional composition or supplement which comprises about 10 E% to about 35 E% protein, from about 8 E% to about 22 E% fat, and from about 55 E% to about 80 E% carbohydrate, to thereby adjust the overall carbohydrate of the diet closer to (or within) the target range of 55 E% to 80 E% carbohydrate. This adjustment in the carbohydrate portion of the diet may improve or maintain cardiovascular health.

Accordingly, some embodiments of the nutritional composition or supplement have one or more features of the diet disclosed above in the “Diets” section of the Detailed Description. For example, some embodiments of the nutritional composition or supplement may comprise one or more of: about 10 E% to about 35 E% protein, from about 8 E% to about 22 E% fat, and from about 55 E% to about 80 E% carbohydrate. Non-limiting particular embodiments include a nutritional composition or supplement comprising about 11 E% to about 28 E% protein, from about 10 E% to about 13 E% fat, and from about 62 E% to about 79 E% carbohydrate.

Methods of improving and/or maintaining cardiovascular health

The diet or compositions of the present invention may be used to improve and/or maintain cardiovascular health.

The present invention provides a method of improving and/or maintaining cardiovascular health in a subject, the method comprising administering the diet of the present invention to said subject.

The present invention provides a method of improving and/or maintaining cardiovascular health in a subject, the method comprising administering one or more compositions to said subject, such that the subject's diet is according to the present invention.

As used herein, "cardiovascular health" may refer to the health of the heart and blood vessels. The term "cardiovascular health" may be defined by metrics such as health behaviours and health factors. Definitions for poor, intermediate, and ideal cardiovascular health are known, for example based on seven metrics defined by the American Heart Association: hypertension, high cholesterol, smoking, body mass index, diabetes, physical activity, and consumption of fruits and vegetables (see e.g. Lloyd-Jones, et al., 2010. Circulation, 121(4), pp.586-613). In some embodiments, the subject's muscle health is determined by an overall CVH score. In some embodiments, poor cardiovascular health is defined as a subject meeting 0-2 of the 7 metrics defined by the American Heart Association.

As used herein, methods of "improving and/or maintaining" cardiovascular health may reduce the severity or delay the onset of symptoms associated with poor cardiovascular health, such as chest pain, shortness of breath, coughing or wheezing, etc.

In some embodiments, improving and/or maintaining cardiovascular health may refer to one or more of the following: (a) reducing the subject's plasma LDL/HDL cholesterol ratio; (b) reducing the subject's plasma total cholesterol; (c) reducing the subject's plasma LDL cholesterol; (d) reducing the subject's plasma apolipoprotein B/apolipoprotein A ratio; and/or (e) reducing the subject's plasma apolipoprotein B.

In some embodiments, improving and/or maintaining cardiovascular health may refer to treating and/or preventing dyslipidaemia, hypercholesterolemia, a dyslipidaemia-related comorbidity, and/or cardiovascular disease. In some embodiments, improving and/or maintaining cardiovascular health may refer to treating and/or preventing dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity. In some embodiments, improving and/or maintaining cardiovascular health may refer to treating and/or preventing cardiovascular disease.

As used herein, the term "preventing" may refer to averting, delaying, impeding or hindering the contraction of the disease. The diet or compositions of the present invention may, for example, prevent or reduce the likelihood of developing or contracting dyslipidaemia, hypercholesterolemia, a dyslipidaemia-related comorbidity and/or cardiovascular disease.

As used herein, the term "treating" may refer to caring for a diseased subject, in order to ameliorate, cure or reduce the symptoms of the disease, or in order to reduce, halt or delay

the progression of the disease. The diet or compositions of the present invention may, for example, ameliorate, cure or reduce the symptoms of dyslipidaemia, hypercholesterolemia, a dyslipidaemia-related comorbidity and/or cardiovascular disease.

Subject

The subject may be any suitable subject. In preferred embodiments, the subject is a human.

In some embodiments, the subject is an adult. In some embodiments, the subject is at least about 20 years of age, at least about 25 years or age, at least about 30 years of age, at least about 35 years of age, at least about 40 years of age, at least about 45 years of age, at least about 50 years of age, at least about 55 years of age, or at least about 60 years of age. In some embodiments, the subject is at least about 40 years of age. In some embodiments, the subject is 69 years of age or less.

In some embodiments, the subject has or is at risk of poor cardiovascular health. In some embodiments, the subject is at risk of poor cardiovascular health. In some embodiments, the subject has poor cardiovascular health.

In some embodiments, the subject has or is at risk of dyslipidaemia, hypercholesterolemia, a dyslipidaemia-related comorbidity and/or cardiovascular disease. In some embodiments, the subject is at risk of dyslipidaemia, hypercholesterolemia, a dyslipidaemia-related comorbidity and/or cardiovascular disease. In some embodiments, the subject has dyslipidaemia, hypercholesterolemia, a dyslipidaemia-related comorbidity and/or cardiovascular disease.

In some embodiments, the subject has one or more, two more, three or more, or four or more of the following: a high plasma LDL/HDL cholesterol ratio, a high plasma total cholesterol level, a high plasma LDL cholesterol level, a high plasma apolipoprotein B/apolipoprotein A ratio level, and/or a high plasma apolipoprotein B level. In some embodiments, the subject has each of the following: a high plasma LDL/HDL cholesterol ratio, a high plasma total cholesterol level, a high plasma LDL cholesterol level, a high plasma apolipoprotein B/apolipoprotein A ratio level, and/or a high plasma apolipoprotein B level.

In some embodiments, the subject has a plasma LDL/HDL cholesterol ratio of about 2.0 or higher, about 2.1 or higher, about 2.2 or higher, about 2.3 or higher, about 2.4 or higher, about 2.5 or higher, about 2.6 or higher, about 2.7 or higher, about 2.8 or higher, about 2.9 or higher, or about 3.0 or higher.

In some embodiments, the subject has a plasma total cholesterol of about 4.0 mmol/L or higher, about 4.1 mmol/L or higher, about 4.2 mmol/L or higher, about 4.3 mmol/L or higher,

about 4.4 mmol/L or higher, about 4.5 mmol/L or higher, about 4.6 mmol/L or higher, about 4.7 mmol/L or higher, about 4.8 mmol/L or higher, about 4.9 mmol/L or higher, about 5.0 mmol/L or higher, about 5.1 mmol/L or higher, about 5.2 mmol/L or higher, about 5.3 mmol/L or higher, about 5.4 mmol/L or higher, about 5.5 mmol/L or higher, about 5.6 mmol/L or higher, about 5.7 mmol/L or higher, about 5.8 mmol/L or higher, about 5.9 mmol/L or higher, or about 6.0 mmol/L or higher.

In some embodiments, the subject has a plasma LDL cholesterol of about 2.5 mmol/L or higher, about 2.6 mmol/L or higher, about 2.7 mmol/L or higher, about 2.8 mmol/L or higher, about 2.9 mmol/L or higher, about 3.0 mmol/L or higher, about 3.1 mmol/L or higher, about 3.2 mmol/L or higher, about 3.3 mmol/L or higher, about 3.4 mmol/L or higher, about 3.5 mmol/L or higher, about 3.6 mmol/L or higher, about 3.7 mmol/L or higher, about 3.8 mmol/L or higher, about 3.9 mmol/L or higher, or about 4.0 mmol/L or higher.

In some embodiments, the subject has a plasma apolipoprotein B/apolipoprotein A ratio of about 0.50 or higher, about 0.55 or higher, about 0.60 or higher, about 0.65 or higher, about 0.70 or higher, about 0.75 or higher, about 0.80 or higher, about 0.85 or higher, or about 0.90 or higher.

In some embodiments, the subject has a plasma apolipoprotein B of about 0.7 g/L or more, about 0.8 g/L or more, about 0.9 g/L or more, about 1.0 g/L or more, about 1.1 g/L or more, about 1.2 g/L or more, or about 1.3 g/L or more.

In some embodiments, the subject has one or more, two or more, three or more, or four or more selected from the following: a plasma LDL/HDL cholesterol ratio of about 2.0 or higher; a plasma total cholesterol of about 4.0 mmol/L or higher; a plasma LDL cholesterol of about 2.5 mmol/L or higher; a plasma apolipoprotein B/apolipoprotein A ratio of about 0.50 or higher; and a plasma apolipoprotein B of about 0.7 g/L or more.

In some embodiments, the subject has each of the following: a plasma LDL/HDL cholesterol ratio of about 2.0 or higher; a plasma total cholesterol of about 4.0 mmol/L or higher; a plasma LDL cholesterol of about 2.5 mmol/L or higher; a plasma apolipoprotein B/apolipoprotein A ratio of about 0.50 or higher; and a plasma apolipoprotein B of about 0.7 g/L or more.

In some embodiments, the subject has one or more, two or more, three or more, or four or more selected from the following: a plasma LDL/HDL cholesterol ratio of about 2.5 or higher; a plasma total cholesterol of about 5.0 mmol/L or higher; a plasma LDL cholesterol of about 3.0 mmol/L or higher; a plasma apolipoprotein B/apolipoprotein A ratio of about 0.70 or higher; and a plasma apolipoprotein B of about 1.0 g/L or more.

In some embodiments, the subject has each of the following: a plasma LDL/HDL cholesterol ratio of about 2.5 or higher; a plasma total cholesterol of about 5.0 mmol/L or higher; a plasma LDL cholesterol of about 3.0 mmol/L or higher; a plasma apolipoprotein B/apolipoprotein A ratio of about 0.70 or higher; and a plasma apolipoprotein B of about 1.0 g/L or more.

In some embodiments, the subject has a low plasma HDL cholesterol level and/or a low plasma apolipoprotein A level.

In some embodiments, the subject has a plasma HDL cholesterol of about 0.9 mmol/L or lower, about 0.8 mmol/L or lower, or about 0.7 mmol/L or lower. In some embodiments, the subject has a plasma apolipoprotein A of about 1.0 g/L or lower, about 0.9 g/L or lower, or about 0.7 g/L or lower.

Lipid biomarkers

In some embodiments, the diet or compositions of the present invention are used to improve and/or maintain one or more lipid biomarkers. The present inventors have surprisingly shown that the diet of the present invention is associated with a lower plasma LDL/HDL cholesterol ratio, lower plasma total cholesterol, lower plasma LDL cholesterol, a lower plasma apolipoprotein B/apolipoprotein A ratio, and lower plasma apolipoprotein B.

The present invention provides a method of improving and/or maintaining one or more lipid biomarkers in a subject, the method comprising administering the diet of the present invention to said subject. The present invention also provides a method of improving and/or maintaining one or more lipid biomarkers in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the diet or compositions of the present invention reduce one or more, two or more, three or more, four or more, or all of the subject's plasma LDL/HDL cholesterol ratio, plasma total cholesterol, plasma LDL cholesterol, plasma apolipoprotein B/apolipoprotein A ratio, and plasma apolipoprotein B. The reduction may be compared to a subject administered a diet which does not fall within the scope of the present invention.

In some embodiments, the diet or compositions of the present invention reduce the subject's plasma LDL/HDL cholesterol ratio. In some embodiments, the subject's plasma LDL/HDL cholesterol ratio is reduced by at least about 0.1, at least about 0.2, at least about 0.3, at least about 0.4, or at least about 0.5. In some embodiments, the subject's plasma LDL/HDL cholesterol ratio is reduced to about 2.4 or lower, about 2.3 or lower, about 2.2 or lower, about 2.1 or lower, or about 2.0 or lower.

In some embodiments, the diet or compositions of the present invention reduce the subject's plasma total cholesterol. In some embodiments, the subject's plasma total cholesterol is reduced by at least about 0.1 mmol/L, at least about 0.2 mmol/L, at least about 0.3 mmol/L, at least about 0.4 mmol/L, or at least about 0.5 mmol/L. In some embodiments, the subject's plasma total cholesterol is reduced to about 5.9 mmol/L or lower, about 5.8 mmol/L or lower, about 5.7 mmol/L or lower, about 5.6 mmol/L or lower, about 5.5 mmol/L or lower, about 5.4 mmol/L or lower, about 5.3 mmol/L or lower, about 5.2 mmol/L or lower, about 5.1 mmol/L or lower, or about 5.0 mmol/L or lower.

In some embodiments, the diet or compositions of the present invention reduce the subject's plasma LDL cholesterol. In some embodiments, the subject's plasma LDL cholesterol is reduced by at least about 0.1 mmol/L, at least about 0.2 mmol/L, at least about 0.3 mmol/L, at least about 0.4 mmol/L, or at least about 0.5 mmol/L. In some embodiments, the subject's plasma LDL cholesterol is reduced to about 3.9 mmol/L or lower, about 3.8 mmol/L or lower, about 3.7 mmol/L or lower, about 3.6 mmol/L or lower, about 3.5 mmol/L or lower, about 3.4 mmol/L or lower, about 3.3 mmol/L or lower, about 3.2 mmol/L or lower, about 3.1 mmol/L or lower, or about 3.0 mmol/L or lower.

In some embodiments, the diet or compositions of the present invention reduce the subject's plasma apolipoprotein B/apolipoprotein A ratio. In some embodiments, the subject's plasma apolipoprotein B/apolipoprotein A ratio is reduced by at least about 0.05, at least about 0.10, at least about 0.15, or at least about 0.20. In some embodiments, the subject's plasma apolipoprotein B/apolipoprotein A ratio is reduced to about 0.70 or lower, about 0.66 or lower, about 0.64 or lower, about 0.62 or lower, or about 0.60 or lower.

In some embodiments, the diet or compositions of the present invention reduce the subject's plasma apolipoprotein B. In some embodiments, the subject's plasma apolipoprotein B is reduced by at least about 0.05 g/L, at least about 0.10 g/L, at least about 0.15 g/L, or at least about 0.20 g/L. In some embodiments, the subject's plasma apolipoprotein B is reduced to about 1.0 g/L or lower, about 0.9 g/L or lower, or about 0.8 g/L or lower.

In some embodiments, the diet or compositions of the present invention increases the subject's HDL cholesterol. In some embodiments, the subject's plasma HDL cholesterol is increased by at least about 0.1 mmol/L, at least about 0.2 mmol/L, at least about 0.3 mmol/L, at least about 0.4 mmol/L, or at least about 0.5 mmol/L. In some embodiments, the subject's plasma HDL cholesterol is increased to about 1.0 mmol/L or higher, about 1.1 mmol/L or higher, about 1.2 mmol/L or higher, about 1.3 mmol/L or higher, or about 1.4 mmol/L or higher.

In some embodiments, the diet or compositions of the present invention increases the subject's plasma apolipoprotein A. In some embodiments, the subject's plasma apolipoprotein A is increased by at least about 0.1 g/L, at least about 0.2 g/L, at least about 0.3 g/L, at least about 0.4 g/L, or at least about 0.5 g/L. In some embodiments, the subject's p plasma apolipoprotein A is increased to about 1.1 g/L or higher, about 1.2 g/L or higher, about 1.3 g/L or higher, about 1.4 g/L or higher, or about 1.5 g/L or higher.

Dyslipidaemia

In some embodiments, the diet or compositions of the present invention are used to treat and/or prevent dyslipidaemia.

The present invention provides a method of treating and/or preventing dyslipidaemia in a subject, the method comprising administering the diet of the present invention to said subject. The present invention also provides a method of treating and/or preventing dyslipidaemia in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the subject has or is at risk of dyslipidaemia. In some embodiments, the subject is at risk of dyslipidaemia. In some embodiments, the subject has dyslipidaemia.

As used herein, "dyslipidaemia" may refer to the imbalance of lipids such as cholesterol, low-density lipoprotein cholesterol, (LDL-C), triglycerides, and high-density lipoprotein (HDL). Dyslipidemia is a major risk factor for coronary heart disease (CHD) (see e.g. Merćep, I., et al., 2022. Pharmaceuticals, 15(7), p.839).

Dyslipidaemia may be diagnosed by any method known in the art. The primary evaluation tool for dyslipidaemia is a fasting lipid panel which consists of total cholesterol, LDL, HDL, and triglycerides. An increased risk of dyslipidaemia may be associated with age, smoking tobacco, alcohol consumption, poor nutrition, obesity, and physical inactivity. Specifically, nutrition risk factors include the insufficient consumption of fruits, nuts/seeds, vegetables, or high consumption of saturated fats (see e.g. Berberich, A.J. and Hegele, R.A., 2022. Endocrine reviews, 43(4), pp.611-653).

In some embodiments, the dyslipidaemia is a secondary dyslipidaemia. Secondary dyslipidaemia is caused by unhealthy lifestyle factors and acquired medical conditions, including underlying diseases and applied drugs. Secondary dyslipidaemia accounts for approximately 30-40% of all dyslipidaemia (see e.g. Yanai, H. and Yoshida, H., 2021. Global health & medicine, 3(1), pp.15-23).

The present invention provides a method of treating and/or preventing secondary dyslipidaemia in a subject, the method comprising administering the diet of the present invention to said subject. The present invention also provides a method of treating and/or preventing secondary dyslipidaemia in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the subject has or is at risk of secondary dyslipidaemia. In some embodiments, the subject is at risk of secondary dyslipidaemia. In some embodiments, the subject has secondary dyslipidaemia.

Hypercholesterolemia

In some embodiments, the diet or compositions of the present invention are used to treat and/or prevent hypercholesterolemia.

The present invention provides a method of treating and/or preventing hypercholesterolemia in a subject, the method comprising administering the diet of the present invention to said subject. The present invention also provides a method of treating and/or preventing hypercholesterolemia in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the subject has or is at risk of hypercholesterolemia. In some embodiments, the subject is at risk of hypercholesterolemia. In some embodiments, the subject has hypercholesterolemia.

Hypercholesterolemia (also known as "high cholesterol") may refer to a type of dyslipidaemia associated with the presence of high levels of cholesterol in the blood. Hypercholesterolemia may be defined as a plasma LDL level >5.0 mmol/L. Hypercholesterolemia may be diagnosed by any method known in the art (e.g. a fasting lipid panel). An increased risk of hypercholesterolemia may be associated with age, smoking tobacco, alcohol consumption, poor nutrition, obesity, and physical inactivity.

Dyslipidaemia-related comorbidities

In some embodiments, the diet or compositions of the present invention are used to treat and/or prevent a dyslipidaemia-related comorbidity.

The present invention provides a method of treating and/or preventing a dyslipidaemia-related comorbidity in a subject, the method comprising administering the diet of the present invention

to said subject. The present invention also provides a method of treating and/or preventing a dyslipidaemia-related comorbidity in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the subject has or is at risk of a dyslipidaemia-related comorbidity. In some embodiments, the subject is at risk of a dyslipidaemia-related comorbidity. In some embodiments, the subject has a dyslipidaemia-related comorbidity.

As used herein, "a dyslipidaemia-related comorbidity" may refer to diseases associated with dyslipidaemia. Dyslipidaemia-related comorbidities may include atherosclerotic cardiovascular disease, xanthomas, xanthelasmas, and corneal arcus (see e.g. Berberich, A.J. and Hegele, R.A., 2022. Endocrine reviews, 43(4), pp.611-653). In some embodiments, the dyslipidaemia-related comorbidity is selected from atherosclerotic cardiovascular disease, xanthomas, carotid bruits, femoral bruits, xanthelasmas, or corneal arcus.

Cardiovascular disease

In some embodiments, the diet or compositions of the present invention are used to treat and/or prevent cardiovascular disease.

The present invention provides a method of treating and/or preventing cardiovascular disease in a subject, the method comprising administering the diet of the present invention to said subject. The present invention also provides a method of treating and/or preventing cardiovascular disease in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the subject has or is at risk of cardiovascular disease. In some embodiments, the subject is at risk of cardiovascular disease. In some embodiments, the subject has cardiovascular disease.

Cardiovascular disease may refer to a group of disorders of the heart and blood vessels, including coronary heart disease, cerebrovascular disease, and rheumatic heart disease (see e.g. Gaziano, T., et al., 2006. Cardiovascular disease. Disease Control Priorities in Developing Countries. 2nd edition). An increased risk of cardiovascular disease may be associated with unhealthful nutrition, physical inactivity, dyslipidemia, hyperglycemia, high blood pressure, obesity, considerations of select patient populations (older age, ethnicity and sex differences), thrombosis/smoking, kidney dysfunction, and genetics/familial hypercholesterolemia (see e.g. Bays, H.E., et al., 2021. American journal of preventive cardiology, 5, p.100149).

In some embodiments, the cardiovascular disease is early cardiovascular disease. Early cardiovascular disease may be associated with vascular and cardiac functional and structural abnormalities (see e.g. Duprez, D.A. and Cohn, J.N., 2008. The Journal of Clinical Hypertension, 10(3), pp.226-231). Early cardiovascular disease may refer to cardiovascular disease in subjects aged about 50 years or younger (see e.g. Ranthe, M.F., et al., 2012. Journal of the American College of Cardiology, 60(9), pp.814-821).

The present invention provides a method of treating and/or preventing early cardiovascular disease in a subject, the method comprising administering the diet of the present invention to said subject. The present invention also provides a method of treating and/or preventing early cardiovascular disease in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the subject has or is at risk of early cardiovascular disease. In some embodiments, the subject is at risk of early cardiovascular disease. In some embodiments, the subject has early cardiovascular disease.

In some embodiments, the cardiovascular disease is an atherosclerotic cardiovascular disease (also known as atherosclerosis), e.g. early atherosclerotic cardiovascular disease. The relationship between dyslipidaemia and atherosclerotic cardiovascular disease is supported by prospective longitudinal cohorts, clinical evidence and genetic linkage studies (see e.g. Lorenzatti, A.J. and Toth, P.P., 2020. European Cardiology Review, 15: e04). In some embodiments, the atherosclerotic cardiovascular disease is selected from coronary heart disease, cerebrovascular disease, angina, acute coronary syndrome, myocardial infarction, stroke, transient ischemic attack, peripheral arterial disease, claudication, and arterial bruits.

The present invention provides a method of treating and/or preventing atherosclerosis in a subject, the method comprising administering the diet of the present invention to said subject. The present invention also provides a method of treating and/or preventing atherosclerosis in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the subject has or is at risk of atherosclerosis. In some embodiments, the subject is at risk of atherosclerosis. In some embodiments, the subject has atherosclerosis.

The present invention provides a method of treating and/or preventing early atherosclerotic cardiovascular disease in a subject, the method comprising administering the diet of the present invention to said subject. The present invention also provides a method of treating

and/or preventing early atherosclerotic cardiovascular disease in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the subject has or is at risk of early atherosclerotic cardiovascular disease. In some embodiments, the subject is at risk of early atherosclerotic cardiovascular disease. In some embodiments, the subject has early atherosclerotic cardiovascular disease.

In some embodiments, the cardiovascular disease is coronary heart disease (also known as coronary artery disease or ischemic heart disease). Genetically determined and metabolically induced disturbances in lipid metabolism, as manifested in several types of dyslipidaemia, have been shown to be causally related to the development of coronary heart disease (see e.g. Kuo, P.T., 1994. Clinical cardiology, 17(10), pp.519-527).

The present invention provides a method of treating and/or preventing coronary heart disease in a subject, the method comprising administering the diet of the present invention to said subject. The present invention also provides a method of treating and/or preventing coronary heart disease in a subject, the method comprising administering one or more composition to said subject, such that the subject's diet is according to the present invention.

In some embodiments, the subject has or is at risk of coronary heart disease. In some embodiments, the subject is at risk of coronary heart disease. In some embodiments, the subject has coronary heart disease.

Methods of determining a diet for improving and/or maintaining cardiovascular health

The present invention provides a method of determining a diet for improving and/or maintaining cardiovascular health in a subject, the method comprising: (a) providing macronutrient requirements for protein, fat, and carbohydrate; and (b) determining a diet that meets said macronutrient requirements. In some embodiments, the method is a computer-implemented method.

The present invention further provides a computer program comprising instructions which, when the program is executed by a computer, cause the computer to carry out a method of determining a diet for improving and/or maintaining cardiovascular health in a subject, the method comprising: (a) providing macronutrient requirements for protein, fat, and carbohydrate; and (b) determining a diet that meets said macronutrient requirements.

The present invention further provides a computer-readable data carrier or data carrier signal having stored thereon a computer program comprising instructions which, when the program

is executed by a computer, cause the computer to carry out a method of determining a diet for improving and/or maintaining cardiovascular health in a subject, the method comprising: (a) providing macronutrient requirements for protein, fat, and carbohydrate; and (b) determining a diet that meets said macronutrient requirements.

The present invention further provides a computer-readable medium comprising instructions which, when executed by a computer, cause the computer to carry out a method of determining a diet for improving and/or maintaining cardiovascular health in a subject, the method comprising: (a) providing macronutrient requirements for protein, fat, and carbohydrate; and (b) determining a diet that meets said macronutrient requirements.

The macronutrient requirements may correspond to those of the diet of the present invention. For example, the macronutrient requirements may be from about 10 E% to about 35 E% protein, from about 8 E% to about 22 E% fat, and from about 55 E% to about 80 E% carbohydrate.

In some embodiments, the macronutrient requirements are:

(a) protein in an amount of from about 10 E% to about 34 E%, from about 10 E% to about 33 E%, from about 10 E% to about 32 E%, from about 10 E% to about 31 E%, from about 10 E% to about 30 E%, from about 11 E% to about 29 E%, or from about 11 E% to about 28 E%;

(b) fat in an amount of from about 8 E% to about 21 E%, from about 8 E% to about 20 E%, from about 8 E% to about 19 E%, from about 8 E% to about 18 E%, from about 9 E% to about 18 E%, from about 10 E% to about 18 E%, from about 10 E% to about 17 E%, from about 10 E% to about 16 E%, from about 10 E% to about 15 E%, from about 10 E% to about 14 E%, or from about 10 E% to about 13 E%; and

(c) carbohydrate in an amount of from 62 E% to 80 E%, from 61 E% to 80 E%, from about 60 E% to about 80 E%, from about 60 E% to about 79 E%, from about 60 E% to about 78 E%, from about 60 E% to about 77 E%, from about 60 E% to about 76 E%, or from about 62 E% to 79 E%.

In some embodiments, the macronutrient requirements are from about 11 E% to about 28 E% protein, from about 10 E% to about 13 E% fat, and from about 62 E% to about 79 E% carbohydrate.

The diet may be determined by any suitable method known in the art and may correspond to any diet described herein. The method of the present invention may be used to determine a

meal plan for the subject. Methods for developing meal plans based on macronutrient distribution are known in the art (see e.g. Ngo, C.H., et al., 2016. J. Comput. Sci., 12(12), pp.582-596).

The diet may provide a total energy intake that fulfils the energy requirements of the subject. For example, the diet may comprise a total energy intake of about 16.0 MJ/day or less. In some embodiments, the diet comprises from about 5.0 MJ/day to about 15.0 MJ/day, from about 5.5 MJ/day to about 14.5 MJ/day, from about 6.0 MJ/day to about 14.0 MJ/day, from about 6.5 MJ/day to about 13.5 MJ/day, from about 7.0 MJ/day to about 13.0 MJ/day, from about 7.5 MJ/day to about 12.5 MJ/day, or from about 8.0 MJ/day to about 12.0 MJ/day.

The present invention provides a diet obtained or obtainable by the method described above.

Methods of determining a diet for a subject

The present invention further provides a method of determining a diet for a subject, the method comprising: (a) determining whether the subject has or is at risk of poor cardiovascular health; and (b) determining a diet for the subject, if the subject has or is at risk of poor cardiovascular health. In some embodiments, the method is a computer-implemented method.

The present invention further provides a computer program comprising instructions which, when the program is executed by a computer, cause the computer to carry out a method of determining a diet, the method comprising: (a) determining whether the subject has or is at risk of poor cardiovascular health; and (b) determining a diet for the subject, if the subject has or is at risk of poor cardiovascular health.

The present invention further provides a computer-readable data carrier or data carrier signal having stored thereon a computer program comprising instructions which, when the program is executed by a computer, cause the computer to carry out a method of determining a diet, the method comprising: (a) determining whether the subject has or is at risk of poor cardiovascular health; and (b) determining a diet for the subject, if the subject has or is at risk of poor cardiovascular health.

The present invention further provides a computer-readable medium comprising instructions which, when executed by a computer, cause the computer to carry out a method of determining a diet, the method comprising: (a) determining whether the subject has or is at risk of poor cardiovascular health; and (b) determining a diet for the subject, if the subject has or is at risk of poor cardiovascular health.

Any suitable method may be used to determine whether the subject has or is at risk of poor cardiovascular health. For example, using a fasting lipid panel which consists of total cholesterol, LDL, HDL, and triglycerides, a lifestyle questionnaire, and/or family history. In some embodiments, the method comprises determining whether the subject has or is at risk of poor cardiovascular health using a fasting lipid panel.

In some embodiments, the subject has or is at risk of poor cardiovascular health if they have one or more, two or more, three or more, four or more selected from the following or if they have each of the following:

(a) a plasma LDL/HDL cholesterol ratio of about 2.0 or higher, about 2.1 or higher, about 2.2 or higher, about 2.3 or higher, about 2.4 or higher, about 2.5 or higher, about 2.6 or higher, about 2.7 or higher, about 2.8 or higher, about 2.9 or higher, or about 3.0 or higher;

(b) a plasma total cholesterol of about 4.0 mmol/L or higher, about 4.1 mmol/L or higher, about 4.2 mmol/L or higher, about 4.3 mmol/L or higher, about 4.4 mmol/L or higher, about 4.5 mmol/L or higher, about 4.6 mmol/L or higher, about 4.7 mmol/L or higher, about 4.8 mmol/L or higher, about 4.9 mmol/L or higher, about 5.0 mmol/L or higher, about 5.1 mmol/L or higher, about 5.2 mmol/L or higher, about 5.3 mmol/L or higher, about 5.4 mmol/L or higher, about 5.5 mmol/L or higher, about 5.6 mmol/L or higher, about 5.7 mmol/L or higher, about 5.8 mmol/L or higher, about 5.9 mmol/L or higher, about or 6.0 mmol/L or higher;

(c) a plasma LDL cholesterol of about 2.5 mmol/L or higher, about 2.6 mmol/L or higher, about 2.7 mmol/L or higher, about 2.8 mmol/L or higher, about 2.9 mmol/L or higher, about 3.0 mmol/L or higher, about 3.1 mmol/L or higher, about 3.2 mmol/L or higher, about 3.3 mmol/L or higher, about 3.4 mmol/L or higher, about 3.5 mmol/L or higher, about 3.6 mmol/L or higher, about 3.7 mmol/L or higher, about 3.8 mmol/L or higher, about 3.9 mmol/L or higher, about or 4.0 mmol/L or higher;

(d) a plasma apolipoprotein B/apolipoprotein A ratio of about 0.50 or higher, about 0.55 or higher, about 0.60 or higher, about 0.65 or higher, about 0.70 or higher, about 0.75 or higher, about 0.80 or higher, about 0.85 or higher, or about 0.90 or higher; and

(e) a plasma apolipoprotein B of about 0.7 g/L or more, about 0.8 g/L or more, about 0.9 g/L or more, about 1.0 g/L or more, about 1.1 g/L or more, about 1.2 g/L or more, or about 1.3 g/L or more.

Any suitable method may be used to determine the diet for the subject. The diet may be a diet according to the present invention. The diet may be determined by a method according to the present invention.

The present invention provides a diet obtained or obtainable by the method described above.

EXAMPLES

The invention is further described with reference to the following examples. It will be appreciated that the invention as claimed is not intended to be limited in any way by these examples.

Example 1 – relationship between dietary macronutrient balance and markers of cardiovascular health

This example uses cardiometabolic data from the UK Biobank cohort and applies a Nutritional Geometry approach to determine the relationship between dietary macronutrient balance and markers of cardiovascular health.

Methodology and model validation

Nutritional Geometry (NG) is a multidimensional framework that models the complex relationships between nutrients and biological parameters. It provides a comprehensive view of how different nutrients interact and influence various biological outcomes. In NG, a model of subject's nutritional relationship with biological parameters is created in a multi-dimensional space. In the case of macronutrients, this space is three-dimensional, i.e., protein, fat and carbohydrate dimensions. To visualize how dietary factors interact to affect biological outcomes, heat maps or response surfaces are generated.

Right-Angled Mixture Triangles (RMTs) are a geometrical tool that allows visualization of nutrients in a multi-dimensional nutrient space. In the context of NG for macronutrients, the vertices of the RMT represent the pure macronutrients (protein, fat, and carbohydrates), and any point within the triangle signifies a mixture of these nutrients in specific ratios. The position of this point indicates the proportions of the mix, providing a clear and intuitive representation of nutrient combinations (see e.g. Simpson, S.J., et al., 2017. Nutrition and Healthy Aging, 4(3), pp.217-226). **Figure 1** shows an example RMT. Diets with different macronutrient compositions can be plotted on the landscape such that the sum of energy from protein, fat and carbohydrates is always 100%. Data for biological outcomes can be superimposed on this landscape as a response surface.

The UK Biobank is a large-scale biomedical database and research resource, established in 2006. Since its creation, it has collected data on half a million UK residents aged between 40 and 69 years old (see e.g. Bycroft, C., et al., 2018. Nature, 562(7726), pp.203-209). UK Biobank is a longitudinal study wherein data is collected from the participants multiple times during an extended period of time, enabling the researchers to follow the onset, development and the progression of diseases. All the data in the UK Biobank database have been checked for mismatches and formatting issues, and validated against a definitive list of coded values. A rich variety of phenotypic and health-related information is available on each participant, including anthropometric measurements, lifestyle indicators, dietary data, biomarkers in blood and urine, and imaging of the body and brain.

Subjects with data available for all variables studied were selected. This yielded a “complete” dataset with about 6000 individuals. The first and ninety-ninth percentile method was used to identify outliers. For the analyses, the dietary data used was collected by four cycles of 24-hour dietary recalls between February 2011 and June 2012. This dataset included data for protein, fat and carbohydrate intakes. For the blood parameters, data from the samples collected in the 2012-2013 cycles was used. The data was adjusted for factors such as energy intake, gender, BMI, age, smoking status and household income.

A Generalized Additive Model (GAM) method was used for data analysis due to its flexibility and the ability to adjust for covariates. To validate the methods, the results of the modelling of UK Biobank data for daily energy intake were compared with published data. Overall, we found that the relationship between macronutrient balance and ad-libitum energy intake were consistent between the two sets of data. Both datasets show a strong influence of dietary protein content on daily calorie intake (see **Figure 2** and Figure 3(b) from Raubenheimer, D., et al., 2015. British Journal of Nutrition, 113(S1), pp.S26-S39.

Macronutrient ranges associated with lower LDL/HDL cholesterol ratio and lower apolipoprotein-B/apolipoprotein-A ratio were identified from visual inspection of the heatmaps (Figures 3 and 4). Wilcoxon testing was then conducted to confirm that these macronutrient ranges were associated with significantly lower ratios of LDL/HDL cholesterol as well as significantly lower ratios of apolipoprotein-B/apolipoprotein-A.

Results and discussion

The GAM method was applied to the selected UK Biobank dataset, for the following biomarkers of cardiovascular health:

- **Total Cholesterol.** Cholesterol is well known for its association with cardiovascular disorders, especially plaque deposits in the arteries that are a hallmark of coronary artery disease (see e.g. Center for Disease Control and Prevention, "Coronary artery disease," 2024).
- **LDL and HDL Cholesterol.** HDL (High-Density Lipoprotein) and LDL (Low-Density Lipoprotein) are two types of lipoproteins that carry cholesterol in the blood. The critical distinction lies in their functions, high HDL levels being protective, and high LDL levels increasing the risk of coronary artery disease (see e.g. Sun, T., et al., 2022. BMC Cardiovascular Disorders, 22(1), p.273).
- **Apolipoproteins A and B.** Apolipoproteins are members of the family of proteins that combine with lipids (fats) to form lipoproteins. Apolipoproteins A and B are strongly linked to cardiovascular disease risk. The apolipoprotein A is found in HDL and the apolipoprotein B is associated with LDL. A high apo-B to apo-A ratio indicates an increased risk of cardiovascular events (see e.g. Lu, M., et al., 2011. Journal of biomedical research, 25(4), pp.266-273; and Kaneva, A.M., et al., 2015. Disease markers, 2015, p.591454).

The RMTs for (a) Total Cholesterol, (b) LDL Cholesterol, and (c) LDL/HDL Cholesterol are shown in **Figures 3A-C**:

- For total cholesterol and LDL-cholesterol, diets containing ≥30 E% protein, ≥ 30 E% fat and ≤ 30 E% carbohydrate led to the highest circulating levels of these lipid species. Conversely, lowest total and LDL-cholesterol levels were observed on diets low in fat, relatively low in protein and high in carbohydrate content (see **Figure 3A** and **Figure 3B**).
- The LDL/HDL ratio was lowest on diets containing relatively low protein, low fat and high carbohydrate (see **Figure 3C**).

The RMTs for (a) Apolipoprotein B and (b) Ratio Apolipoprotein B/ Apolipoprotein A are shown in **Figures 4A-B**. The results for apolipoprotein are consistent with the results for LDL and HDL:

- For both LDL-cholesterol (**Figure 3B**) and apolipoprotein B (**Figure 4A**), diets rich in protein and fat generated maximum levels.
- The response surface for the ratio apo-B/apo-A (**Figure 4B**) is also consistent with LDL/HDL ratio with minimum values observed on diets with low fat, lower protein and high carbohydrate content.

In summary, the results surprisingly show that a diet comprising about 10-35 E% protein, about 8-22 E% fat, and about 55-80 E% carbohydrate are associated with improvements in lipid biomarkers of cardiovascular health.

EMBODIMENTS

Various preferred features and embodiments of the present invention will now be described with reference to the following numbered paragraphs (paras).

1. A diet for use in improving or maintaining cardiovascular health in a subject, wherein the diet comprises a total energy intake of 16.0 MJ/day or less, and wherein the diet comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

2. The diet for use according to para 1, wherein the diet comprises protein in an amount of at least 11 E%, at least 12 E%, at least 13 E%, at least 14 E%, or at least 15 E%.

3. The diet for use according to para 1 or 2, wherein the diet comprises protein in an amount of 34 E% or less, 33 E% or less, 32 E% or less, 31 E% or less, 30 E% or less, 29 E% or less, 28 E% or less, 27 E% or less, 26 E% or less, or 25 E% or less.

4. The diet for use according to any preceding para, wherein the diet comprises protein in an amount of from 10 E% to 34 E%, from 10 E% to 33 E%, from 10 E% to 32 E%, from 10 E% to 31 E%, from 10 E% to 30 E%, from 11 E% to 29 E%, or from 11 E% to 28 E%.

5. The diet for use according to any preceding para, wherein the diet comprises fat in an amount of at least 9 E%, at least 10 E%, at least 11 E%, or at least 12 E%.

6. The diet for use according to any preceding para, wherein the diet comprises fat in an amount of 21 E% or less, 20 E% or less, 19 E% or less, 18 E% or less, 17 E% or less, 16 E% or less, 15 E% or less, 14 E% or less, or 13 E% or less.

7. The diet for use according to any preceding para, wherein the diet comprises fat in an amount of from 8 E% to 21 E%, from 8 E% to 20 E%, from 8 E% to 19 E%, from 8 E% to 18 E%, from 9 E% to 18 E%, from 10 E% to 18 E%, from 10 E% to 17 E%, from 10 E% to 16 E%, from 10 E% to 15 E%, from 10 E% to 14 E%, or from 10 E% to 13 E%.

8. The diet for use according to any preceding para, wherein the diet comprises carbohydrate in an amount of at least 56 E%, at least 57 E%, at least 58 E%, at least 59 E%, at least 60 E%, at least 61 E%, at least 62 E%, at least 63 E%, at least 64 E%, or at least 65 E%.

9. The diet for use according to any preceding para, wherein the diet comprises carbohydrate in an amount of 79 E% or less, 78 E% or less, 77 E% or less, 76 E% or less, or 75 E% or less.

10. The diet for use according to any preceding para, wherein the diet comprises carbohydrate in an amount of from 60 E% to 80 E%, from 60 E% to 79 E%, from 61 E% to 79 E%, or from 62 E% to 79 E%.

11. The diet for use according to any preceding para, wherein the diet comprises from 11 E% to 28 E% protein, from 10 E% to 13 E% fat, and from 62 E% to 79 E% carbohydrate.

12. The diet for use according to any preceding para, wherein the diet comprises a total energy intake of 15.5 MJ/day or less, 15.0 MJ/day or less, 14.5 MJ/day or less, 14.0 MJ/day or less, 13.5 MJ/day or less, 13.0 MJ/day or less, 12.5 MJ/day or less, 12.0 MJ/day or less, 11.5 MJ/day or less, 11.0 MJ/day or less, 10.5 MJ/day or less, or 10.0 MJ/day or less.

13. The diet for use according to any preceding para, wherein the diet comprises a total energy intake of 7.0 MJ/day or more, 7.5 MJ/day or more, or 8.0 MJ/day or more.

14. The diet for use according to any preceding para, wherein the diet is administered for at least one week, at least two weeks, at least three weeks, or at least four weeks.

15. The diet for use according to any preceding para, wherein the diet is administered for at least one month, at least two months, at least three months, at least six months, at least nine months, or at least twelve months.

16. The diet for use according to any preceding para, wherein the diet is administered for at least one year, at least two years, at least three years, at least four years, or at least five years.

17. The diet for use according to any preceding para, wherein the diet comprises at least 4 food groups per day, at least 5 food groups per day, at least 6 food groups per day, or at least 7 food groups per day.

18. The diet for use according to any preceding para, wherein the diet comprises dietary fibre in an amount of from 10 g/1000 kcal to 16 g/1000 kcal, from 11 g/1000 kcal to 15 g/1000 kcal, or from 12 g/1000 kcal to 14 g/1000 kcal.

19. The diet for use according to any preceding para, wherein the subject is human.

20. The diet for use according to any preceding para, wherein the subject is an adult.

21. The diet for use according to any preceding para, wherein the subject is at least 40 years of age.

22. The diet for use according to any preceding para, wherein the subject has or is at risk of poor cardiovascular health.

23. The diet for use according to any preceding para, wherein the subject has or is at risk of dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity.

24. The diet for use according to any preceding para, wherein the subject has or is at risk of cardiovascular disease, optionally wherein the subject has or is at risk of atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease.

25. The diet for use according to any preceding para, wherein the subject has one or more selected from the following:

(i) a plasma LDL/HDL cholesterol ratio of 2.5 or higher, 2.6 or higher, 2.7 or higher, 2.8 or higher, 2.9 or higher, or 3.0 or higher;

(ii) a plasma total cholesterol of 5.0 mmol/L or higher, 5.1 mmol/L or higher, 5.2 mmol/L or higher, 5.3 mmol/L or higher, 5.4 mmol/L or higher, 5.5 mmol/L or higher, 5.6 mmol/L or higher, 5.7 mmol/L or higher, 5.8 mmol/L or higher, 5.9 mmol/L or higher, or 6.0 mmol/L or higher;

(iii) a plasma LDL cholesterol of 3.0 mmol/L or higher, 3.1 mmol/L or higher, 3.2 mmol/L or higher, 3.3 mmol/L or higher, 3.4 mmol/L or higher, 3.5 mmol/L or higher, 3.6 mmol/L or higher, 3.7 mmol/L or higher, 3.8 mmol/L or higher, 3.9 mmol/L or higher, or 4.0 mmol/L or higher;

(iv) a plasma apolipoprotein B/apolipoprotein A ratio of 0.70 or higher, 0.80 or higher, or 0.90 or higher; and

(v) a plasma apolipoprotein B of 1.0 g/L or more, 1.1 g/L or more, 1.2 g/L or more, or 1.3 g/L or more.

26. The diet for use according to any preceding para, wherein administration of the diet to the subject:

(i) reduces the subject's plasma LDL/HDL cholesterol ratio, optionally wherein the subject's plasma LDL/HDL cholesterol ratio is reduced by at least 0.1, at least 0.2, at least 0.3, at least 0.4, or at least 0.5;

(ii) reduces the subject's plasma total cholesterol, optionally wherein the subject's plasma total cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L;

(iii) reduces the subject's plasma LDL cholesterol, optionally wherein the subject's plasma LDL cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L;

(iv) reduces the subject's plasma apolipoprotein B/apolipoprotein A ratio, optionally wherein the subject's plasma apolipoprotein B/apolipoprotein A ratio is reduced by at least 0.05, at least 0.10, at least 0.15, or at least 0.20; and/or

(v) reduces the subject's plasma apolipoprotein B, optionally wherein the subject's plasma apolipoprotein B is reduced by at least 0.05 g/L, at least 0.10 g/L, at least 0.15 g/L, or at least 0.20 g/L.

27. The diet for use according to any preceding para, wherein administration of the diet to the subject treats or prevents dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity.

28. The diet for use according to para 27, wherein the dyslipidaemia-related comorbidity is xanthomas, carotid bruits, femoral bruits, xanthelasmas, or corneal arcus.

29. The diet for use according to any preceding para, wherein administration of the diet to the subject treats or prevents cardiovascular disease.

30. The diet for use according to para 29, wherein the cardiovascular disease is atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease.

31. A nutritional composition or supplement for use in improving or maintaining cardiovascular health in a subject, wherein the nutritional composition or supplement comprises 70 E% carbohydrate or more, and wherein the nutritional composition or supplement is administered to the subject such that the subject's diet comprises a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

32. The nutritional composition or supplement for use according to para 31, wherein the diet is defined according to any of paras 1-18.

33. The nutritional composition or supplement for use according to para 31 or 32, wherein the subject is defined according to any of paras 19-25.

34. The nutritional composition or supplement for use according to any of paras 31-33, wherein the effect of administering the nutritional composition or supplement to the subject is defined according to any of paras 26-30.

35. The nutritional composition or supplement for use according to any of paras 31-34, wherein the nutritional composition or supplement comprises carbohydrate in an amount of 75 E% or more, 80 E% or more, 85 E% or more, 90 E% or more, or 95 E% or more.

36. The nutritional composition or supplement for use according to any of paras 31-35, wherein the nutritional composition or supplement comprises fat in an amount of 15 E% or less, 10 E% or less, or 5 E% or less.

37. The nutritional composition or supplement for use according to any of paras 31-36, wherein the nutritional composition or supplement comprises protein in an amount of 20 E% or less, 15 E% or less, 10 E% or less, or 5 E% or less.

38. The nutritional composition or supplement for use according to any of paras 31-37, wherein the nutritional composition or supplement comprises protein in an amount of 15 E% or less, fat in amount of 10 E% or less, and carbohydrate in an amount of 75 E% or more.

39. A method of determining a diet for improving or maintaining cardiovascular health in a subject, the method comprising:

(a) providing macronutrient requirements for protein, fat, and carbohydrate, wherein the macronutrient requirements are from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate; and

(b) determining a diet comprising a total energy intake of 16.0 MJ/day or less that meets said macronutrient requirements.

40. The method according to para 39, wherein the diet is defined according to any of paras 1-18.

41. The method according to para 39 or 40, wherein the subject is defined according to any of paras 19-25.

42. The method according to any of paras 39-41, wherein the effect of administering the diet to the subject is defined according to any of paras 26-30.

43. A method of determining a diet for a subject, the method comprising:

(a) determining whether the subject has or is at risk of poor cardiovascular health; and

(b) determining a diet for the subject, wherein if the subject has or is at risk of poor cardiovascular health the diet comprises a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

44. The method according to para 43, wherein the diet is defined according to any of paras 1-18.

45. The method according to para 43 or 44, wherein the subject has or is at risk of poor cardiovascular health if they have one or more of the following:

(i) a plasma LDL/HDL cholesterol ratio of 2.5 or higher, 2.6 or higher, 2.7 or higher, 2.8 or higher, 2.9 or higher, or 3.0 or higher;

(ii) a plasma total cholesterol of 5.2 mmol/L or higher, 5.3 mmol/L or higher, 5.4 mmol/L or higher, 5.5 mmol/L or higher, 5.6 mmol/L or higher, 5.7 mmol/L or higher, 5.8 mmol/L or higher, 5.9 mmol/L or higher, or 6.0 mmol/L or higher;

(iii) a plasma LDL cholesterol of 3.4 mmol/L or higher, 3.5 mmol/L or higher, 3.6 mmol/L or higher, 3.7 mmol/L or higher, 3.8 mmol/L or higher, 3.9 mmol/L or higher, or 4.0 mmol/L or higher;

(iv) a plasma apolipoprotein B/apolipoprotein A ratio of 0.70 or higher, 0.80 or higher, or 0.90 or higher; or

(v) a plasma apolipoprotein B of 1.0 g/L or more, 1.1 g/L or more, 1.2 g/L or more, or 1.3 g/L or more.

46. The method according to any of paras 43-45, wherein the effect of administering the diet to the subject is defined according to any of paras 26-30.

47. The method according to any of paras 39-46, wherein the method is a computer-implemented method.

48. A computer program comprising instructions which, when the program is executed by a computer, cause the computer to carry out the method of any of paras 39-47.

49. A computer-readable data carrier having stored thereon the computer program of para 48.

50. A computer-readable medium comprising instructions which, when executed by a computer, cause the computer to carry out the method of any of paras 39-47.

51. A diet determined by the method of any of paras 39-47.

52. A method of treating or preventing dyslipidaemia, hypercholesterolemia, a dyslipidaemia-related comorbidity, and/or cardiovascular disease and/or improving or maintaining cardiovascular health in a subject, the method comprising administering a diet to said subject, wherein the diet comprises a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

53. The method according to para 52, wherein the diet is defined according to any of paras 1-18.

54. The method according to para 52 or 53, wherein the subject is defined according to any of paras 19-25.

55. The method according to any of paras 52-54, wherein the effect of administering the diet to the subject is defined according to any of paras 26-30.

56. A method of improving or maintaining cardiovascular health in a subject, the method comprising administering a nutritional composition or supplement comprising 70 E% carbohydrate or more to said subject, wherein the nutritional composition or supplement is administered to the subject such that the subject's diet comprises a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

57. The method according to para 56, wherein the diet is defined according to any of paras 1-18.

58. The method according to para 56 or 57, wherein the subject is defined according to any of paras 19-25.

59. The method according to any of paras 56-58, wherein the effect of administering the nutritional composition or supplement to the subject is defined according to any of paras 26-30.

60. The method according to any of paras 56-59, wherein the nutritional composition or supplement is defined according to any of paras 35-38.

61. A nutritional composition or supplement, for use in improving or maintaining cardiovascular health in a subject, wherein the nutritional composition or supplement comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

62. The nutritional composition or supplement according to para 61, wherein the nutritional composition or supplement comprises protein in an amount of at least 11 E%, at least 12 E%, at least 13 E%, at least 14 E%, or at least 15 E%.

63. The nutritional composition or supplement according to para 61 or 62, wherein the nutritional composition or supplement comprises protein in an amount of 34 E% or less, 33 E% or less, 32 E% or less, 31 E% or less, 30 E% or less, 29 E% or less, 28 E% or less, 27 E% or less, 26 E% or less, or 25 E% or less.

64. The nutritional composition or supplement according to any of para 61-63, wherein the nutritional composition or supplement comprises protein in an amount of from 10 E% to 34 E%, from 10 E% to 33 E%, from 10 E% to 32 E%, from 10 E% to 31 E%, from 10 E% to 30 E%, from 11 E% to 29 E%, or from 11 E% to 28 E%.

65. The nutritional composition or supplement according to any of para 61-64, wherein the nutritional composition or supplement comprises fat in an amount of at least 9 E%, at least 10 E%, at least 11 E%, or at least 12 E%.

66. The nutritional composition or supplement according to any of para 61-65, wherein the nutritional composition or supplement comprises fat in an amount of 21 E% or less, 20 E% or less, 19 E% or less, 18 E% or less, 17 E% or less, 16 E% or less, 15 E% or less, 14 E% or less, or 13 E% or less.

67. The nutritional composition or supplement according to any of para 61-66, wherein the nutritional composition or supplement comprises fat in an amount of from 8 E% to 21 E%, from 8 E% to 20 E%, from 8 E% to 19 E%, from 8 E% to 18 E%, from 9 E% to 18 E%, from 10 E% to 18 E%, from 10 E% to 17 E%, from 10 E% to 16 E%, from 10 E% to 15 E%, from 10 E% to 14 E%, or from 10 E% to 13 E%.

68. The nutritional composition or supplement according to any of para 61-67, wherein the nutritional composition or supplement comprises carbohydrate in an amount of at least 56 E%, at least 57 E%, at least 58 E%, at least 59 E%, at least 60 E%, at least 61 E%, at least 62 E%, at least 63 E%, at least 64 E%, or at least 65 E%.

69. The nutritional composition or supplement according to any of para 61-68, wherein the nutritional composition or supplement comprises carbohydrate in an amount of 79 E% or less, 78 E% or less, 77 E% or less, 76 E% or less, or 75 E% or less.

70. The nutritional composition or supplement according to any of para 61-69, wherein the nutritional composition or supplement comprises carbohydrate in an amount of from 60 E% to 80 E%, from 60 E% to 79 E%, from 61 E% to 79 E%, or from 62 E% to 79 E%.

71. The nutritional composition or supplement according to any of para 61-70, wherein the nutritional composition or supplement comprises from 11 E% to 28 E% protein, from 10 E% to 13 E% fat, and from 62 E% to 79 E% carbohydrate.

72. The nutritional composition or supplement according to any of para 61-71, wherein the nutritional composition or supplement is administered for at least one week, at least two weeks, at least three weeks, or at least four weeks.

73. The nutritional composition or supplement according to any of para 61-72, wherein the nutritional composition or supplement is administered for at least one month, at least two months, at least three months, at least six months, at least nine months, or at least twelve months.

74. The nutritional composition or supplement according to any of para 61-73, wherein the nutritional composition or supplement is administered for at least one year, at least two years, at least three years, at least four years, or at least five years.

75. The nutritional composition or supplement according to any of para 61-74, wherein the nutritional composition or supplement comprises dietary fibre in an amount of from 10 g/1000 kcal to 16 g/1000 kcal, from 11 g/1000 kcal to 15 g/1000 kcal, or from 12 g/1000 kcal to 14 g/1000 kcal.

76. The nutritional composition or supplement according to any of para 61-75, wherein the subject is human.

77. The nutritional composition or supplement according to any of para 61-76, wherein the subject is an adult.

78. The nutritional composition or supplement according to any of para 61-77, wherein the subject is at least 40 years of age.

79. The nutritional composition or supplement according to any of para 61-78, wherein the subject has or is at risk of poor cardiovascular health.

80. The nutritional composition or supplement according to any of para 61-79, wherein the subject has or is at risk of dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity.

81. The nutritional composition or supplement according to any of para 61-80, wherein the subject has or is at risk of cardiovascular disease, optionally wherein the subject has or is at risk of atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease.

82. The nutritional composition or supplement according to any of para 61-81, wherein the subject has one or more selected from the following:

(i) a plasma LDL/HDL cholesterol ratio of 2.5 or higher, 2.6 or higher, 2.7 or higher, 2.8 or higher, 2.9 or higher, or 3.0 or higher;

(ii) a plasma total cholesterol of 5.0 mmol/L or higher, 5.1 mmol/L or higher, 5.2 mmol/L or higher, 5.3 mmol/L or higher, 5.4 mmol/L or higher, 5.5 mmol/L or higher, 5.6 mmol/L or higher, 5.7 mmol/L or higher, 5.8 mmol/L or higher, 5.9 mmol/L or higher, or 6.0 mmol/L or higher;

(iii) a plasma LDL cholesterol of 3.0 mmol/L or higher, 3.1 mmol/L or higher, 3.2 mmol/L or higher, 3.3 mmol/L or higher, 3.4 mmol/L or higher, 3.5 mmol/L or higher, 3.6 mmol/L or higher, 3.7 mmol/L or higher, 3.8 mmol/L or higher, 3.9 mmol/L or higher, or 4.0 mmol/L or higher;

(iv) a plasma apolipoprotein B/apolipoprotein A ratio of 0.70 or higher, 0.80 or higher, or 0.90 or higher; and

(v) a plasma apolipoprotein B of 1.0 g/L or more, 1.1 g/L or more, 1.2 g/L or more, or 1.3 g/L or more.

83. The nutritional composition or supplement according to any of para 61-82, wherein administration of the nutritional composition or supplement to the subject:

(i) reduces the subject's plasma LDL/HDL cholesterol ratio, optionally wherein the subject's plasma LDL/HDL cholesterol ratio is reduced by at least 0.1, at least 0.2, at least 0.3, at least 0.4, or at least 0.5;

(ii) reduces the subject's plasma total cholesterol, optionally wherein the subject's plasma total cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L;

(iii) reduces the subject's plasma LDL cholesterol, optionally wherein the subject's plasma LDL cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L;

(iv) reduces the subject's plasma apolipoprotein B/apolipoprotein A ratio, optionally wherein the subject's plasma apolipoprotein B/apolipoprotein A ratio is reduced by at least 0.05, at least 0.10, at least 0.15, or at least 0.20; and/or

(v) reduces the subject's plasma apolipoprotein B, optionally wherein the subject's plasma apolipoprotein B is reduced by at least 0.05 g/L, at least 0.10 g/L, at least 0.15 g/L, or at least 0.20 g/L.

84. The nutritional composition or supplement according to any of para 61-83, wherein administration of the nutritional composition or supplement to the subject treats or prevents dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity.

85. The nutritional composition or supplement according to para 84, wherein the dyslipidaemia-related comorbidity is xanthomas, carotid bruits, femoral bruits, xanthelasmas, or corneal arcus.

86. The nutritional composition or supplement according to any of para 61-85, wherein administration of the nutritional composition or supplement to the subject treats or prevents cardiovascular disease.

87. The nutritional composition or supplement according to para 86, wherein the cardiovascular disease is atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease.

88. A nutritional composition or supplement for use in improving or maintaining cardiovascular health in a subject who is consuming an initial diet, wherein the nutritional composition or supplement is administered to the subject such that the subject's modified diet comprises, or is closer to, one or more of a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

89. The nutritional composition or supplement according to para 88, wherein the initial diet is defined according to any of paras 1-18.

90. The nutritional composition or supplement according to para 88, wherein the initial diet is not a diet defined according to any of paras 1-18.

91. The nutritional composition or supplement according to para 88-90, wherein the subject is defined according to any of paras 19-25.

92. The nutritional composition or supplement according to any of paras 88-91, wherein the effect of administering the nutritional composition or supplement to the subject is defined according to any of paras 26-30.

93. A method of determining a nutritional composition or supplement for improving or maintaining cardiovascular health in a subject, the method comprising:

(a) providing macronutrient requirements for protein, fat, and carbohydrate, wherein the macronutrient requirements are from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate; and

(b) determining a nutritional composition or supplement comprising that meets said macronutrient requirements.

94. The method according to para 93, wherein the subject is defined according to any of paras 19-25.

95. The method according to any of paras 93 and 94, wherein the effect of administering the nutritional composition or supplement to the subject is defined according to any of paras 26-30.

96. A method of determining a nutritional composition or supplement for a subject, the method comprising:

(a) determining whether the subject has or is at risk of poor cardiovascular health; and

(b) determining a nutritional composition or supplement for the subject, wherein if the subject has or is at risk of poor cardiovascular health, the nutritional composition or supplement comprises a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

97. The method according to para 96, wherein the subject has or is at risk of poor cardiovascular health if they have one or more of the following:

(i) a plasma LDL/HDL cholesterol ratio of 2.5 or higher, 2.6 or higher, 2.7 or higher, 2.8 or higher, 2.9 or higher, or 3.0 or higher;

(ii) a plasma total cholesterol of 5.2 mmol/L or higher, 5.3 mmol/L or higher, 5.4 mmol/L or higher, 5.5 mmol/L or higher, 5.6 mmol/L or higher, 5.7 mmol/L or higher, 5.8 mmol/L or higher, 5.9 mmol/L or higher, or 6.0 mmol/L or higher;

(iii) a plasma LDL cholesterol of 3.4 mmol/L or higher, 3.5 mmol/L or higher, 3.6 mmol/L or higher, 3.7 mmol/L or higher, 3.8 mmol/L or higher, 3.9 mmol/L or higher, or 4.0 mmol/L or higher;

(iv) a plasma apolipoprotein B/apolipoprotein A ratio of 0.70 or higher, 0.80 or higher, or 0.90 or higher; or

(v) a plasma apolipoprotein B of 1.0 g/L or more, 1.1 g/L or more, 1.2 g/L or more, or 1.3 g/L or more.

98. The method according to any of paras 96 and 97, wherein the effect of administering the nutritional composition or supplement to the subject is defined according to any of paras 26-30.

99. The method according to any of paras 93-98, wherein the method is a computer-implemented method.

100. A computer program comprising instructions which, when the program is executed by a computer, cause the computer to carry out the method of any of paras 93-98.

101. A computer-readable data carrier having stored thereon the computer program of para 100.

102. A computer-readable medium comprising instructions which, when executed by a computer, cause the computer to carry out the method of any of paras 93-98.

103. A nutritional composition or supplement determined by the method of any of paras 93-98.

104. A method of treating or preventing dyslipidaemia, hypercholesterolemia, a dyslipidaemia-related comorbidity, and/or cardiovascular disease and/or improving or maintaining cardiovascular health in a subject, the method comprising administering a nutritional composition or supplement to said subject, wherein the nutritional composition or supplement comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

105. The method according to para 104, wherein the subject is defined according to any of paras 19-25.

106. The method according to any of paras 104 and 105, wherein the effect of administering the nutritional composition or supplement to the subject is defined according to any of paras 26-30.

107. A method of improving or maintaining cardiovascular health in a subject who is consuming an initial diet, the method comprising administering a nutritional composition or supplement to the subject such that the subject's modified diet comprises, or is closer to, one or more of a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

108. The method according to para 107, wherein the initial diet is defined according to any of paras 1-18.

109. The method according to para 107, wherein the initial diet is not a diet defined according to any of paras 1-18.

110. The method according to any of para 107-109, wherein the subject is defined according to any of paras 19-25.

111. The method according to any of paras 107-110, wherein the effect of administering the nutritional composition or supplement to the subject is defined according to any of paras 26-30.

Although the invention has been described by way of example, it should be appreciated that variations and modifications may be made without departing from the scope of the invention as defined in the claims. Furthermore, where known equivalents exist to specific features, such equivalents are incorporated as if specifically referred in this specification.

CLAIMS

1. A predetermined diet for use in improving or maintaining cardiovascular health in a subject, wherein the diet comprises a total energy intake of 16.0 MJ/day or less, and wherein the diet comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

2. The diet for use according to claim 1, wherein the diet comprises:

(a) protein in an amount of from 10 E% to 34 E%, from 10 E% to 33 E%, from 10 E% to 32 E%, from 10 E% to 31 E%, from 10 E% to 30 E%, from 11 E% to 29 E%, or from 11 E% to 28 E%;

(b) fat in an amount of from 8 E% to 21 E%, from 8 E% to 20 E%, from 8 E% to 19 E%, from 8 E% to 18 E%, from 9 E% to 18 E%, from 10 E% to 18 E%, from 10 E% to 17 E%, from 10 E% to 16 E%, from 10 E% to 15 E%, from 10 E% to 14 E%, or from 10 E% to 13 E%; and/or

(c) carbohydrate in an amount of from 60 E% to 80 E%, from 60 E% to 79 E%, from 61 E% to 79 E%, or from 62 E% to 79 E%.

3. The diet for use according to claim 1 or 2, wherein the diet is administered to the subject for at least one month, at least two months, at least three months, at least six months, at least nine months, or at least twelve months.

4. The diet for use according to any preceding claim, wherein the diet comprises at least 4 food groups per day, at least 5 food groups per day, at least 6 food groups per day, or at least 7 food groups per day.

5. The diet for use according to any preceding claim, wherein the subject is human, preferably wherein the subject is an adult, more preferably wherein the subject is at least 40 years of age.

6. The diet for use according to any preceding claim, wherein the subject has or is at risk of poor cardiovascular health, optionally wherein:

(a) the subject has or is at risk of dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity;

(b) the subject has or is at risk of cardiovascular disease, optionally wherein the subject has or is at risk of atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease; and/or

(c) the subject has one or more selected from the following: (i) a plasma LDL/HDL cholesterol ratio of 2.5 or higher, 2.6 or higher, 2.7 or higher, 2.8 or higher, 2.9 or higher, or 3.0 or higher; (ii) a plasma total cholesterol of 5.0 mmol/L or higher, 5.1 mmol/L or higher, 5.2 mmol/L or higher, 5.3 mmol/L or higher, 5.4 mmol/L or higher, 5.5 mmol/L or higher, 5.6 mmol/L or higher, 5.7 mmol/L or higher, 5.8 mmol/L or higher, 5.9 mmol/L or higher, or 6.0 mmol/L or higher; (iii) a plasma LDL cholesterol of 3.0 mmol/L or higher, 3.1 mmol/L or higher, 3.2 mmol/L or higher, 3.3 mmol/L or higher, 3.4 mmol/L or higher, 3.5 mmol/L or higher, 3.6 mmol/L or higher, 3.7 mmol/L or higher, 3.8 mmol/L or higher, 3.9 mmol/L or higher, or 4.0 mmol/L or higher; (iv) a plasma apolipoprotein B/apolipoprotein A ratio of 0.70 or higher, 0.80 or higher, or 0.90 or higher; and (v) a plasma apolipoprotein B of 1.0 g/L or more, 1.1 g/L or more, 1.2 g/L or more, or 1.3 g/L or more.

7. The diet for use according to any preceding claim, wherein administration of the diet to the subject treats or prevents dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity, optionally wherein the dyslipidaemia-related comorbidity is xanthomas, carotid bruits, femoral bruits, xanthelasmas, or corneal arcus.

8. The diet for use according to any preceding claim, wherein administration of the diet to the subject treats or prevents cardiovascular disease, optionally wherein the cardiovascular disease is atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease.

9. The diet for use according to any preceding claim, wherein administration of the diet to the subject:

(i) reduces the subject's plasma LDL/HDL cholesterol ratio, optionally wherein the subject's plasma LDL/HDL cholesterol ratio is reduced by at least 0.1, at least 0.2, at least 0.3, at least 0.4, or at least 0.5;

(ii) reduces the subject's plasma total cholesterol, optionally wherein the subject's plasma total cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L;

(iii) reduces the subject's plasma LDL cholesterol, optionally wherein the subject's plasma LDL cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L;

(iv) reduces the subject's plasma apolipoprotein B/apolipoprotein A ratio, optionally wherein the subject's plasma apolipoprotein B/apolipoprotein A ratio is reduced by at least 0.05, at least 0.10, at least 0.15, or at least 0.20; and/or

(v) reduces the subject's plasma apolipoprotein B, optionally wherein the subject's plasma apolipoprotein B is reduced by at least 0.05 g/L, at least 0.10 g/L, at least 0.15 g/L, or at least 0.20 g/L.

10. A nutritional composition or supplement for use in improving or maintaining cardiovascular health in a subject, wherein the nutritional composition or supplement comprises 70 E% carbohydrate or more, and wherein the nutritional composition or supplement is administered to the subject such that the subject's diet comprises a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

11. The nutritional composition or supplement for use according to claim 10, wherein the nutritional composition or supplement comprises: (a) carbohydrate in an amount of 75 E% or more, 80 E% or more, 85 E% or more, 90 E% or more, or 95 E% or more; (b) fat in an amount of 15 E% or less, 10 E% or less, or 5 E% or less; and/or (c) protein in an amount of 20 E% or less, 15 E% or less, 10 E% or less, or 5 E% or less.

12. A method of determining a diet for improving or maintaining cardiovascular health in a subject, the method comprising:

(a) providing macronutrient requirements for protein, fat, and carbohydrate, wherein the macronutrient requirements are from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate; and

(b) determining a diet comprising a total energy intake of 16.0 MJ/day or less that meets said macronutrient requirements.

13. A method of determining a diet for a subject, the method comprising:

(a) determining whether the subject has or is at risk of poor cardiovascular health; and

(b) determining a diet for the subject, wherein if the subject has or is at risk of poor cardiovascular health the diet comprises a total energy intake of 16.0 MJ/day or less,

from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

14. A computer program comprising instructions which, when the program is executed by a computer, cause the computer to carry out the method of claim 12 or 13.

15. A diet determined by the method of claim 12 or 13.

16. A nutritional composition or supplement for use in improving or maintaining cardiovascular health in a subject, wherein the nutritional composition or supplement comprises from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

17. The nutritional composition or supplement according to claim 16, wherein the nutritional composition or supplement comprises:

(a) protein in an amount of from 10 E% to 34 E%, from 10 E% to 33 E%, from 10 E% to 32 E%, from 10 E% to 31 E%, from 10 E% to 30 E%, from 11 E% to 29 E%, or from 11 E% to 28 E%;

(b) fat in an amount of from 8 E% to 21 E%, from 8 E% to 20 E%, from 8 E% to 19 E%, from 8 E% to 18 E%, from 9 E% to 18 E%, from 10 E% to 18 E%, from 10 E% to 17 E%, from 10 E% to 16 E%, from 10 E% to 15 E%, from 10 E% to 14 E%, or from 10 E% to 13 E%; and/or

(c) carbohydrate in an amount of from 60 E% to 80 E%, from 60 E% to 79 E%, from 61 E% to 79 E%, or from 62 E% to 79 E%.

18. The nutritional composition or supplement according to claim 16 or 17, wherein the nutritional composition or supplement is administered to the subject for at least one month, at least two months, at least three months, at least six months, at least nine months, or at least twelve months.

19. The nutritional composition or supplement according to any of claims 16-18, wherein the subject is human, preferably wherein the subject is an adult, more preferably wherein the subject is at least 40 years of age.

20. The nutritional composition or supplement according to any of claims 16-19, wherein the subject has or is at risk of poor cardiovascular health, optionally wherein:

(a) the subject has or is at risk of dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity;

(b) the subject has or is at risk of cardiovascular disease, optionally wherein the subject has or is at risk of atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease; and/or

(c) the subject has one or more selected from the following: (i) a plasma LDL/HDL cholesterol ratio of 2.5 or higher, 2.6 or higher, 2.7 or higher, 2.8 or higher, 2.9 or higher, or 3.0 or higher; (ii) a plasma total cholesterol of 5.0 mmol/L or higher, 5.1 mmol/L or higher, 5.2 mmol/L or higher, 5.3 mmol/L or higher, 5.4 mmol/L or higher, 5.5 mmol/L or higher, 5.6 mmol/L or higher, 5.7 mmol/L or higher, 5.8 mmol/L or higher, 5.9 mmol/L or higher, or 6.0 mmol/L or higher; (iii) a plasma LDL cholesterol of 3.0 mmol/L or higher, 3.1 mmol/L or higher, 3.2 mmol/L or higher, 3.3 mmol/L or higher, 3.4 mmol/L or higher, 3.5 mmol/L or higher, 3.6 mmol/L or higher, 3.7 mmol/L or higher, 3.8 mmol/L or higher, 3.9 mmol/L or higher, or 4.0 mmol/L or higher; (iv) a plasma apolipoprotein B/apolipoprotein A ratio of 0.70 or higher, 0.80 or higher, or 0.90 or higher; and (v) a plasma apolipoprotein B of 1.0 g/L or more, 1.1 g/L or more, 1.2 g/L or more, or 1.3 g/L or more.

21. The nutritional composition or supplement according to any of claims 16-20, wherein administration of the nutritional composition or supplement to the subject treats or prevents dyslipidaemia, hypercholesterolemia, and/or a dyslipidaemia-related comorbidity, optionally wherein the dyslipidaemia-related comorbidity is xanthomas, carotid bruits, femoral bruits, xanthelasmas, or corneal arcus.

22. The nutritional composition or supplement according to any of claims 16-21, wherein administration of the nutritional composition or supplement to the subject treats or prevents cardiovascular disease, optionally wherein the cardiovascular disease is atherosclerotic cardiovascular disease, early cardiovascular disease, and/or coronary heart disease.

23. The nutritional composition or supplement according to any of claims 16-22, wherein administration of the nutritional composition or supplement to the subject:

(i) reduces the subject's plasma LDL/HDL cholesterol ratio, optionally wherein the subject's plasma LDL/HDL cholesterol ratio is reduced by at least 0.1, at least 0.2, at least 0.3, at least 0.4, or at least 0.5;

(ii) reduces the subject's plasma total cholesterol, optionally wherein the subject's plasma total cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L;

(iii) reduces the subject's plasma LDL cholesterol, optionally wherein the subject's plasma LDL cholesterol is reduced by at least 0.1 mmol/L, at least 0.2 mmol/L, at least 0.3 mmol/L, at least 0.4 mmol/L, or at least 0.5 mmol/L;

(iv) reduces the subject's plasma apolipoprotein B/apolipoprotein A ratio, optionally wherein the subject's plasma apolipoprotein B/apolipoprotein A ratio is reduced by at least 0.05, at least 0.10, at least 0.15, or at least 0.20; and/or

(v) reduces the subject's plasma apolipoprotein B, optionally wherein the subject's plasma apolipoprotein B is reduced by at least 0.05 g/L, at least 0.10 g/L, at least 0.15 g/L, or at least 0.20 g/L.

24. A nutritional composition or supplement, for use in improving or maintaining cardiovascular health in a subject who is consuming an initial diet, wherein the nutritional composition or supplement is administered to the subject such that the subject's modified diet comprises, or is closer to, one or more of a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

25. The nutritional composition or supplement according to claim 24, wherein the nutritional composition or supplement comprises: from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

26. A method of determining a nutritional composition or supplement for improving or maintaining cardiovascular health in a subject, the method comprising:

(a) providing macronutrient requirements for protein, fat, and carbohydrate, wherein the macronutrient requirements are from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate; and

(b) determining a nutritional composition or supplement that meets said macronutrient requirements.

27. A method of determining a nutritional composition or supplement for a subject, the method comprising:

(a) determining whether the subject has or is at risk of poor cardiovascular health; and

(b) determining a nutritional composition or supplement for the subject, wherein if the subject has or is at risk of poor cardiovascular health, the nutritional composition or supplement comprises a total energy intake of 16.0 MJ/day or less, from 10 E% to 35 E% protein, from 8 E% to 22 E% fat, and from 55 E% to 80 E% carbohydrate.

28. A computer program comprising instructions which, when the program is executed by a computer, cause the computer to carry out the method of claim 26 or 27.

29. A nutritional composition or supplement determined by the method of claim 26 or 27.