Cardiovascular Disease Prevention:

What the nutritional science shows us

Global Centre for
Nutrition and Health

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Chair in Global Nutrition (Health & Disease), Ulster University | Visiting Professor: Imperial; Parma; Wollongong
Co-Founder, BMJ Nutrition, Prevention & Health

- **WHO WE ARE & WHAT WE DO TOWARDS NUTRITION CAPACITY BUILDING**
- REVIEW OF CAUSAL PATHWAYS INVOLVING CONVENTIONAL & EMERGING RISK FACTORS
- FAQs IN DIET, NUTRITION & CVD
- FUTURE RESEARCH DIRECTIONS

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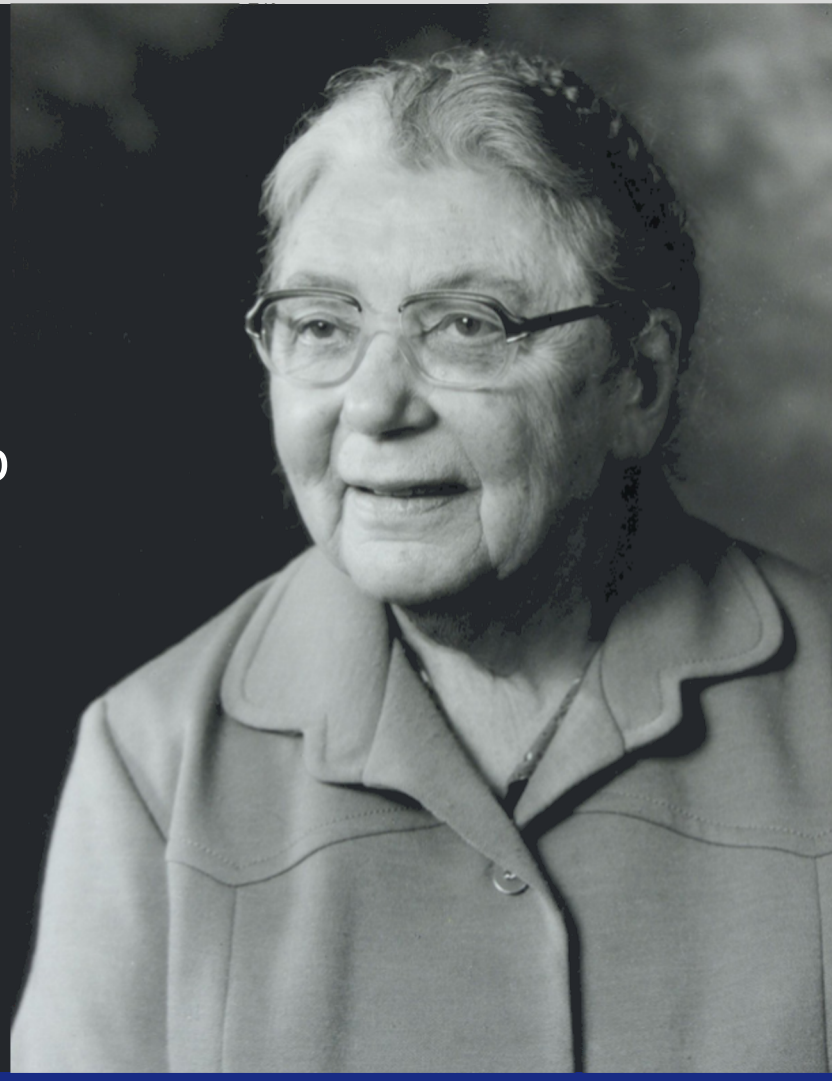
Nutrition and Health

Dr Elsie Widdowson, RD, PhD, CH, CBE, FRS

MRC | Elsie Widdowson Laboratory

- A **true pioneer** of nutrition science
- Working with Dr Robert McCance, published the **first issue of *The Composition of Foods***
- An effective example of the **dietitian-doctor partnership**
- Seminal work laid the foundations for the **Elsie Widdowson Laboratory** in Cambridge (houses the NNEdPro Global Centre for Nutrition and Health)

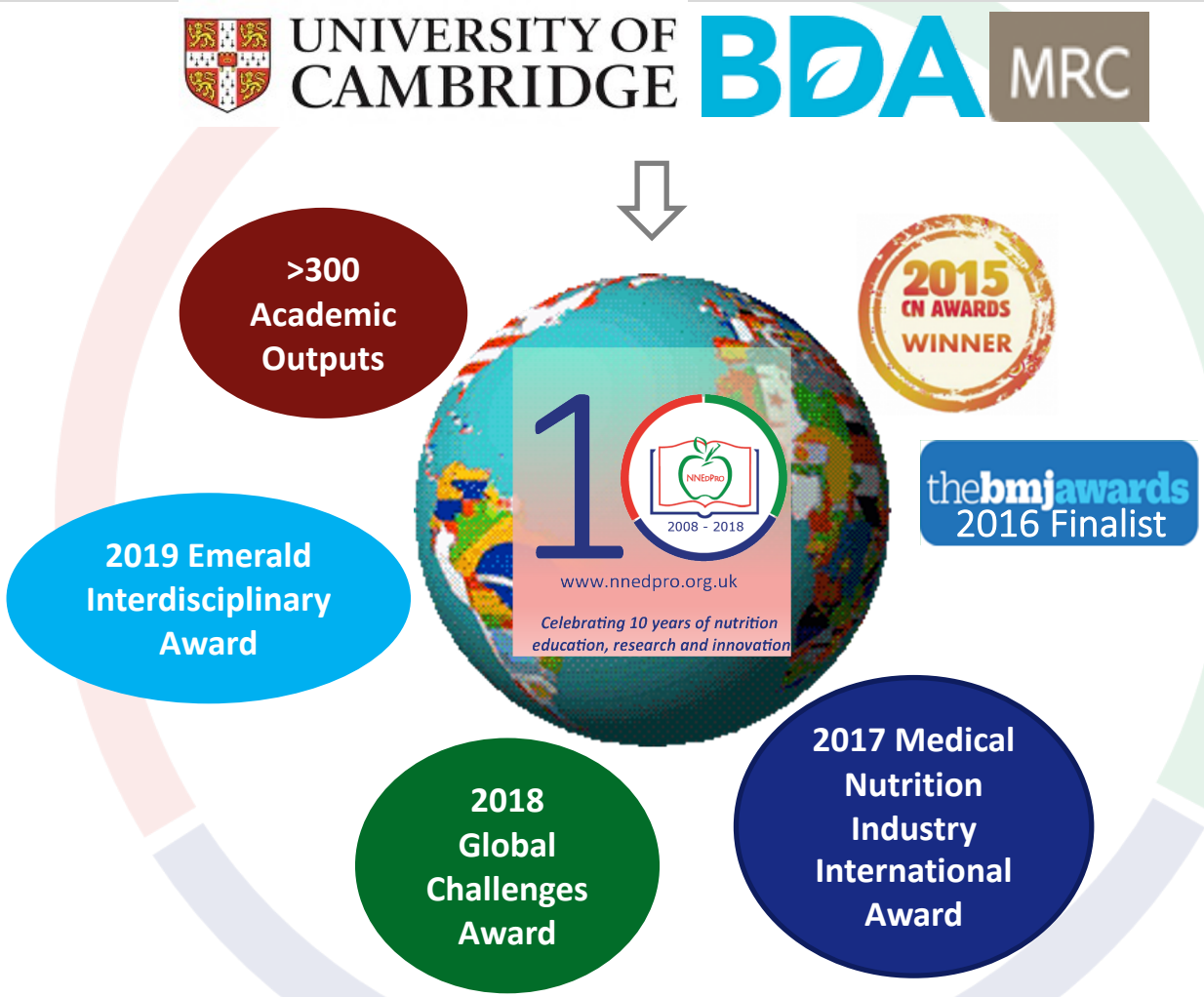


The NNEdPro Global Centre…

An award winning, international and interdisciplinary think-tank, training academy and knowledge network engaged in education, research and implementation

A strategic partnership between doctors, dietitians, nutritionists, nurses, researchers, educators, other professionals, patients and the public

Anchored in Cambridge but working without borders both in the UK and globally!



Key Collaborations and Strategic Partnerships

Academic Institutions

Ulster University

UNIVERSITÀ DEGLI STUDI DI PARMA

Imperial College London

UNIVERSITY OF CAMBRIDGE

Specialist Organisations

BDA The Association of UK Dietitians

BMJ

Society for Nutrition Education and Behavior

LGC

CAMBRIDGE UNIVERSITY Health Partners

Swiss Re Institute

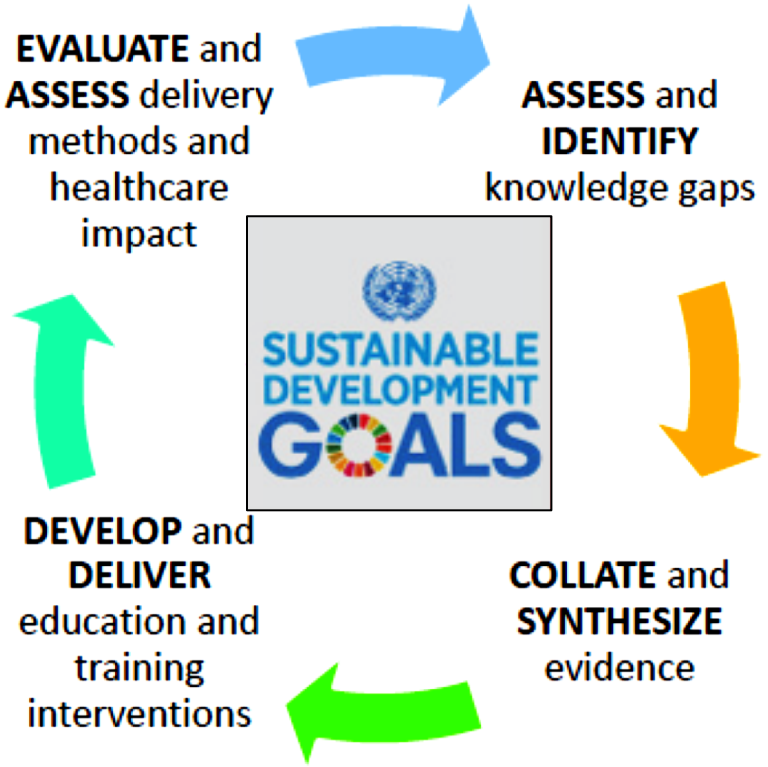
LORD RANA FOUNDATION CHARITABLE TRUST

ERimNN

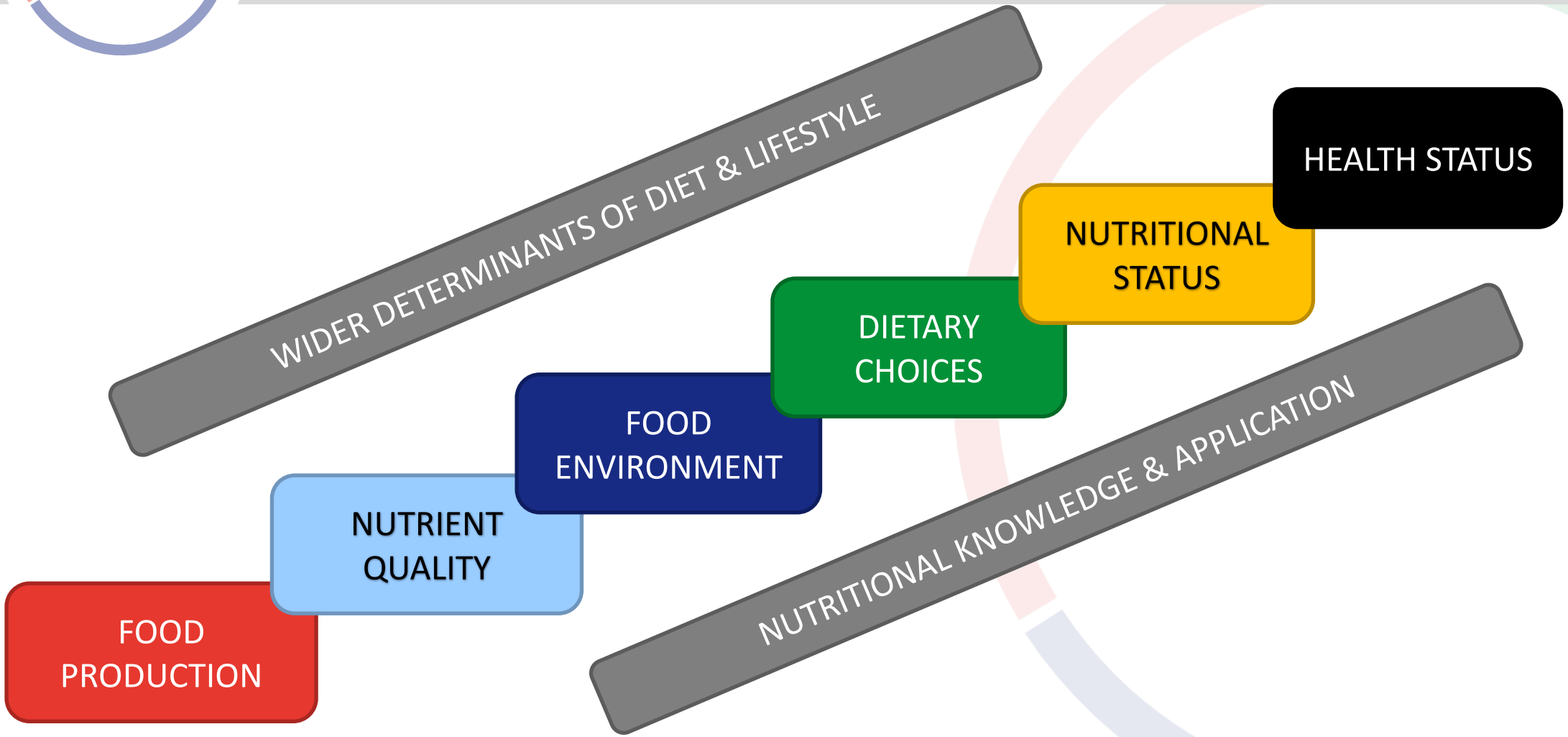
Our Aim...

To develop a critical mass of self-sustaining knowledge, skills and capacity in Nutrition and Health, within the global healthcare and public health workforce, resulting in significantly improved health practices and outcomes.

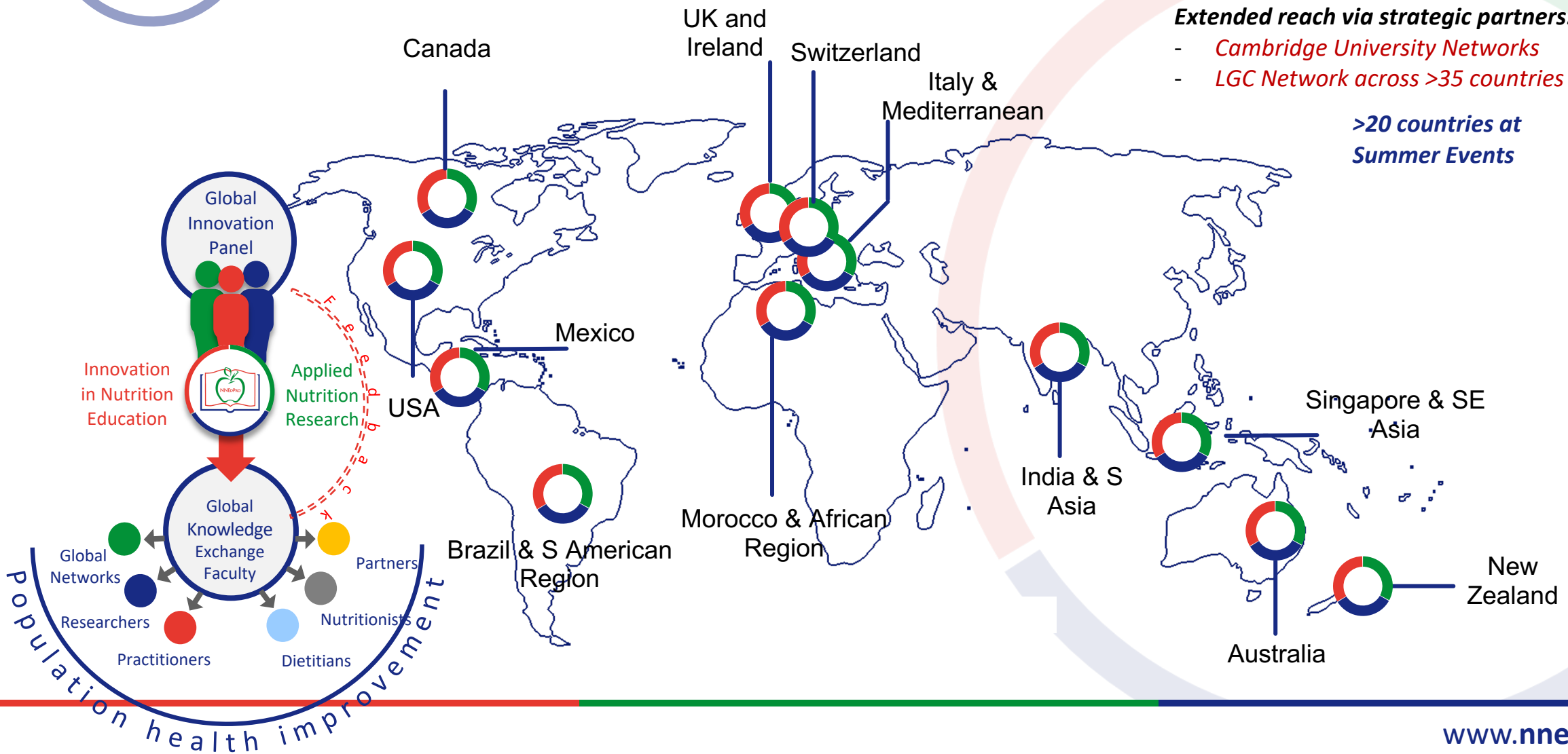
UNITED NATIONS DECADE OF
ACTION ON NUTRITION
2016-2025



Our Framework → Step-ladder from Food to Health…



KEY NETWORKS → Local to Global…



Extended reach via strategic partners:

- *Cambridge University Networks*
- *LGC Network across >35 countries*

>20 countries at Summer Events

A Global Hub for Emerging Knowledge…

"The creation of BMJ Nutrition, Prevention and Health is timely as we seek to make key contributions to the UN decade of action on nutrition (2016-25) by strengthening the translation of nutrition science for disease prevention and best healthcare practice."

Open access

Tackling a tidal wave: sound nutrition knowledge today for a better tomorrow…

Sumantra Ray

NNEdPro

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CPD accredited comprehensive Foundation Certificate Course in Applied Human Nutrition for professionals interested in nutrition and its health applications

12 - 16 July 2020



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Including dietary assessment, body composition and energy metabolism

Nutrition Research Methods
Including nutritional epidemiology, nutrigenetics, nutrigenomics and diet-microbe interactions in the gut

Nutrition in Disease Prevention
Including non-communicable diseases, musculoskeletal health and neurodegenerative diseases

Nutrition in Healthcare
Including hydration and clinical leadership, clinical ethics, malnutrition in practice and ageing

Nutrition Public Health and Policy
Including global nutrition, nutrition and health claims regulation, policy formulation and industry

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- 40 contact hours, practical and/or **interactive** sessions, **self-directed learning and small group work,** individual mentoring & **case studies.**
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Plenary sessions and interactive panel with key opinion leaders on global systems perspective

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17th July 2020
Homerton College
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From 09:00 to 17:00
Followed by a mini-symposium and network reception

A 2020 evaluation of global knowledge networks in the UN Decade of Action on Nutrition (2016-2025)

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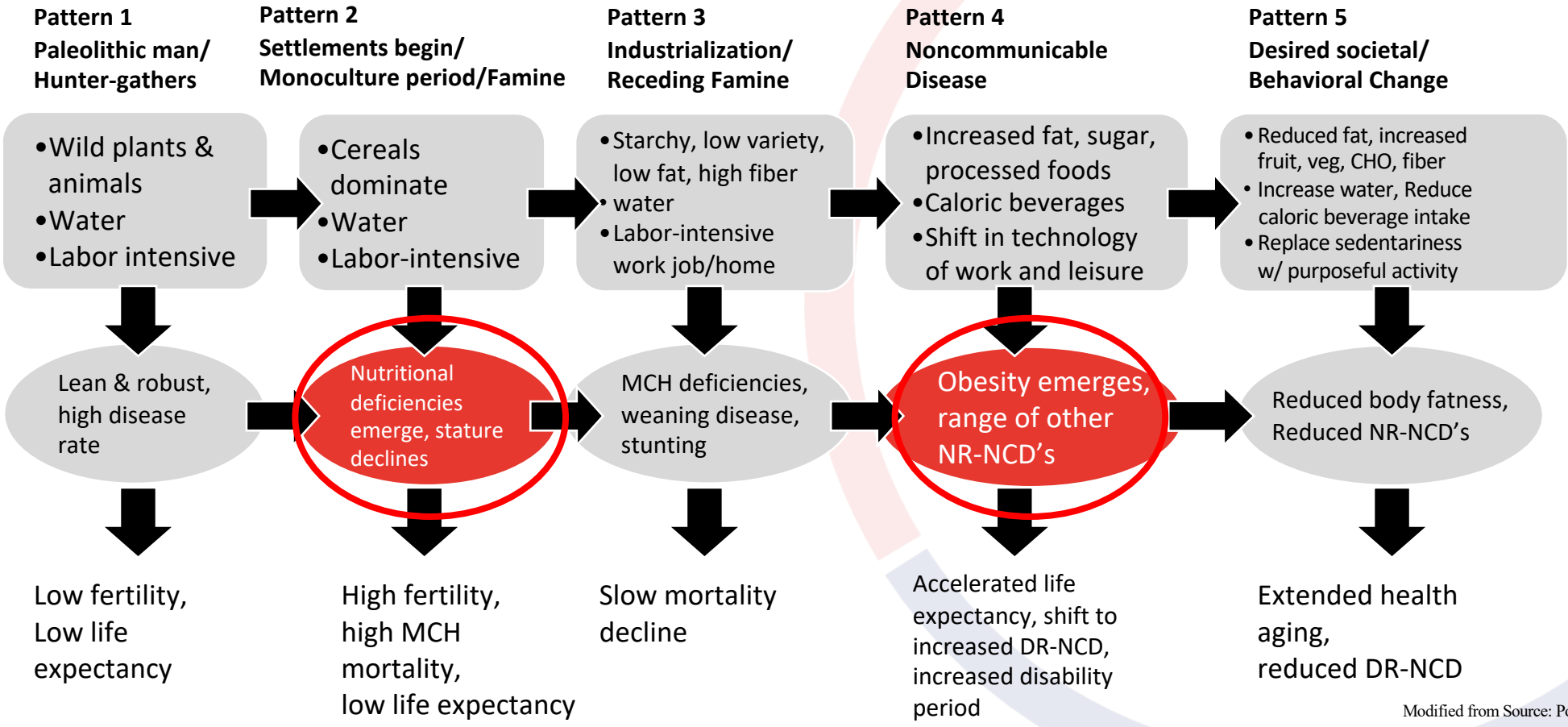
Abstract submissions of original research are accepted by email to **info@nnedpro.org.uk**
Max. 250 words
Email Subject Heading: Summit 2020 Poster Abstract
Deadline: 30th June 2020

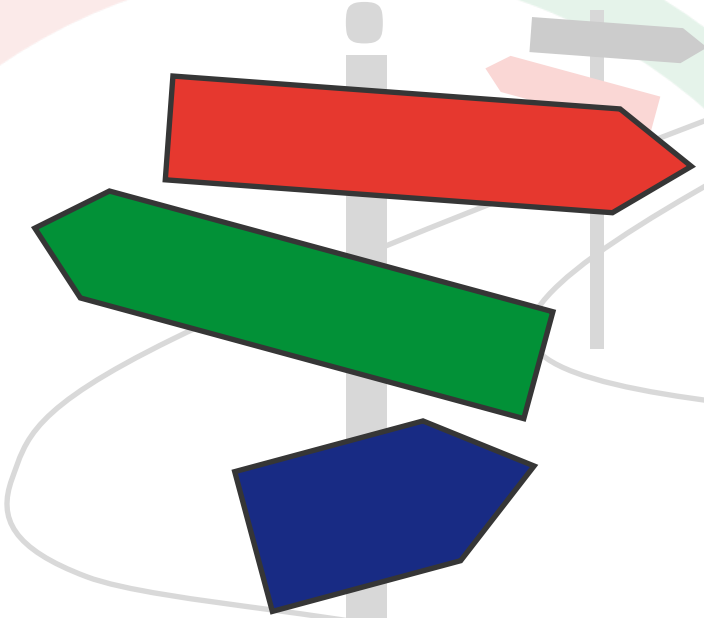
Concept: Global Nutrition Transition

Urbanization, economic growth, technological changes for work, leisure, & food processing, mass media growth



Modified from Source: Popkin 2002 revised 2006.

Conundrum: Double Nutritional Burden



- Co-existence of under and over-nutrition (and associated chronic diseases e.g. CVD)
- Can occur in the same countries, communities and even individuals
- One of the greatest challenges to national policy health policy and resources…

Solution: Research for Education/Implementation

Research Institutions e.g. MRC HNR/EWL
Generating Nutrition Evidence from Molecules to Mankind…

NNEdPro
Translating Nutrition Evidence to Healthcare Practitioners…

Informing Health Policy and Clinical Practice

Population Health

Translation into societal and cultural context

Epidemiology / trials / surveillance

Aetiological studies Behavioural science

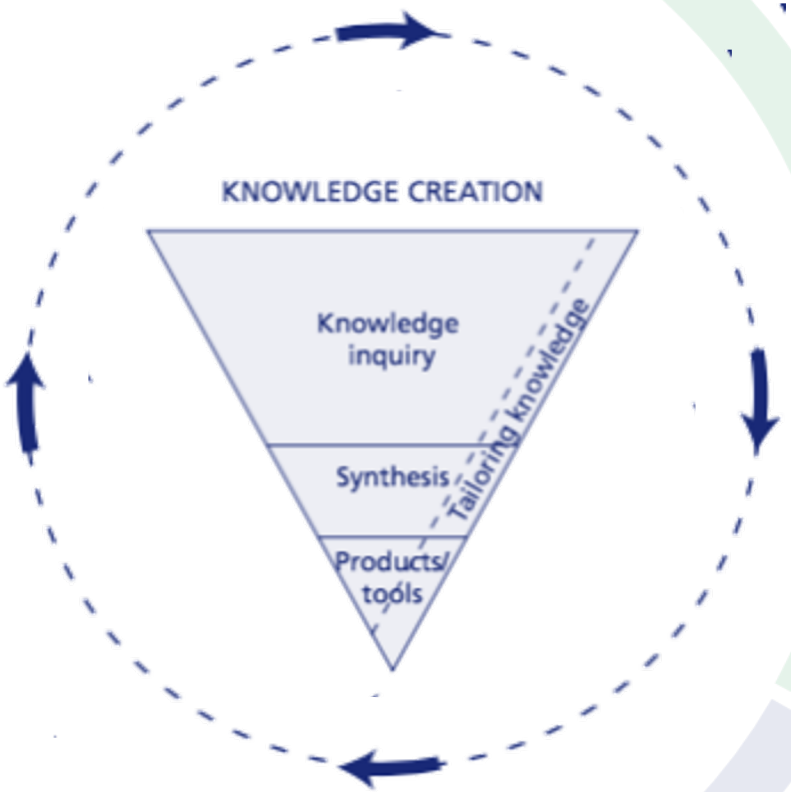
Human physiology Intermediary metabolism

Innovative methodologies Biomarkers, 'omics'

Underpinning mechanism

Discovery science Hypothesis generation

Basic Sciences



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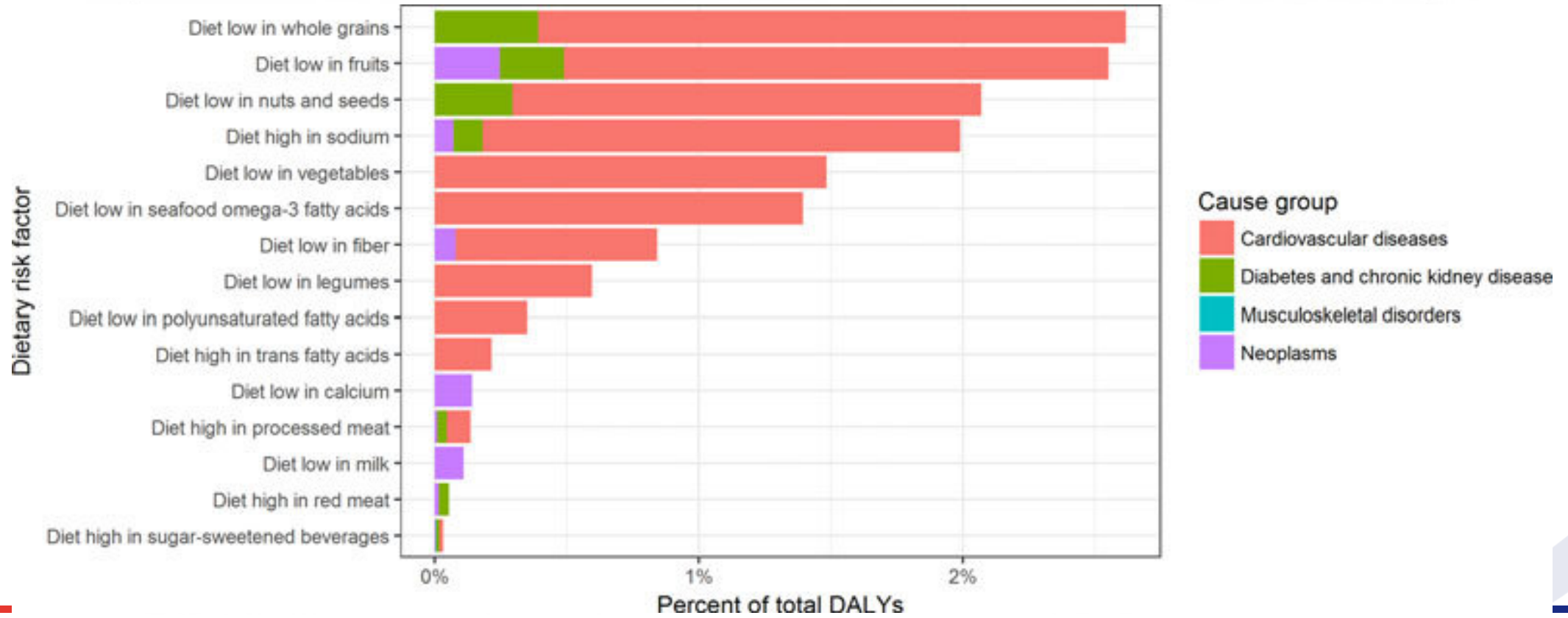
A Review of Causal Pathways involving Conventional and Emerging Risk Factors for Cardio-metabolic/-vascular Disease

M Lima do Vale, L Buckner, S Ashraf, **S Ray**

February 2019

Burden of Cardiovascular Disease/Risk

- CVDs are the number one cause of mortality worldwide (>1/3 deaths)
- UK healthcare spending on CVD is greater than any other EU country
- Over half of CVD treatment in the UK is for preventable conditions



Low Risk

High Risk

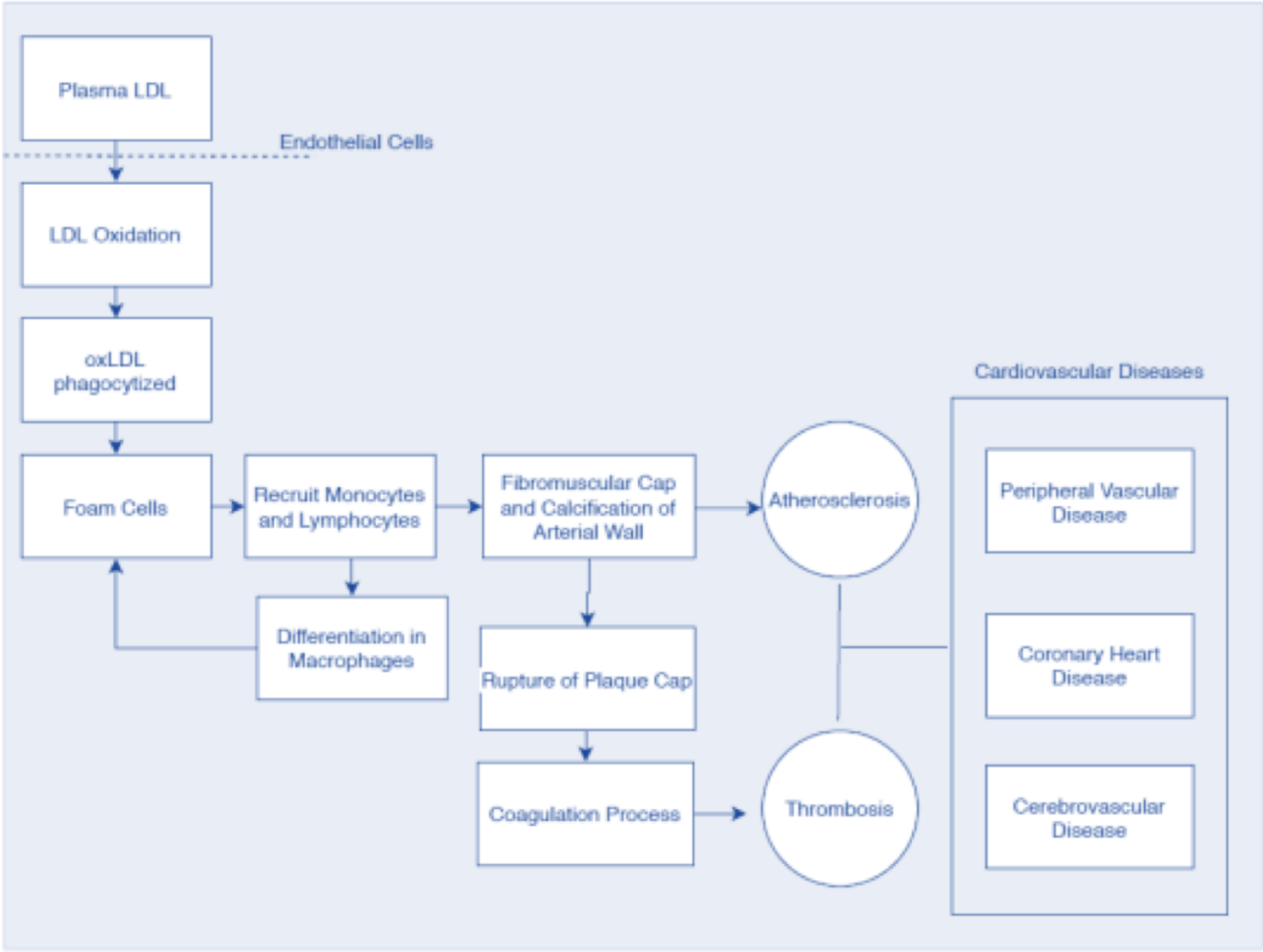
Cardiovascular Disease

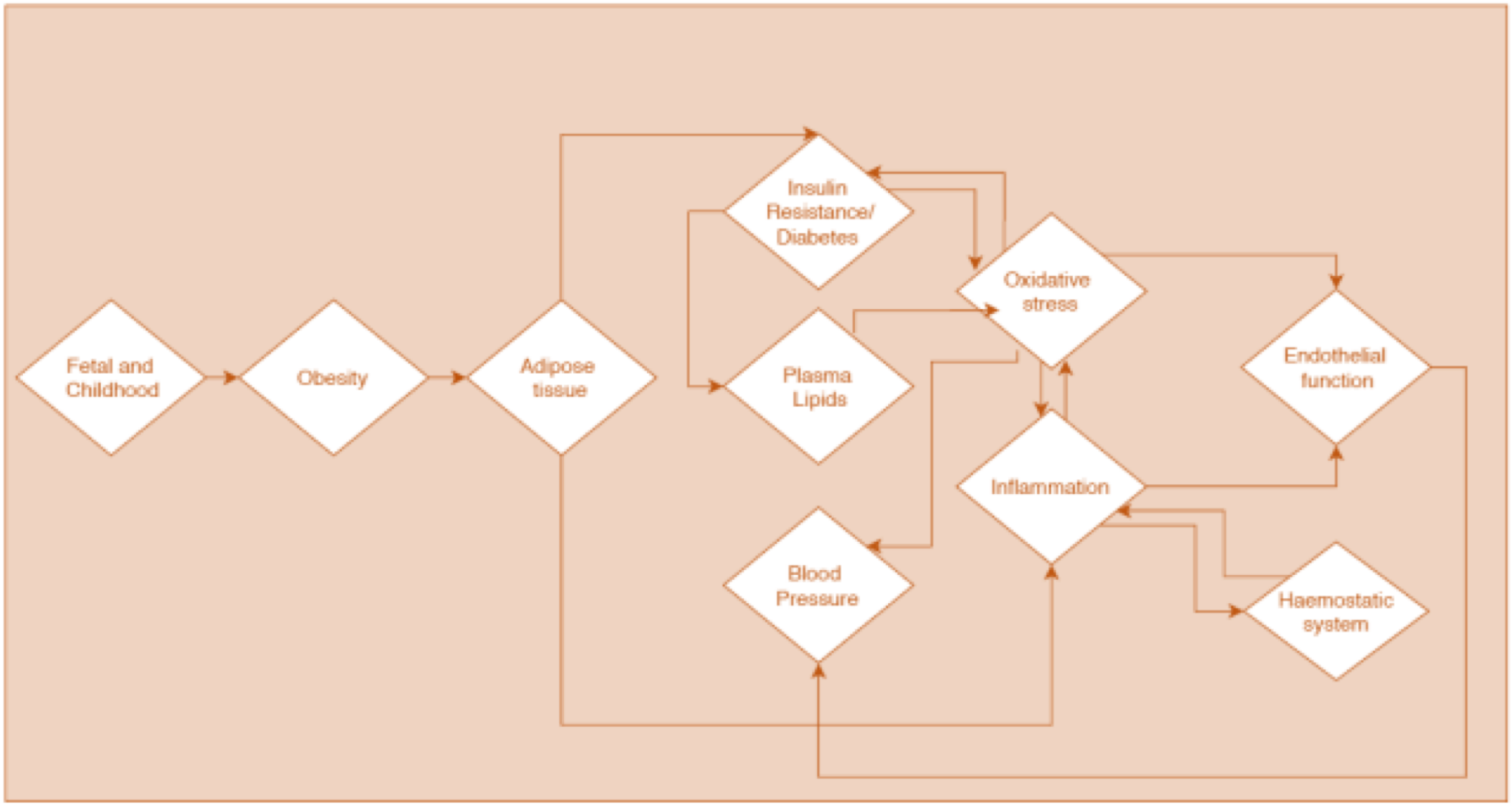
Diet, Nutrition and Emerging Risk Factors

Second Edition

The Report of a
British Nutrition
Foundation Task Force

http://www.wiley.com/go/bnf/cardiovascular_diseases


Plasma LDL
Endothelial Cells
LDL Oxidation
oxLDL phagocytized
Foam Cells
Recruit Monocytes and Lymphocytes
Fibromuscular Cap and Calcification of Arterial Wall
Atherosclerosis
Differentiation in Macrophages
Rupture of Plaque Cap
Coagulation Process
Thrombosis
Cardiovascular Diseases
Peripheral Vascular Disease
Coronary Heart Disease
Cerebrovascular Disease


Fetal and Childhood
Obesity
Adipose tissue
Insulin Resistance/ Diabetes
Plasma Lipids
Oxidative stress
Endothelial function
Inflammation
Blood Pressure
Haemostatic system

FETAL AND CHILDHOOD ORIGINS

- RCTs suggest macro/micronutrient supplementation during pregnancy to address low birth weight might improve children's insulin resistance and blood pressure; RCTs on gestational diabetes suggest positive impact on offspring birthweight, but no impact on children´s BMI.

- Consistent evidence from observational data linking lower birth weight and faster weight or body mass index (BMI) gain in childhood and adolescence with higher metabolic risk in adulthood; systematic review evaluating the metabolic outcomes of rapid weight gain and catch-up growth experienced in infancy across those born term, prematurely or small for gestational age is underway (van der Haak, Wood, Sweeney, & Munn, 2019). Further research to understand the windows of opportunity and the value of interventions during infancy and childhood are required.

- Consistent epidemiological data suggest a protective effect of breastfeeding versus bottle in obesity and type 2 diabetes, and adult blood pressure and lipids. Experimental studies found association between increased duration of breastfeeding and faster weight gain at 3 months, but not after 12 months. Emerging observational studies report protective effect of breastfeeding on other CVD factors, such as triglycerides levels (Umer et al., 2019).

OBESITY, FAT DISTRIBUTION AND ADIPOSE TISSUE

- Consistent evidence support the relevance of genetic profiles to obesity and fat distribution. There is also consistent observational evidence linking obesity and fat distribution with CVD. Some studies suggest that obesity become less relevant after adjustment for other conventional risk factors (e.g., blood pressure, diabetes, total, and high density lipoprotein (HDL) cholesterol), which point to the relevance mediation factors.

- CVD risk among metabolically healthy obese is not consistent in a key systematic review (Eckel, Meidtner, Kalle-Uhlmann, Stefan, & Schulze, 2015). An updated systematic-review is underway (Tian, Liu, Feng, Lou, & Dong, 2019).

- The adipose tissue act as an active endocrine and paracrine organ which can increase CVD risk, insulin resistance, dyslipidemia, hypertension, haemostasis. Except for Acylation-Stimulating Protein (ASP), an important marker for abnormal lipid metabolism and accumulation of fat tissue, much of the evidence for relationship between adipose tissue factors and CVD risk factors comes from in vitro and animal studies. Recent reviews might help to understand the role of each factor on the CVD risk (Dutheil et al., 2018; Ha & Bauer, 2018).

INSULIN RESISTANCE, TYPE 2 DIABETES AND METABOLIC SYNDROME

- There is consistent observational evidence linking insulin resistance and type 2 diabetes with CVD. Glucose management interventions that improve insulin resistance and type 2 diabetes have mixed CVD outcomes (Burggraaf & Castro Cabezas, 2017). It has been suggested that other risk factors may overwhelm any benefit that intensive treatment of hyperglycemia (Leon, 2015).

- Few studies on the link between insulin resistance and diabetes with other CVD risk factors are synthesised despite recent evidence suggesting the key roles that insulin resistance play on classical and less conventional mechanisms for CVD. Van Gaal, Mertens and Block (2006) present a comprehensive discussion of the role of insulin resistance.

LIPID RELATED FACTORS

- Consistent observational evidence shows association between triglyceride, but association become less relevant after adjustment for cholesterol levels or others risk factors. In genetic studies triglycerides were associated with remnant cholesterol, HDL cholesterol and with triglyceride rich lipoproteins.

- Consistent epidemiological data suggest HDL is inversely correlated with CVD risk, but in genetic studies and RCTs improvements in HDL do not reduce CVD risk. HDL seems to be related with endothelial function.

- Consistent observational evidence support the role of small LDL and Remnant Like Particles in CVD, even after adjustment for other risk factors.

INFLAMMATION

- Consistent observational evidence link inflammatory disorders and inflammation markers (C reactive protein, fibrinogen, IL-18, albumin and leukocyte) with CVD.

- Although limited, genetic studies support heritability of inflammatory biomarkers, but also showed that not all inflammatory have causal relevance for CVD, including CRP, fibrinogen and Lipoprotein Associated Phospholipase A2. Genes associated with IL-6 impairment were found to be associated with other inflammatory markers and with CVD.

- Experimental studies seems to support the relevance of CRP and IL-6 levels, as well as IL-1βIL-1β for effective mitigation of inflammation risk. Although whether specifically targeting them would prove to be beneficial in reducing CVD risk remains unclear (Moore, 2019).

- Observational evidence show that inflammation is associated with other risk factors, including BMI, insulin resistance and lipid levels. It is important to note that obesity (Nakayama & Wang, 2010) and insulin resistance (Ormazabal et al., 2018) are thought to lead to inflammation with alterations in lipid metabolism (Feingold & Grunfeld, 2000).

ENDOTHELIAL FUNCTION

- Consistent observational evidence links endothelial dysfunction with CVD but there is missing evidence on links to CVD events.

- Observational evidence suggest endothelial dysfunction is linked to other CVD risk factors, such as smoking, obesity, hypertension, type 2 diabetes and inflammation. Existing evidence support two-way relationship, where endothelial dysfunction may be a predisposing factor, or an anticipating marker for the development of hypertension and diabetes (Versari, Daghini, Virdis, Ghiadoni, & Taddei, 2009) and inflammation (Senoner & Dichtl, 2019).

- There has been growing interest in the role of dietary patterns and nutritional factors in endothelial function, with some experimental studies indicating benefits from weight loss, consumption of fruits and vegetables, polyunsaturates, vitamin C and R and flavanols. Other systematic reviews exploring the role of diet and nutrition on endothelial function have been published, and they support the benefits of fruits and vegetables (Defagó, Elorriaga, Irazola, & Rubinstein, 2014) , n−3 fatty acids, antioxidant vitamins (especially vitamins E and C), folic acid, and L-arginine on vascular endothelial function (Brown & Hu, 2001).

Oxidative Stress

- A limited number of prospective studies suggested a link between oxidized LDL and myeloperoxidase and CVD. Additional reviews describing associations between oxidative stress and CVD have been published recently, and they describe many case control and cohort studies, where higher level of circulating ox-LDL was significantly associated with CVD events, yet not consistently. The same was observed for the relationship between sources of Reactive Species of Oxygen (ROS), many of which were not included in the Task force report that should be taken in consideration (Cervantes Gracia, Llanas-Cornejo, & Husi, 2017; Pignatelli, Menichelli, Pastori, & Violi, 2018).

- No genetic studies to support causality inferences were identified.

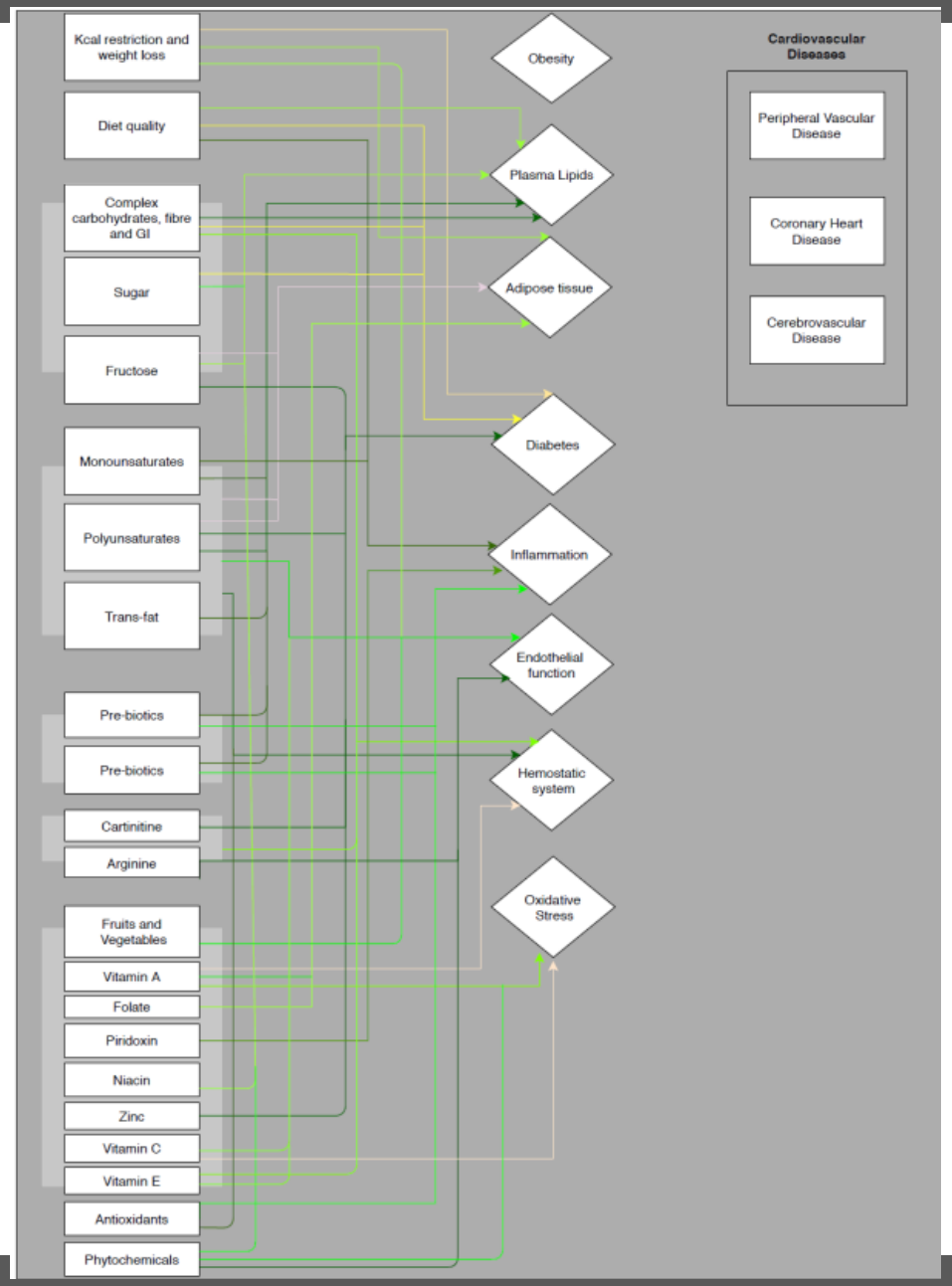
- Existing studies, support the notion that oxidative stress may cause insulin resistance (Henriksen, Diamond-Stanic, & Marchionne, 2011; Hurrle & Hsu, 2017), abnormal coagulation (Pashkow, 2011) and endothelial dysfunction (Higashi, Maruhashi, Noma, & Kihara, 2014); Oxidative stress has also been considered cause and consequence of hypertension (González, 2014; Grossman, 2008) and inflammatory processes (Chatterjee, 2016).

HAEMOSTATIC FACTORS

- Observational data suggest a link between many components of the coagulation system with CVD, with reviews and meta-analysis focused on vWf, fibrinogen and plasminogen supporting such association. Prospective studies suggest a link between Factor VII, VIII, IX, X and XII, but the association between platelets and CVD remain conflicting. Cross-sectional studies suggest the relevance of thrombomodulin.

- Genetic studies seem to support the relevance of factor VII, XII, prothrombin, and plasminogen for CVD. Fibrinogen seem to be relevant only for pulmonary embolism.

- Animal and cross-sectional studies identified a link between haemostatic factors and obesity and endothelial dysfunction. Intervention studies have shown that energy restriction combined with physical activity improves the haemostatic risk profile in obese subjects (Bastard et al., 2000; Gallistl, Sudi, Aigner, & Borkenstein, 2001), supporting the causal link between obesity and haemostatic factors. A potential explanation for the association between coagulation and endothelial dysfunction might be attributed to the fact that NO reduction in endothelial dysfunction might trigger coagulation cascades (Galley & Webster, 2004; Van Hinsbergh, 2012).


Kcal restriction and weight loss
Diet quality
Complex carbohydrates, fibre and GI
Sugar
Fructose
Monounsaturates
Polyunsaturates
Trans-fat
Pre-biotics
Pre-biotics
Cartinitine
Arginine
Fruits and Vegetables
Vitamin A
Folate
Piridoxin
Niacin
Zinc
Vitamin C
Vitamin E
Antioxidants
Phytochemicals
Obesity
Plasma Lipids
Adipose tissue
Diabetes
Inflammation
Endothelial function
Hemostatic system
Oxidative Stress
Cardiovascular Diseases
Peripheral Vascular Disease
Coronary Heart Disease
Cerebrovascular Disease

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WHAT MIGHT MORE NOVEL RISK FACTORS ADD TO WHAT WE KNOW ABOUT CVD?

- Although cigarette smoking, elevated blood pressure, and cholesterol account for many cases of cardiovascular disease, there is reason to believe that other risk factors may account for some of the differences in cardiovascular disease rates within and between populations.

- A better understanding of the role of these additional risk factors may help to identify other ways of predicting individuals at risk and identifying additional approaches for treatment and prevention.

Are changes in diet and lifestyle becoming less important as treatment for CVD and its risk factors improve?

- The National Health Service in England spent around £6.8 billion on cardiovascular disease in 2012/2013, the majority from spending on secondary care.

- Encouraging changes to diet and lifestyle can prevent heart disease without the side effects associated with surgery and drug therapy. Being physically active and eating a balanced diet can also tackle several cardiovascular risk factors simultaneously.

- Lifestyle changes remain critical to reducing the prevalence of heart disease and stroke.

Are small babies more likely to become obese in adult life?

- Adult BMI is positively related to birthweight, so smaller babies are more likely to have a low adult BMI, and larger babies to have a high adult BMI. Since obesity is defined by BMI, smaller babies are less likely to become obese.

- For any level of adult BMI, there is evidence that smaller babies have less lean (muscle) tissue, and that they also distribute their fat differently, developing relatively more abdominal fat, which is known to be more harmful in terms of cardiovascular disease risk than peripheral fat (on the arms and legs), than heavier babies.

How is diabetes linked to CVD? Can lifestyle changes reduce the risk of developing type 2 diabetes?

- People with diabetes are at greater risk of CVD, although the reasons for this are not fully understood. It is thought that if blood insulin and glucose levels are higher than normal and not controlled, this may affect the lining of arterial walls, increasing susceptibility to atherosclerosis.

- As well as insulin resistance and high glucose levels, people with type 2 diabetes tend to have central obesity, high blood pressure, and abnormal lipid concentrations. The combination of these risk factors is often called the metabolic syndrome and is associated with an increased risk of cardiovascular disease.

- Being physically active, maintaining a healthy bodyweight, and eating a healthy diet that does not contain too much fat, particularly saturates, and free sugars, but contains plenty of fibre-rich foods, such as wholegrain cereals and fruit and vegetables, can lower the risk of developing T2D.

What causes insulin resistance?

- Insulin resistance is thought to be caused by both genetic and lifestyle factors.
- Physical inactivity, a diet high in saturates and with a high glycaemic index or load, excess alcohol consumption, and increased bodyweight, high blood pressure, and a low level of HDL are linked to the incidence of insulin resistance, and may trigger the condition in people who are genetically prone.
- All these factors are also linked to an increased risk of CVD, and this may be one reason why there is a high incidence of heart disease and stroke in T2D.

Weight Loss: Should low-carbohydrate, high-fat diets be encouraged as a method of? Is there a role for high-protein diets?

- For those who need to lose weight, the key aspect is reducing energy intake below energy expenditure. This is best done through a combination of increased physical activity and reduced energy intake.

- The macronutrient source of the energy (i.e. fat versus carbohydrate) is generally of secondary importance, although it may influence adherence to different dietary regimens.

- The low-carbohydrate approach to dieting has attracted considerable publicity, but a systematic review of the evidence has demonstrated that weight loss while on such diets is primarily the result of a decrease in energy intake, rather than being associated with reduced carbohydrate per se. While it was previously not known in detail whether there were any possible adverse effects of very low-carbohydrate intakes, and in particular their effect in people with cardiovascular disease, dyslipidaemia, type 2 diabetes or hypertension, it is now more widely accepted that there are potential short-term benefits of low- carbohydrate diets for people with type 2 diabetes.

- When low-carbohydrate diets are adopted, intakes of protein tend to be high. High-protein diets are thought to be effective due to their high palatability and the satiating effect of protein. High-protein, low-energy intermittent fasting regimens have been found to reduce body mass index in obese adults, and result in less weight regain compared to a ‘heart healthy’ diet.

Does dietary fibre have a role in CVD risk?

- The evidence supporting a relationship between a fibre-rich diet and reduced risk of heart disease and type 2 diabetes has accumulated over the past few decades since the dietary reference value (DRV) for fibre was last considered. In its review of carbohydrates and health, the Scientific Advisory Committee on Nutrition (SACN) reviewed the evidence that has since become available, and found strong evidence from prospective studies that increased intakes of dietary fibre (particularly from cereals and wholegrains) lowered the risk of heart disease, type 2 diabetes and stroke.

- Randomised controlled trials have also suggested that higher intake of some specific types of fibre, such as oat bran and beta-glucans, improve blood lipid levels. Based on this evidence, SACN recommended that the UK population's fibre intake should be increased to an average of 30 g AOAC fibre a day for adults, from the previous recommendation equivalent to 24 g AOAC fibre per day (AOAC is the method now used for defining dietary fibre for food labelling purposes).

- By comparison, current intakes in adults are around 18 g per day. Targets have also been set for children (15 g/day for 2–5 year-olds, 20 g/ day for 5–11 year-olds and 25 g/day for 11–16 year-olds).

Why has advice to reduce the risk of cardiovascular disease focused so much on fat in the diet?

- Dietary fats are important determinants of CVD because of their effects on blood cholesterol levels. Human intervention studies have shown that blood cholesterol can be influenced by the balance of different types of fatty acids in the diet; blood levels of low-density lipoprotein cholesterol are lowered when some saturates (e.g. myristic and palmitic acid) are replaced by monounsaturates, polyunsaturates, or complex carbohydrate. Fatty acids may also affect cardiovascular disease risk via other mechanisms (e.g. by influencing clotting).

- Current recommendations advise people to cut down on the amount of saturates in the diet (principally found in butter, full-fat dairy products, fatty meat products, and confectionery such as biscuits and cakes). While blood cholesterol is an important risk factor for heart disease, it has been suggested that even if everyone in the UK population managed to reduce their cholesterol levels below 6.5 mmol/l, there would only be around a 10% reduction in heart disease because it is a multifactorial disease.

- Thus, advice to reduce risk of CVD must also include advice to change other aspects of the diet (e.g. to eat more fruit and vegetables, cut down on free sugars, reduce salt intake, and eat more fibre and wholegrain foods), as well as stopping smoking, taking more exercise, and maintaining a healthy weight.

WHAT IS THE ROLE OF CHOLESTEROL?

- Cholesterol is a lipid found in the bloodstream and in all cells It is also a key component in the manufacture of hormones and bile acids. Some foods, such as meat, poultry, shellfish, eggs, and dairy products, contain dietary cholesterol. Organ meats, such as liver, are especially high in cholesterol, while it is not found at all in foods of plant origin. However, only a small proportion of cholesterol in the body comes from the cholesterol in food. It is made mostly in the liver and this process is stimulated by saturates.

- There are two main types of blood cholesterol, which are often referred to as ‘good’ and ‘bad’ cholesterol. Low-density lipoprotein (LDL) is the main cholesterol carrier in the blood. If too much LDL-cholesterol circulates in the blood, it can build up in the lining of the arteries and form atheroma (or fatty deposits). These can cause the arteries to narrow in a process called atherosclerosis. An elevated level of LDL-cholesterol is associated with increased risk of CVD. It has therefore been traditionally referred to as ‘bad’ cholesterol. However, research now tells us we also need to consider other types of ‘bad’ cholesterol, known as intermediate density lipoprotein (IDL), very low-density lipoprotein (VLDL), and lipoprotein(a) in order to understand the risk that cholesterol poses to health. While a low level of HDL-cholesterol may increase the risk of atherosclerosis. Recently, non-HDL cholesterol has become a commonly used marker for a blood lipid pattern associated with increased risk of CVD.

Triglycerides and Lipoproteins?

- Triglycerides are carried in the blood bound to proteins forming very low, low, and high-density lipoproteins. Like cholesterol, triglyceride in the blood comes either from the diet or from its synthesis in the liver. High triglyceride levels are associated with increased risk of CVD and stroke.

- What are apolipoproteins? Apolipoproteins are proteins that are mostly formed in the liver and intestine. They play an important role in the production and transport of cholesterol around the body. There are at least nine types of apolipoprotein, including apoA-1, apoB, and apoE. Each type bonds with cholesterol in the blood to form either the protective cholesterol, HDL, or the more harmful cholesterol, LDL.

- High levels of certain apolipoproteins may increase risk of heart disease, diabetes, or stroke. For example, high levels of apoB are associated with higher risk of heart disease as it is the main protein in LDL-cholesterol. In contrast, high levels of other apolipoproteins can protect against coronary disease. For example, apoA-1 is the major protein in the more protective HDLcholesterol. High levels of apoE can affect the removal of cholesterol in the blood, and also influence the progression of CVD, depending on the subtype of the apolipoprotein. ApoE2 appears to play a protective role as it is associated with lower LDL levels

WHAT SORTS OF FATS ARE IN FOODS?

- Fat in food is composed mainly of triglycerides, which contain two main types of fatty acids: saturates and unsaturates. Saturates are predominantly found in animal fats, such as butter, full-fat dairy products and fatty meat products. Unsaturates can be either polyunsaturates or monounsaturates.

- There are two main types of polyunsaturates: n-6 fatty acids obtained predominantly from the seeds of plants, such as sunflower oil or soya oil, and n-3 fatty acids, some of which are predominantly from seeds (e.g. rapeseed and linseed), and others that are present in large amounts in fish oils and have attracted particular attention.

- All foods contain a combination of saturates, polyunsaturates, or monounsaturates, but the proportion of each varies greatly with different foods.

What effects do dietary fatty acids have on blood lipids? What about trans fatty acids?

- Saturates in our diets raise blood cholesterol levels more than anything else, including trans fatty acids as they are consumed in greater quantities than trans fatty acids. n-6 polyunsaturates lower total cholesterol levels primarily by lowering LDL-cholesterol levels associated with coronary heart disease. Monounsaturates have also been found to help lower the amount of LDL-cholesterol in the blood. One of the ways in which the long-chain n-3 polyunsaturates found in oil-rich fish may protect against heart disease is via their ability to lower blood triglyceride levels. There is also some evidence that high intakes of these fatty acids may additionally protect against heart disease by positive effects on other blood lipids (e.g. by lowering small, dense LDLs, and reducing remnant lipoproteins). Their effect on blood cholesterol levels, however, is less clear, and it may be that individuals react differently to these fatty acids. The extent to which the n-3 fatty acids present in seeds (e.g. flaxseeds, walnuts, and hempseeds) can simulate the effects of those from oil-rich fish remains to be clarified. However, the available evidence suggests that fish oil supplements (marine derived omega-3 fatty acids) have no beneficial effects on risk of heart disease.

- Trans fatty acids are produced during the process of hydrogenation of unsaturated fats and are principally found in manufactured products (e.g. biscuits, cakes, and chocolates) and some ready meals. They have a particularly adverse effect on lipoproteins [they increase LDL- cholesterol and Lp(a) and decrease HDL-cholesterol], and have been shown to increase risk of CVD. In the UK, however, they contribute a relatively small proportion of total energy.

Why do nutritionists and dietitians promote the 5 A Day message?

- There is a considerable body of evidence that has shown diets rich in fruit, vegetables, and other plant foods to be associated with a reduced risk of a number of diseases, including high blood pressure, obesity, heart disease, and stroke, type 2 diabetes and some cancers (including mouth, throat, stomach, colon, and lung cancers).

- It has been estimated that diet is likely to contribute to the development of one-third of all cancers, and that eating more fruits and vegetables is the second most important cancer prevention strategy, after stopping smoking. Eating lots of fruit and vegetables has also been associated with lower risk of age-related eye conditions such as cataracts and macular degeneration and chronic lung disorders. This has led to the recommendation by the World Health Organization to eat at least 400 g of fruit and vegetables every day, which has been translated by the Department of Health into advice for the UK population to eat at least five portions of a variety of fruit and vegetables each day.

- The range of nutrients and phytochemicals present varies considerably between different types of fruit and vegetables. So, advice with regard to consumption of these foods should focus on variety, to ensure that a wide array of nutrients and bioactive substances are consumed. There is also likely to be a displacement effect by eating more fruit and vegetables as we tend to eat less high fat and energy dense foods that may increase risk of obesity, CVD, and diabetes.

Can supplements be as effective as fruit and vegetables in reducing your risk of cardiovascular disease?

- Intervention trials have not supported the notion that supplements provide the same protection against chronic diseases as increasing fruit and vegetable intake.

- This might be because it is the cocktail effect of the many substances present in whole fruit and vegetables, including fibre, vitamins, minerals, and plant bioactives, such as polyphenols and carotenoids that confer the health properties or that the substances tested are not those responsible.

What have we learnt about the role of diet in heart disease since the last Task Force 2005?

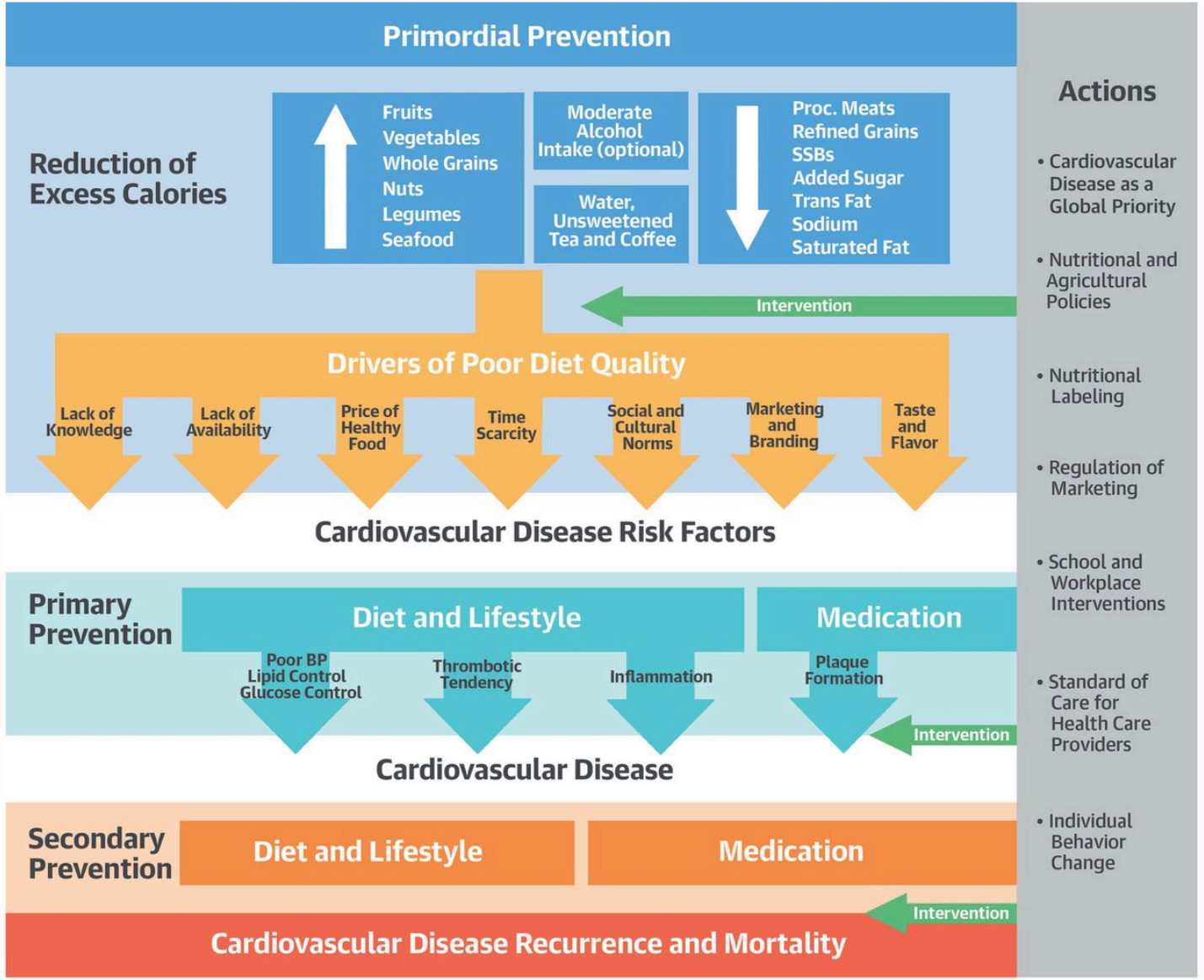
- In particular, there is now strong evidence that homocysteine levels can be reduced by supplementation with folic acid, however, randomised controlled trials have not found any evidence that this helps prevent heart disease.

- Evidence for a role of adverse nutrition in early life as a risk factor for heart disease later in life has also strengthened and both over- and undernutrition during pregnancy are now believed to be linked to increased risk of high blood pressure, insulin resistance and type 2 diabetes in the offspring in later life.

- Furthermore, interest is now growing in a number of newer risk factors, including the role of the gut microbiome and how it is influenced by the diet.

IN SUMMARY...

CENTRAL ILLUSTRATION: Flow Diagram of the Development of CVD and Possible Prevention by a Healthy Diet

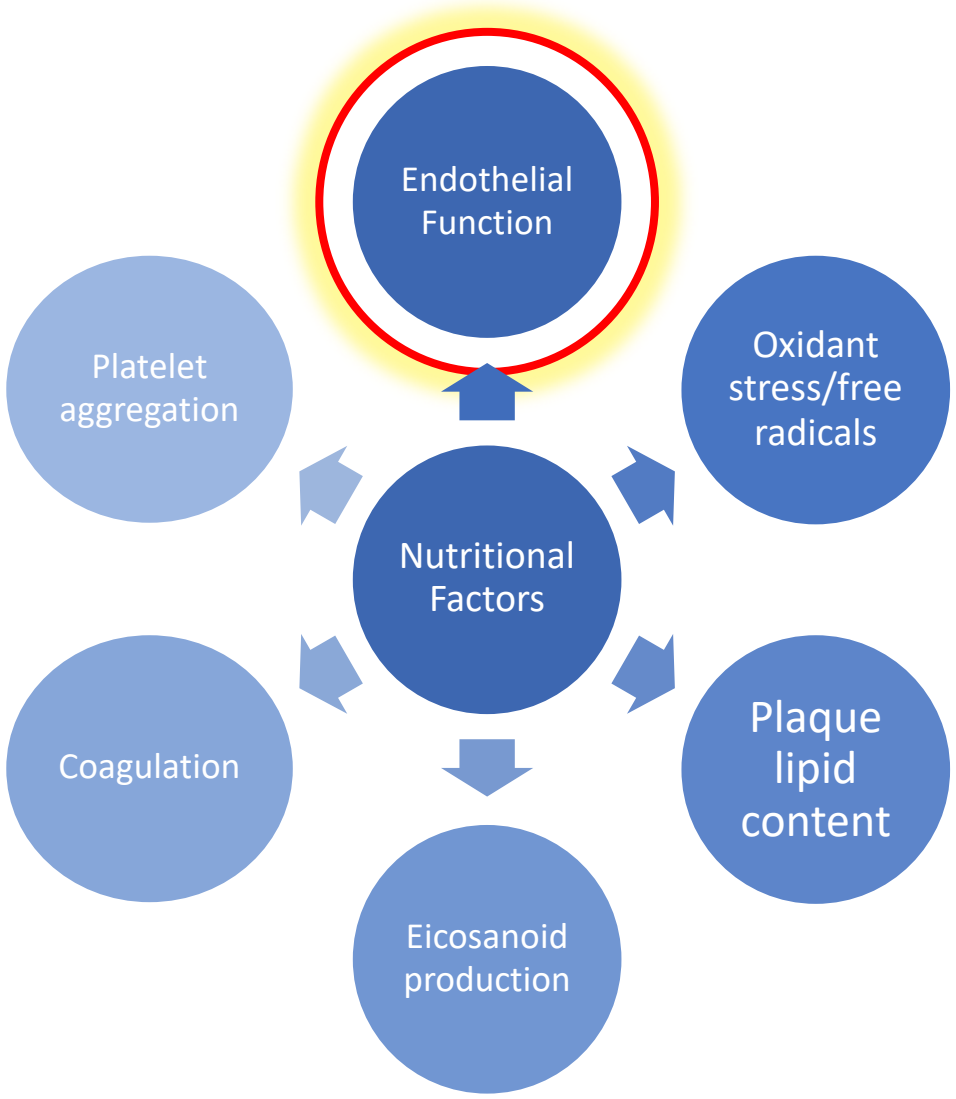


Yu, E. et al. J Am Coll Cardiol. 2018;72(8):914-26.

- WHO WE ARE & WHAT WE DO TOWARDS NUTRITION CAPACITY BUILDING
- REVIEW OF CAUSAL PATHWAYS INVOLVING CONVENTIONAL & EMERGING RISK FACTORS
- FAQs IN DIET, NUTRITION & CVD
- **FUTURE RESEARCH DIRECTIONS**

Global Centre for
Nutrition and Health

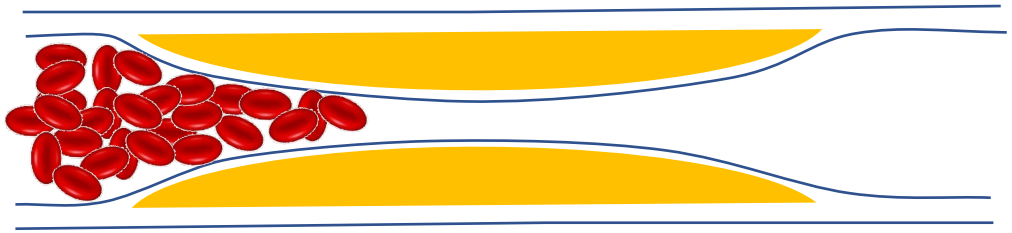
The Role of Nutrition in Atherosclerosis



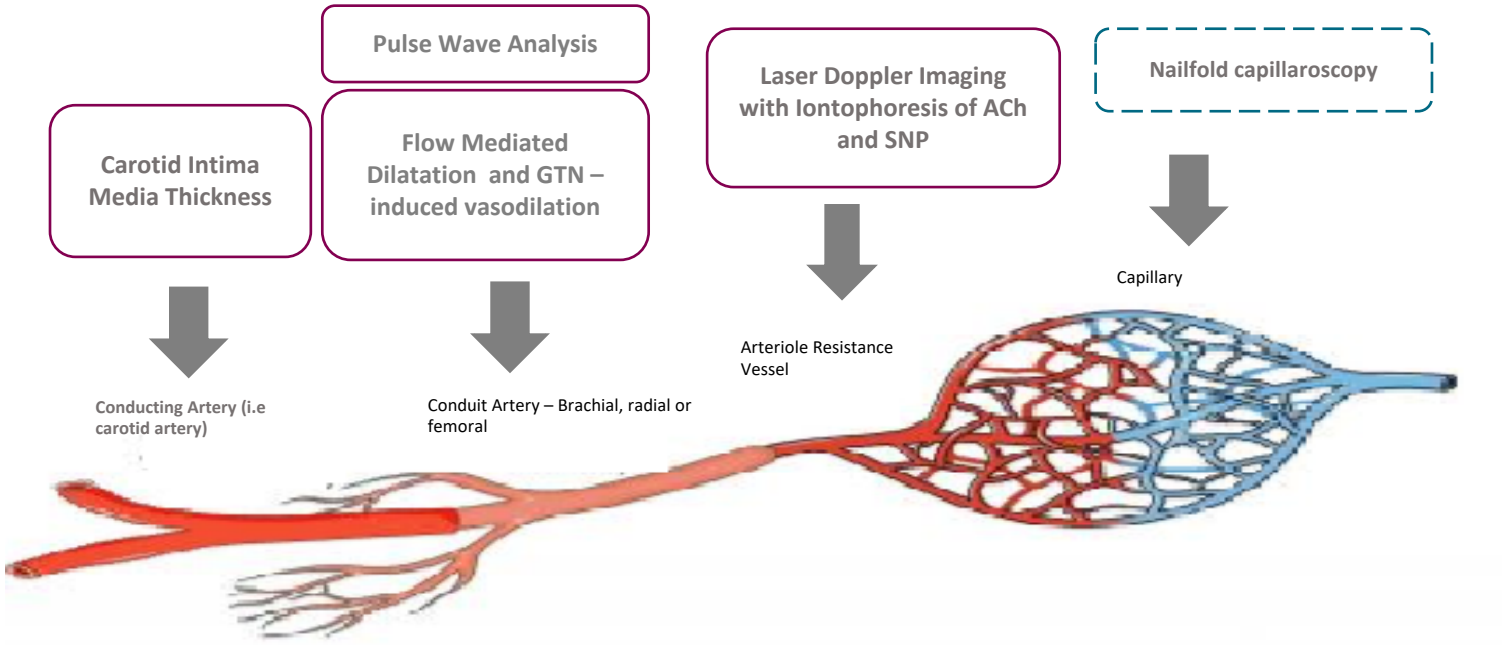
Endothelial Dysfunction

- Dilatation
- Growth inhibition
- Antithrombosis
- Anti-inflammation

- Constriction
- Growth promotion
- Prothrombosis
- Proinflammation

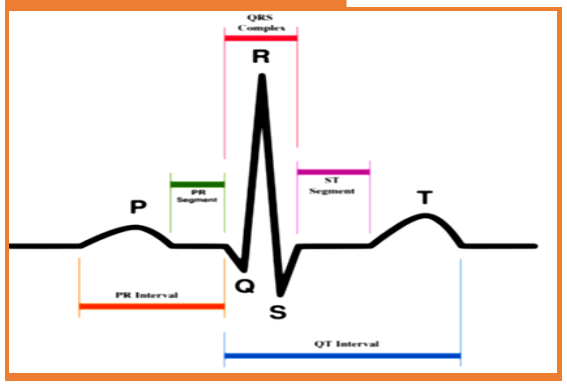


Measures of endothelial function

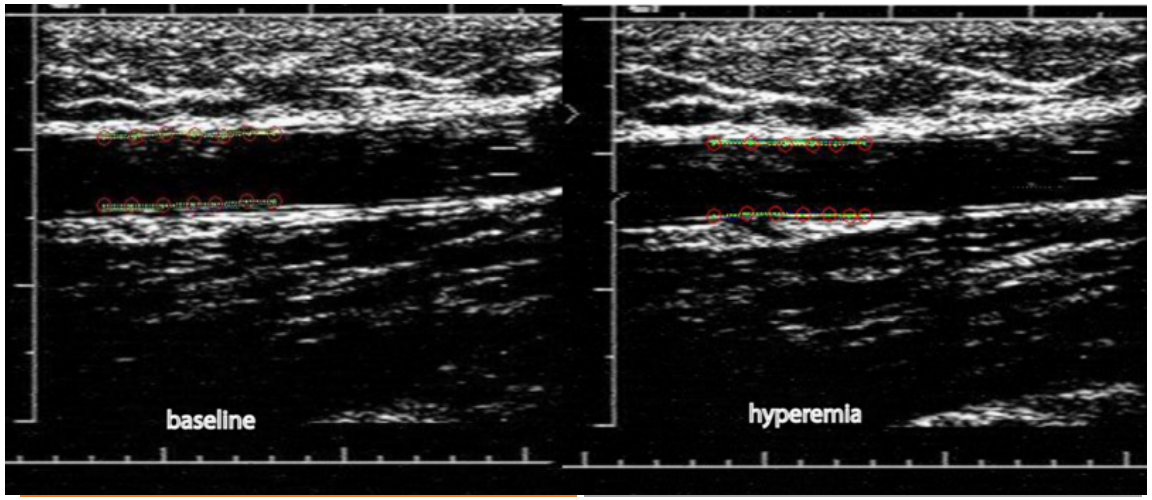


NVS Vascular Function Assessment Lab (vFAL)

ECG



Ambulatory Blood Pressure



Blood Pressure

Anthropometrics

Pulse Wave Analysis

Carotid Intimal Media Thickness

EXPERIMENTAL
Phytonutrients and Vascular Function

Berry RCTs

RCT on effects of a wide range of fruit and vegetable extracts on vascular/endothelial function and metabolic risk

Hydration sub study

Vascular function study linked with a metabolic trial of green tea/coffee polyphenols

Vascular function acute trial comparing techniques using a hazelnut extract intervention

EPIDEMIOLOGICAL
Population Diet and CVD Risk

Longitudinal analyses of dietary patterns and vascular function in the 1946 British birth cohort, including derivation of novel intermediates from stored samples

NSHD

Cross-sectional analyses of diet and CVD risk data and database formulation from the UK NDNS repository

NDNS

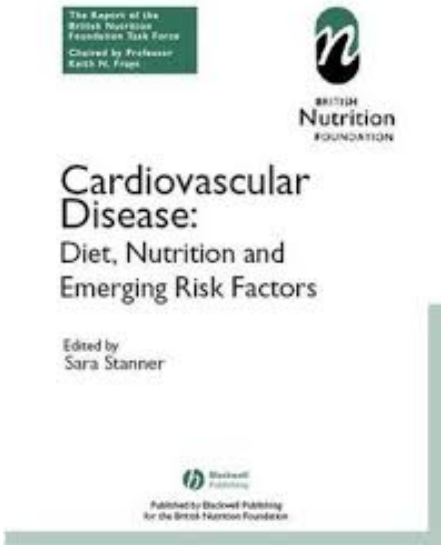
Clinic based studies in the NHS

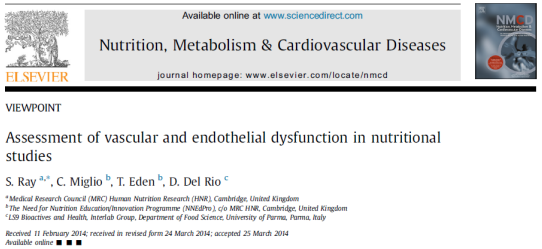
NHS

TRANSLATIONAL:

Evidence Synthesis and Knowledge Exchange

- Evidence synthesis and knowledge exchange, including key contributions to the second edition of the Task Force on Cardiovascular Disease: Diet, Nutrition and Emerging Risk Factors by British Nutrition Foundation
  - ***Supplement: NUTRTIONAL MANAGEMENT OF ACUTE STROKE***
- Development of a consensus forum on vascular measures in nutritional studies (including hydration)
- Driving quality in research methods across nutrition and healthcare sciences





A Way Forward & A Role for Research…

- Current evidence is limited by **heterogeneity** in the design of studies, lack of controls, relatively short intervention periods, low power and lack of long term followup amongst cohorts
- **Large**, well-powered, long-term and systematically inter-related human dietary intervention required alongside observational and intervention cohorts possibly with nested case-control studies
- **Small**, mechanistic studies can further test unanswered questions from larger population studies
- A geographically focussed **feasibility model** approach with scalability may be better than widely 'representative' population sample in the first instance
- **Capacity** building and specialist capability development are key…

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With acknowledgements to the ASLM organisers and NNEdPro colleagues