



Workshop Report

A symposium and workshop report from the Global Nutrition and Epidemiologic Transition Initiative: nutrition transition and the global burden of type 2 diabetes

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Abstract

The present report summarises the symposium 'Nutrition Transition and the Global Burden of Type 2 Diabetes' and a workshop on strategies for dietary interventions to prevent type 2 diabetes held by the Global Nutrition and Epidemiologic Transition Initiative, Boston, MA, USA in November 2011. The objectives of this event were to bring attention to the global epidemic of type 2 diabetes in light of the ongoing nutrition transition worldwide, especially in low- and middle-income countries, and to highlight the present evidence on key dietary risk factors contributing to the global diabetes burden. The meeting put forward ideas for further research on this topic and discussed practical recommendations to design and implement culturally appropriate dietary interventions with a focus on improving carbohydrate quality to help alleviate this growing health problem.

Key words: Nutrition transition: Type 2 diabetes: Global health: Dietary intervention

As a global epidemiological transition has shifted the burden of mortality from infectious to chronic diseases, type 2 diabetes has reached epidemic proportions in many countries around the world, including low- and middle-income countries^(1,2). This increase has been partly attributed to rapid economic and nutritional changes, fuelled by global free trade^(1,3). Traditional staple foods, once rich in whole grains and dietary fibre, have been replaced by highly refined carbohydrates, such as polished white rice and refined flours. This nutrition transition has resulted in a major reduction in the quality of carbohydrates in the diet. Research has shown that the consumption of high-quality carbohydrates, such as whole grains, can reduce the risk of diabetes by improving blood glucose and insulin levels^(4,5). Reincorporating such traditional foods in the regular diet of countries undergoing nutrition/epidemiological transition may be a cost-effective, feasible and sustainable approach to diabetes prevention, particularly

in low- and middle-income countries, simultaneously managing undernutrition and infectious diseases.

It is paramount to bring attention to the global type 2 diabetes epidemic in light of the ongoing nutrition transition worldwide, and identify key dietary risk factors contributing to the global diabetes burden. To this end, the Global Nutrition and Epidemiologic Transition Initiative (GNET) convened on 15–16 November 2011 in Boston, MA, to present a symposium and workshop on this timely topic and to help researchers and clinical and public health professionals gain knowledge to frame practical, innovative and culturally appropriate interventions to prevent and mitigate this growing health problem.

The objectives of the symposium were to:

- (1) Bring together experts in the fields of global health, type 2 diabetes and nutrition to showcase the present state of knowledge in these areas.

Abbreviations: DPP, Diabetes Prevention Program; FGD, focus group discussion; GI, glycaemic index; GL, glycaemic load; GNET, Global Nutrition and Epidemiologic Transition; POUNDS LOST, Preventing Overweight Using Novel Dietary Strategies.

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- (2) Illustrate the undergoing burden of disease in low- and middle-income countries, focusing on type 2 diabetes and nutrition transition, and the implications for the design and implementation of dietary interventions.
- (3) Explain the present evidence on the contribution of diet quality, with emphasis on carbohydrate, on type 2 diabetes and cardio-metabolic outcomes.
- (4) Engage in cross-disciplinary discussion to gain a clear understanding of the aforementioned topics, and put forth ideas for further research and solutions to the global burden of diabetes.

The objectives of the workshops were to:

- (1) Learn and practise skills required to successfully design and implement global dietary interventions for diabetes prevention, as taught by experts in each topic.
- (2) Engage in interactive discussion to help understand the acquired skills and lessons, and how these can be properly implemented in each country setting.
- (3) Formulate how the new skills and lessons may boost collaborative efforts between GNET members to help achieve its goals and overall mission, in terms of organisation, operation and advancing research and science.

The GNET is a collaborative multi-national academic working group launched by researchers from the Departments of Epidemiology and Nutrition at the Harvard School of Public Health. Its mission is to develop novel approaches to improve the carbohydrate quality of staple foods to prevent the global diabetes epidemic and enable healthier and more enjoyable lifestyles. The GNET is comprised of leading researchers in nine countries from Asia, Africa, the Middle East and Latin America, who are at various stages of designing and implementing pilot projects and dietary interventions to assess the effect of substituting whole-grain alternatives for refined carbohydrate staples on intermediate markers of diabetes risk. The studies also assess the cultural acceptability and feasibility of these interventions in local communities. Results from the studies will help design larger multi-site interventions that will test whether whole-grain dietary modifications can have a long-lasting, measurable impact. The present report summarises the information and ideas put forth by GNET investigators and invited speakers who are experts in the fields of global health, type 2 diabetes and nutrition, with the goal of advancing GNET's mission and highlighting the urgency of solving the global type 2 diabetes epidemic. The workshop may be seen in its entirety at <http://hsph.me/gnet>

Summary of keynote presentations

Double burden of under- and overnutrition

The Symposium was opened by Dr Benjamin Caballero (John Hopkins School of Public Health, Baltimore, MD, USA) who discussed the double burden of under- and overnutrition in developing countries. Dr Caballero highlighted data from the WHO Global Health Risk Report 2009, which illustrates an epidemiological transition, with overweight and obesity causing more deaths than underweight and the burden of diseases

related to poor diet and physical inactivity in low- and middle-income countries being equivalent to that of HIV/AIDS and tuberculosis combined⁽⁶⁾. A recent study shows dramatic increases in the prevalence of overweight and obesity worldwide in the last 28 years⁽⁷⁾, which will translate into excessive rates of consequent morbidities and mortality. An increase in BMI was noted in all but eight countries of the 199 included in the study. The age-standardised worldwide prevalence of obesity doubled from 4.8% in men and 7.9% in women in 1980, to 9.8% in men and 13.8% in women by 2008, rendering 34% of the world adult population as obese (502 million people) or overweight (1.5 billion). However, many countries need to concurrently manage chronic diseases and the health consequences of undernutrition. In 2010, the undernourished population worldwide reached 1 billion, with 64% living in Asia and the Pacific region, and 26% in sub-Saharan Africa⁽⁸⁾. Dr Caballero cited five key drivers of the epidemiological transition and double burden of disease:

- (1) Increased life expectancy.
- (2) Urbanisation.
- (3) Economic growth and increases in household income.
- (4) Globalised food production and marketing, including availability and price.
- (5) Unhealthy lifestyles: physical inactivity and poor diets.

He explained that the epidemiological transition is driven by an increase in life expectancy that occurs when countries gain control over infectious diseases⁽⁶⁾. Increased life expectancy then leads to an increased proportion of adults aged 65 years and older, and thus, to an increase in chronic diseases. As for urbanisation, such lifestyles are characterised by unhealthy behaviours such as decreased physical activity, excess energy intake and smoking, which lead to an adverse cardio-metabolic profile and increased prevalence of chronic diseases. This is of concern as most predictions indicate that nearly 80% of the population growth in developing countries will be in urban areas by the year 2030⁽⁹⁾.

Economic growth and increased household income are also strongly linked to obesity. This link is due, in part, to increased availability of food (i.e. more energy) and decreased physical activity. In China, physical activity has decreased dramatically as the level of urbanisation has increased⁽¹⁰⁾. The ongoing trends of higher availability of animal food products, refined carbohydrates and vegetable oils, as reported by FAO data, as well as more food markets that sell processed, as opposed to fresh, foods are worrisome. Also of concern is the increased number of multi-national low-priced food chains and street vendors selling processed foods in poor areas. For example, the growth rate of markets for fruits and fresh products in developing countries is 10–15%, compared to 30–35% for processed foods⁽¹¹⁾. Similarly, consumption of sugar-sweetened beverages, laden with extra empty energy, has increased with economic growth, becoming a major contributor to excess energy intake worldwide.

Another driver of the epidemiological and nutrition transition is the proportion of income that people spend on food, because price has a great impact on people's purchasing choices, especially when large proportions of the income are



spent on food⁽¹²⁾. Many people living in developing countries spend a considerable amount of their income on food, and in such underprivileged circumstances, purchasing cheaper processed foods becomes economically sensible. In response, the demand for these poor-quality foods keeps growing, compared to that of more expensive fresh produce.

Dr Caballero stated that the double burden of under- and overweight that many countries are facing may be due to the unfortunate reality that economic growth and higher income do not necessarily translate into improved health outcomes. Overall, increasing the gross national product results in only a 10% decrease in underweight status for children under 5 years⁽¹³⁾, and reductions in mortality have a beneficial effect mostly among high socio-economic groups⁽¹⁴⁾. Therefore, millions of children remain affected by acute and chronic malnutrition. He stressed the point that low birth weight is not a main contributor to undernutrition, but rather large decreases in weight-for-age; in children aged around 3 months, living in developing countries is the major problem⁽¹⁵⁾. Many interventions conducted during the first 12 months of life have effectively reduced infant mortality, but the downside is that these children develop significantly higher body fat, fasting insulin and insulin resistance later in life⁽¹⁶⁾. Therefore, the challenge for future interventions and programmes is to prevent this decline in weight-for-age at 3 months, with subsequent regain of weight in the first year of life.

Dr Caballero concluded the presentation by explaining the concept of 'risk transition', where the balance between traditional and modern risk factors defines the level of mortality a country faces⁽⁶⁾. Traditional risks include undernutrition, indoor air pollution, contaminated water and inadequate sanitation and hygiene. Modern risks are those associated with poor urban air quality and road traffic safety, occupational risks, physical inactivity, poor diets, overweight and tobacco use. As traditional risks decline, modern risks tend to rise. Yet, a country's socio-economic development has a dramatic effect on the impact of modern risks. In low-income countries, urbanisation and higher life expectancy lead to increased prevalence of modern risks, while still sustaining the impact of traditional risks on health. But, as a low-income country, the resources to design and implement policies to simultaneously manage traditional and modern risks are limited. Understanding the driving forces of these risk factors and how they affect disease risk is important for developing effective strategies to improve global health.

Nutrition transitions and diabetes in developing countries

Dr K. M. Venkat Narayan (Emory University, Atlanta, GA, USA) highlighted the present evidence for the prevention of type 2 diabetes, with special emphasis on randomised controlled trials. He then described a community-based intervention being conducted in India to illustrate diabetes prevention translational research in the context of a middle-income country.

Several diabetes prevention trials have been conducted to date: notably the Diabetes Prevention Program (DPP)⁽¹⁷⁾, the Finnish Diabetes Prevention Study⁽¹⁸⁾ and the Da Qing IGTT

and Diabetes Study⁽¹⁹⁾. Dr Narayan summarised findings from DPP, a multi-ethnic clinical trial conducted in twenty-seven centres across the USA in over 3000 adults who were at high risk (i.e. had impaired glucose tolerance) for type 2 diabetes and were randomised to one of three intervention arms: intensive diet and lifestyle modifications, oral glucose medication (metformin) or standard lifestyle advice as placebo. The average length of follow-up was approximately 3 years; however, the multi-centre trial was terminated early by the Data Safety and Monitoring Board, given the proven efficacy of the two interventions compared to placebo. Dramatically, the diet and lifestyle intervention proved more effective than the drug intervention, reducing incidence of type 2 diabetes by 58 (95% CI 48, 66)%, while metformin did so by 31 (95% CI 17, 43)%. The DPP demonstrated that a structured lifestyle intervention effectively lowered the incidence of type 2 diabetes among study participants. Furthermore, the Da Qing trial showed that the benefits of lifestyle in preventing diabetes have been sustained for over 20 years, while the Finnish Study and DPP have shown sustained benefits at 10 years of follow-up. Analysis from DPP and the Finnish trial indicate that lifestyle interventions negate the risks conferred by several of the known major genes for diabetes.

The trials described above have been conducted in populations with pre-diabetes, defined as having impaired glucose tolerance based on a 2-h glucose concentration between 1400 and 2000 mg/l and/or impaired fasting glucose concentration between 1000 and 1260 mg/l. Dr Narayan posited that given the very low incidence of diabetes in people with normal glucose tolerance, prevention trials in people without pre-diabetes would not be effective due to the large number of participants and study duration that would be required⁽²⁰⁾. He proposes that although people with diagnosed pre-diabetes may only comprise less than one-third of the total population, given the high conversion rate to diabetes and the number of those people who go on to develop type 2 diabetes, it would be more effective to target this population, emphasising again that there is more evidence from intervention trials to support effectiveness and cost-effectiveness in persons with pre-diabetes. He reminded the audience that present treatments, at best, lower incidence rates, but even with intensive pharmacological or lifestyle interventions, most persons with pre-diabetes will develop diabetes within 10–20 years.

Dr Narayan suggested that key components of successful lifestyle programmes for diabetes prevention should be multi-faceted and typically include a diet component (e.g. energy reduction, lowering fat intake, increasing fibre, etc.), weight reduction or maintenance, physical activity and behaviour change counselling. He discussed his skepticism over approaches testing changes in single items. To put these ideas into context, he gave an example from a community-based intervention presently being conducted in India. The Diabetes Community Lifestyle Improvement Program⁽²¹⁾ is a randomised controlled trial conducted in healthy adults aged 20–65 years with BMI ≥ 23 kg/m² and pre-diabetes. Investigators randomised 600 participants to either an intervention

tailored after the DPP or a control arm receiving standard-of-care treatment. The outcomes included diabetes incidence, changes in clinical characteristics and cost-effectiveness. This trial will be the first to evaluate a wider group of persons with impaired glucose tolerance and/or impaired fasting glucose, and to be conducted in a low- or middle-income country, using low-cost approaches to lifestyle modification. Results will inform future translational research for diabetes prevention.

Carbohydrate intake and cardio-metabolic risk

Dr Frank B. Hu (Harvard School of Public Health, Boston, MA, USA) proceeded to illustrate the present evidence for the link between carbohydrate quality and quantity and cardio-metabolic risk. Dr Hu began by stressing the alarming projections of incidence of type 2 diabetes around the world, with the epicentre being developing countries, namely India, China, the Middle East, Latin America and the Caribbean, although sub-Saharan Africa is also expected to show a rapid increase⁽²⁾. There is convincing evidence that changes in lifestyle, particularly dietary habits, are major contributors to this disease. Much of the evidence about the association of diet and diabetes comes from large prospective epidemiological studies, including two major cohorts from the Harvard School of Public Health: the Nurses' Health Study and the Health Professional Follow-Up Study. The repeated dietary measurements in this type of design are valuable for studying the effects of long-term diet on disease outcomes, and may help decrease measurement error and increase analytical power.

These epidemiological studies suggest that BMI, as a measure of obesity, is a major risk factor for diabetes^(22,23). Thus, weight control is one of the best strategies to prevent and control diabetes. Several lifestyle intervention trials conducted in various populations across the world have also consistently demonstrated that diet and physical activity can reduce risk of diabetes, especially among those at high risk because of obesity. Both observational and randomised trial data provide strong evidence of the impact of lifestyle on diabetes. In fact, Dr Hu has shown that type 2 diabetes can be almost entirely preventable, with a 90% reduction in risk, by following five primary preventative factors⁽²⁴⁾:

- (1) Consuming a healthy diet (defined as the upper quintiles of a healthy diet score).
- (2) Having normal BMI ($< 25 \text{ kg/m}^2$).
- (3) Participating in moderate/vigorous exercise ($\geq 30 \text{ min/d}$).
- (4) Non-smoking.
- (5) Consuming alcohol at half a drink to one drink per d.

Regarding diet, Dr Hu pointed out that the evidence shows that the quality of the foods and nutrients, rather than quantity of nutrients, has a greater influence on disease. For example, some types of dietary fats and carbohydrates are highly associated with risk of diabetes, with protective effects obtained from consumption of polyunsaturated fats (such as vegetable oils, nuts), whole grains and fruits and vegetables, while risk can increase with higher intake of red and processed meats, refined carbohydrates, potato chips, fries, margarine, butter

and added sugars such as sugar-sweetened beverages. Thus, the source and quality of the food has a high impact on disease. Many obesogenic foods are not only high in unhealthy fats, but also, or rather, comprised of low-quality carbohydrates⁽²⁵⁾. According to Dr Hu, this highlights an important strategy for obesity and diabetes prevention: not only should we eat less, but also eat better. It also suggests that present metrics and guidelines (fat content, energy density and total sugars) might not be as helpful in prevention and control, and the focus should be on diet (especially carbohydrate) quality and the extent of food processing.

Several metrics have been used to assess the complexity of carbohydrate quality, including glycaemic index (GI, indicates quality) and glycaemic load (GL, indicates quality and quantity), amount of fibre, whole *v.* refined grains and liquid *v.* solid energies. There is also a recently defined carbohydrate quality ranking score developed by Dr Walter Willett that places empty sugary energy (such as sugar-sweetened beverages) at the bottom with a value of zero, while foods with > 100 score include intact whole grains, parboiled brown rice and legumes, which are high-quality foods. There is convincing evidence that foods high in GI (score of > 70) and GL, such as potatoes, white bread, pastries, most rice, most breakfast cereals and low-fat snacks, increase the risk of diabetes^(5,26). Dr Hu pointed out that some of those foods, *i.e.* potatoes, bread and rice, are staples in the diet of many countries.

The associations with GI are modified by several factors, such as BMI, as the effect of GI on CHD is strongest for obese/overweight individuals⁽²⁷⁾. This implies a biological interaction between BMI and GL, which may explain why traditional societies that were physically active better tolerated refined carbohydrates, while sedentarism may boost obesity and insulin resistance from refined carbohydrates consumption. Another modifying factor may be moderate alcohol intake, which has been shown to blunt the effect of a high-GL diet⁽²⁸⁾. Higher GL is associated with increased risk of diabetes, but this association is attenuated for those with moderate intake of alcohol, probably by blunting the effect of high GL on glucose and insulin sensitivity. Moreover, the effect of a predisposing genetic variant in *TCF7L2*, which is related to β -cell function, becomes more pronounced on high GL or low cereal intake⁽²⁹⁾.

Dietary fibre intake is another metric of carbohydrate quality. A meta-analysis has shown a beneficial effect of fibre from cereal but not from fruits and vegetables⁽³⁰⁾. The reasons are still unclear, but Dr Hu proposed that cereals may have a combination of other beneficial nutrients such as Mg, antioxidants and polyphenols. Dr Hu discussed the tremendous impact of industrial refining and processing on the quality of food. For example, milling grains removes the germ, which contains most of the nutrients and fibre, leaving the endosperm of the grain which is mainly starch (glucose). Many minerals and vitamins are lost even after enriching or fortifying. Thus, whole grains with minimal processing are healthier and associated with a reduction in risk of diabetes⁽⁴⁾, compared to refined grains, which have lower carbohydrate quality and lower micronutrient and fibre content. A major staple food highly subjected to processing and polishing is white

rice. Indeed, a meta-analysis that included studies from China and the USA showed a clear dose–response of white rice consumption and risk of type 2 diabetes⁽³¹⁾. Substituting brown rice may significantly reduce this risk⁽³²⁾.

Liquid energy provides another metric of carbohydrate intake. Soft drinks and sugar-sweetened beverages are a major source of excess energy in the diet. Experimental studies show that these beverages provide little satiety and induce unique adverse metabolic effects, as the simple sugars induce β -cell dysfunction, inflammation and insulin resistance. Intake of sugar-sweetened beverages have been consistently associated with cardio-metabolic disorders and type 2 diabetes⁽³³⁾, with pronounced risk in Asians and African-Americans; substituting them for healthy beverages such as tea, low-fat milk, coffee and water may reduce the risk significantly. Coffee intake has been shown to lower the risk of diabetes⁽³⁴⁾, probably due to healthy bioactive compounds such as polyphenols and minerals. Although studies on diet soda are complicated by confounding by indication or reverse causation (diet soda intake being a marker for dieting behaviours in overweight individuals) that abolishes its association with diabetes⁽³⁵⁾, this artificially sweetened beverage may not be a healthy alternative, as its taste may induce cravings for sweets in some people.

Dr Hu concluded his presentation by providing some advice as to how to improve diet quality in order to prevent diabetes. The evidence shows that consuming whole grains, decreasing consumption of total carbohydrates and foods of high GI and increasing intake of cereal fibres, especially soluble fibre, seem to be helpful strategies⁽³⁶⁾. The goal is to shift carbohydrate quality and improve diet overall along with other healthy lifestyle behaviours. Dr Hu stresses that these small diet and lifestyle changes can make a big difference and provide a remarkable opportunity for prevention.

Diet quality, glycaemic index and risk of diabetes

The last speaker was Dr David Jenkins (University of Toronto, Toronto, Canada), who discussed diet quality, as it relates to risk of diabetes and cardiovascular disease, with an emphasis on carbohydrates and GI. Dr Jenkins' began by describing the findings of Denis Burkitt in the 1970s when the Western world was experiencing a radical change by consuming more animal protein and less plant-based protein, less fibre and an overall diet containing more fat, saturated fat, sugar and salt. He also highlighted the debate regarding the role of saturated fat in risk of heart disease by contrasting Ancel Key's original Seven-Countries Study, which showed a positive correlation between cholesterol and CHD⁽³⁷⁾, with a meta-analysis of studies conducted since the 1980s showing that saturated fat did not have a significant effect compared to carbohydrates⁽³⁸⁾. These findings provide a rationale to look beyond saturated fat and examine the role of slow-release (*lente*) carbohydrates on risk of diabetes and heart disease in more detail, the idea being that the rate of glucose absorption is slowed by utilising a larger part of the small intestine, resulting in a more gradual rise in post-prandial blood glucose. Using acarbose, an α -glucosidase inhibitor,

as a model, the benefits of reducing hyperglycaemia were demonstrated in the Study to Prevent Non-insulin Dependent Diabetes Mellitus (STOP-NIDDM) trial, where acarbose resulted in a 49% reduction in CHD and a 34% reduction in hypertension⁽³⁹⁾. As said by Dr Jenkins, 'this study was considered the trial analogue for the low-GI diet'. These findings were supported by others, including the Nurses' Health Study, which found that a high-GL diet and low intake of cereal fibre increased risk of diabetes over 2-fold⁽⁴⁰⁾.

Dr Jenkins pointed out that if packaged foods are being used for a dietary intervention, it is important to consider that GI values may change in relation to changes in product formulation made by manufacturers. Thus, 'it is very important to know the GI of the actual items being used'. The following is a list of low-GI foods recommended by Dr Jenkins, which can be used in dietary interventions and otherwise: steel-cut oats, barley, bulgur (cracked wheat), pasta (whole wheat), parboiled rice, lentils, chick peas, dried beans, pumpernickel bread and temperate climate fruit. In general, these are traditional foods, but modern versions such as pumpernickel bread often contain added sugars to enhance palatability, which may raise GI values. Dr Jenkins discussed evidence showing benefits of low- *v.* high-GI diets on glycosylated Hb and glycated proteins, HDL-cholesterol, C-reactive protein and clotting factors, as well as data from over eleven studies that have shown higher risk of CHD for high-GL diets. Dr Jenkins also discussed his recent trial of low-GI fruit intake, which found that the highest quartile of intake had the greatest reduction in glycosylated Hb, suggesting that consumption of temperate climate fruit (berries, citrus, apples) may be important for reducing risk of diabetes⁽⁴¹⁾. In contrast, tropical fruits such as mangos and pineapple tend to have higher GI values.

Dr Jenkins considered the data showing the health benefits of plant-based fat and protein to be of particular importance. In the Nurses' Health Study, it was shown that greater intake of a plant-based diet of fat and protein reduced risk of CHD⁽⁴²⁾ and diabetes⁽⁴³⁾, compared to an animal-based diet. In both diets, intakes of carbohydrates were restricted. According to Dr Jenkins, these findings 'are useful as we go into the post-Atkins era'. Interestingly, the upper decile of animal fat and protein intake increased the risk of diabetes by about 60% when the analysis was not adjusted for BMI, suggesting the role of BMI in mediating this association. Dr Jenkins specifically discussed the beneficial effects of pulses, which are a good source of plant protein on glycated proteins, and of nuts, which are a good source of plant fat and protein, on risk of diabetes and CHD.

Dr Jenkins concluded that the quality of carbohydrates appears to have a greater effect on CHD than saturated fat. It also appears that risk of CHD and diabetes is reduced when carbohydrate is replaced by vegetable oils and proteins. Foods that therefore warrant special consideration for inclusion in the diet are those that provide more plant fat and protein and low-GI carbohydrates, which are high in fibre, in order to consume fewer high-GI carbohydrates. These beneficial foods include whole grains (especially barley, parboiled rice, cracked wheat and steel-cut oats), legumes (which increase protein and are staples in Latin American and Indian diets), nuts to reduce

GL and increase plant oils and protein and temperate climate fruit for their slow-release fructose, which may have a catalytic effect on glucose uptake.

Summary of workshops

Design of dietary interventions

The speakers and the participants at the Symposium commented on the need for global dietary interventions that incorporate culturally appropriate, high-quality foods, as a potential way to identify prevention strategies for type 2 diabetes and its risk factors. To discuss this, several workshops presented research tools necessary to achieve this.

First, Dr Vincent Carey (Brigham and Women's Hospital, Boston, MA, USA) discussed statistical considerations for the design of dietary interventions. Many of the examples presented by Dr Carey were obtained from his experience working with the Optimal Macronutrient Intake Trial for Heart Health (Omini Heart) Trial^(44,45) and the Preventing Overweight Using Novel Dietary Strategies (POUNDS LOST) Trial⁽⁴⁶⁾. Dr Carey noted that preferences among competing designs emerge through formal evaluation of their capacities to reduce bias, improve adherence and maximise efficiency. Participant non-compliance, drop-outs, carryover effects in cross-over settings and *ad hoc* approaches to multiple testing are typical threats to validity of study interpretations; effects of each of these should be reckoned in the design selection process. Important steps that help to improve study reliability and impact are: (1) knowing the variability of the outcome measure, (2) defining the desired effect size, (3) properly identifying, tracking and accommodating for potential confounders and (4) setting an adequate sample size and power. Dr Carey suggested that directly handling threats to study interpretability and uncertainties about outcome variability and effect sizes during the design phase is essential to successful study implementation and interpretation. Strong biostatistics support is crucial in the design and analysis phases of dietary interventions. Dr Carey also pointed out that there are multiple ways to measure compliance; for example, reported overall dietary intake or meeting specific dietary composition targets, and attendance at group counselling or educational trainings.

Dr Carey proceeded to discuss other important factors that should be carefully considered at the design phase. First, researchers should define how to randomise the diets (choosing in an informed way among approaches based on permuted blocks, biased coin-toss simulations or other algorithms) and whether (and which) covariates should be used to randomise or for adjustment in *post hoc* analysis. Also, the basic design of the study (cross-over, parallel or other comparative frameworks) and length of the intervention periods should be determined early on to help formulate the analytical approach. Cross-over designs are particularly useful to interpret the efficacy of dietary interventions and allow a simple analytical approach, but generalisability is limited and patient burden may be excessive. Long-term feeding studies have eligibility restrictions, and self-selection may inhibit generalisability and interpretation of results.

Researchers should also anticipate effects of emerging knowledge (within the study context or in the general setting of nutritional science) on ethics of continuing or stopping a clinical experiment. Futility analyses allow valid interpretation of a study that is terminated if no effect is observed at a pre-defined time point. Research into adaptive trial designs provides useful guidance on approaches that can be used, with appropriate prior planning, if design decisions concerning important parameters such as outcome variability have been taken in error.

Implementation of dietary interventions

Proper implementation is as essential to the success of a dietary intervention as is its design. Accordingly, Kathy McManus (Brigham and Women's Hospital, Boston, MA, USA) provided an overview of essential elements in conducting dietary interventions and gave specific examples from the POUNDS LOST trial, a trial of over 800 free-living overweight participants across two sites, designed to test the effects of four diets varying in macronutrient composition on weight loss and long-term weight maintenance⁽⁴⁶⁾. Ms McManus identified six key elements in conducting dietary interventions:

- (1) A well-designed dietary intervention that meets the aims and objectives of the study.
- (2) A detailed manual of operations prior to onset of the study.
- (3) Initial and on-going staff training to ensure integrity and expertise of staff.
- (4) Procedures to monitor progress of the intervention and maintain compliance.
- (5) Strategies to ensure retention of all randomised participants.
- (6) A decision-making process for handling unexpected issues.

As with any study, in a dietary intervention, investigators must formulate the hypothesis for the study, followed by specific aims and expected outcomes and then create the actual diet intervention. At this stage, it is important to think about other confounders or potential issues that may affect the diets. For example: Are the diets nutritionally sound? If it is a weight loss trial, is there a potential for micronutrient deficiency? If intake of one macronutrient is lowered, then what will be the replacement? Conducting pilot studies can be informative to answer these questions. Prior to POUNDS LOST, a pilot study of a Mediterranean diet *v.* a low-fat diet found that it was very difficult to convince participants to eat a higher-fat diet to lose weight during the 'fat phobia craze of the 1990s'. This was an unexpected finding that took several months to reverse through intensive education and relationship building with participants.

The importance of having a working manual of operations, which documents details of the study including specific aims, background, recruitment, diet intervention, outcomes, safety considerations, statistical methods and quality control, was also discussed. Specific components found in the diet intervention section of a manual of operations were discussed in detail, as follows:

- (1) Specifics of the diet: What is the intervention and how will the goals be met? If foods or supplements are being used, the type and quantity must be determined and they must be similar in look, feel and taste across arms to prevent bias. Focus groups can be helpful for accessing acceptability of test foods among participants.
- (2) Staffing: Number and level of experience of the staff should be based on study design, intensity of the intervention and number of participants. POUNDS LOST had 400 participants at once in one site, requiring six full-time dietitians. Most interventions should include dietitians/nutritionists.
- (3) Types of education materials: Will they be developed or purchased? Materials should be suited to the level of education of participants and must be equal in delivery and calibre for each treatment arm to prevent bias. For some basic instructions, pictures may be helpful.
- (4) Frequency and mode of contact: Outline the frequency of visits, whether they are individual or group-based, in-person or by phone or email, duration, information to be discussed and who will conduct the sessions. In POUNDS LOST, logistics and content for each session were created prior to the onset of the study.
- (5) Forms and data collection sheets: Participant modules and leader guides should be created to ensure equality across groups. Follow-up forms should be standardised for consistent data collection over time. In POUNDS LOST, dietitians used individual follow-up forms to access goals and chart progress.

As mentioned by Ms McManus, one of the most important components in a dietary intervention is training staff on components of the manual of operations. Staff must be equally trained on specifics of the intervention diets, how to conduct the sessions, the study materials and forms, tracking and monitoring of the diet and the tools used. In POUNDS LOST, the staff had initial and ongoing training on motivational interviewing and behavioural modification, and were evaluated by experts throughout the trial to ensure that they understood the concepts and were delivering the information correctly. Developing a plan for tracking the diet is also a crucial component of a dietary intervention. Selection of the appropriate diet assessment tool should be based on whether a quantitative or qualitative analysis is desired. Self-monitoring of the diet is important for multiple reasons, including supporting participants' diet modification and raising awareness and accountability. To improve accuracy of self-monitoring, recording should be structured and occur at the time of the activity, as bias can occur when individuals try to recall diet, and 'having biased data is worse than having no data at all'.

Because compliance and attendance are critical for success of a dietary intervention, it is important to define them and describe how they will be handled, as well as develop specific strategies to improve them by identifying potential reasons for poor attendance/compliance. Another crucial component of a dietary intervention is retention of randomised participants, which involves identifying participants at

risk for dropping out, establishing procedures of how to handle at-risk and drop-out participants and establishing strategies for contacting inactive participants. The final key component to consider in a dietary intervention is to formulate a decision-making process prior to the onset of the trial for unexpected issues that may occur, and require a formal system for handling issues. In POUNDS LOST, this was done through trial-wide committees, including a steering committee, diet intervention committee, retention committee and quality control committee.

Ms McManus commented that even in intense trials such as POUNDS LOST, participant burden can be handled and diminished. For example, the trial had an extensive screening process to understand if the individual was ready to participate and motivated to adhere to the diets. She commented that 'we were very up-front about study commitments to ensure that there were no surprises'. She also mentioned that it is important to set the bar high from the beginning in long-term studies, and to ask participants to consistently keep food records, as those who do tend to have better results. Ms McManus also commented that a potential way to handle the situation of when control subjects compensate and lose weight, regardless, or to motivate controls to stay in the study, is by providing the option of doing a cross-over study and promising all participants the benefits of the intervention diet at some point. It is also important to ensure that preparation of food items in substitution studies is standardised.

Qualitative data collection for dietary interventions: focus group discussions

Dr Ana Lindsay (Harvard Medical School, Boston, MA, USA) proceeded to provide suggestions to design, conduct and analyse focus group discussions (FGD) as part of qualitative data collection for dietary interventions. FGD may be used to obtain data and insight that would be less accessible without the interactions intrinsic of a group setting⁽⁴⁷⁾, allowing participants to hear from each other and prompting them to remember and share points relevant to the topic. The group effect provides a 'common language' for them to talk from their point of view. Thus, FGD are best suited to discuss general opinions rather than detailed topics.

To design an informative FGD, first define its purpose and develop the questions or moderator's guide. Much effort should be devoted to this part, as it will define the data that will be obtained. To help construct the guide, review the literature available on similar topics and consider framing the questions under a behavioural theory if appropriate. The length of the guide should be short so that participants are not overwhelmed. Questions should induce discussion rather than definite answers. Include 'probes' within the guide to keep the flow and pace of the discussion and to obtain in-depth responses. Particularly applicable to international settings, it is important to translate the guide accurately and to use a native speaker to make sure the vernacular language is appropriate. Similarly important is selecting the right moderator, who will have a key role in running the group and extracting useful information.

This person should be familiar with the topic, but preferably neutral, to avoid any preconceptions, and should have ample practice to keep the conversation dynamic and flowing, but under control, and to intervene in the discussion without inhibiting or biasing it.

One useful suggestion from Dr Lindsay is to pilot test the question guide using a small group (about four participants) of people with similar characteristics to the ones for the formal discussion. Use this opportunity to take notes and revise the guide as needed before actual implementation. Other relevant forms and information that should be prepared and included as part of the discussion are a short socio-demographic survey, informed consent, contact information form, receipt form for incentives, additional recruitment flyers and any other relevant questionnaires (i.e. socio-economic or acculturation scales). Several suggestions when recruiting and setting the discussions include:

- (1) Recruitment should be conducted at the same site and time, and using the same technique when possible. Some sources include membership lists, advertising and flyers. The 'snowball technique' (asking each participant to help enroll new participants) is also useful. Purposive sampling (specific recruitment strategies to obtain a target group) should be considered if the research question demands it; for example, sampling from government assistance eligible mothers rather than all mothers. In all cases, be clear about the selection criteria and expectations for participation.
- (2) The sample size and design depend on the overall goal and questions to be discussed. Group size is usually six to twelve participants, with a minimum of six to ensure a good discussion but limit to twelve to avoid overwhelming the group. Homogeneous groups (those with similar inclusion criteria) may require fewer participants, but should have at least four. Recruit more participants than needed because of possible cancellations and no-shows.
- (3) It is important to arrange participants based on the questions and expected answers. An overall group may be acceptable, but it may also be relevant to have different settings; e.g. one group for mothers and a separate one for child-care providers.
- (4) Be attentive for status differential among participants that may make an impact on the responses. For example, avoid family members or friends, co-workers or extreme differences in personal characteristics (such as opposite socio-economic strata).
- (5) The number of discussion groups to conduct varies, but it is usually four per topic. It may be necessary to follow a 'saturation strategy': conduct focus groups until obtaining the same answers repeatedly, at which point you may not need further discussions.
- (6) Consider the logistics. For example, choose a location and a sitting arrangement that allows for an open discussion, prepare and bring sufficient copies of all forms (including two copies per person of the informed consent), supplies and equipment (including materials

to take notes and recording devices), arrange for refreshments and for child care if necessary and compile and bring incentives if they will be provided.

- (7) Always call or send reminders the day before the discussion.

When implementing the FGD, inform participants of confidentiality agreements and remind them that they can speak at any time, but politely, and that there are no specific answers expected for each question. The moderator is available to clarify but not answer questions directly. Assign a note taker so that the moderator focuses on keeping the discussion flowing within a relaxed environment, by becoming very familiar with the guide in advance. An 'ice-breaker' question not related to the topic of research usually helps sets a comfortable mood. It is important to think of the participants as the experts and have each of them express their views without anyone dominating the conversation.

Immediately after each discussion session, collect all forms and recordings, and debrief the proceedings with team members, including the assistant and note taker. The pre-analysis part consists of reviewing the audio recording and notes, recording non-verbal behaviours (attitude, moods and reactions) and summarising the discussion right after the session. Dr Lindsay recommended for the audio to be transcribed as soon as possible after each session; it is not necessary to wait until completing all sessions. Prompt pre-analysis and transcription of the first audio recordings can help improve the next sessions. The recordings should be transcribed by the researcher or a trained staffer, but the person must be a native speaker who understands the discussion. Transcriptions require several careful readings and revisions.

To code the information, Dr Lindsay mentioned that using either analytical software or traditional coding (a framework with coloured blocks on copies of original transcripts) provides similar processes and results. First, the coders – at least two – should code relevant overarching as well as specific themes, using a working definition or theory, and following the original research questions and guides. Defining codes and themes should be a thorough process, and she suggested a 'saturation' approach to completing it: stop when no more themes emerge. After identifying large-scale ideas, she suggested finding units (the smallest amount of data, such as a phrase or paragraph that provides information on a theme), categorising those units and then selecting and sorting the final categories, based on defined inclusion criteria. Analysts should be in consensus about defining and setting the final categories.

Some of Dr Lindsay's suggestion for summarising and presenting FGD results include using direct quotes from participants when appropriate, and not using terminology that quantifies data (e.g. use 'most' rather than 'two-thirds of participants'). To close, Dr Lindsay reminded the audience that the results of FGD are only descriptive, not generalisable and cannot be applied to individuals, even if similar to participants. A good measure of validity is how transferable the results are into other contexts, and how well can they be applied by other researchers.

Discussion

Several prominent global organisations, including the United Nations, the WHO and the International Diabetes Federation, have embraced the chronic disease epidemic and the double burden of undernutrition in developing countries as a major priority, posing the need for global awareness on this challenging topic, as well as timely discussion for both general and country-specific strategies to reduce these alarming trends. The GNET-sponsored Symposium and Workshop on Nutrition Transition and Global Burden of Type 2 Diabetes partly met this need by highlighting these issues and providing strong evidence for the nutrition contribution, especially carbohydrate quality, to diabetes risk, as well as specific suggestions on proper design and implementation of population-based dietary interventions, with an emphasis on international settings, as an approach to help alleviate the burden of diabetes. The present report makes those outcomes accessible to the general nutrition and public health community, in order to broaden and sustain GNET's efforts worldwide.

At the end of the Symposium, a question and answer session posed interesting discussion points and remaining questions on the topic. For example, Dr Narayan was asked to comment on what kind of strategies can help reach out to the communities that need it. He suggested that we should identify key leaders and enroll them to work on the issues at hand, but also to have flexibility around the situation. He used the example in India, where the major group in need is the low socio-economic group, and they approached family and community leaders to help increase health knowledge among those groups.

Dr Jenkins was asked to comment on the utility of doing trials that assess the effect of substituting one item for another, which intuitively seem scalable *v.* doing a composite trial that changes multiple components of the diet within several dimensions. Dr Jenkins said that because diet, the economy, the environment and agriculture are all linked, multi-level approaches would be useful in tackling and promoting change for these issues at the same time. He commented that as with any approach, we have to answer the question of 'if we put that package together, will it work?' He also said that single-change efforts can make a difference in public health, but often those differences need to be much larger to see an effect in a clinical trial; composite trials may then be useful in obtaining more public health and clinical impact.

Dr Jenkins was also asked why physicians in practice, especially in low- and middle-income countries, do not promote nutrition education. Dr Jenkins thinks this is because we have not yet managed to create the environments for people to obtain the healthy foods that they need. He commented that 'physicians that are burdened with high patient loads know that the pharmacy has the prescription, but do not know if the market has the food'.

Dr Walter Willett, chair of the Department of Nutrition at Harvard School of Public Health and founding member of GNET, agreed with Dr Jenkins that we should consider 'the whole package' and target multiple levels in interventions in

order to have more impact on health. This would mean engaging relevant industries, such as agriculture or medicine, considering other food components and weighing the evidence of epidemiological and interventional studies across the globe. He also commented on which type of results and evidence we should focus on: do we need to prove reduction in type 2 diabetes incidence or are metabolic measures such as insulin and glucose levels appropriate? Dr Willett also posed the question of target audience: the general population or high-risk groups? He said that such questions may not have a definitive answer, but that for health issues such as type 2 diabetes, almost everyone is at potential risk. Thus, action must be taken early before there is further physiological damage.

Dr Willett provided an important argument as to why dietary interventions may be beneficial on a large scale even when trials may show small effects. He used the example of a 3% reduction in smoking in community interventions *v.* 12% when such efforts were implemented on a larger scale. He remarked that 'trials predict what will happen in the population in the long term and in the real world, and that is what we aim for with these diet interventions'. Dr Willett encouraged the audience to promote changes in the culture in order to change the diet. Such efforts may help garner the best possible evidence to then take action and show a real impact.

In addition to the discussion session, GNET distributed a short survey to gather input from attendees about the event and next steps. Some key topics that participants suggested should be discussed in the future include:

- (1) Using dietary interventions and evidence-based science to formulate public policy around type 2 diabetes prevention.
- (2) Translational research: from community/population interventions to clinical applications.
- (3) Domestic and international agriculture and food policy, and implications on chronic diseases.
- (4) The implications of the United Nations High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases (September 2011).
- (5) How the nutrition transition and major food production and food insecurity trends in the USA make an impact on global trends of diabetes and chronic disease.
- (6) Cultural barriers and perceptions that may influence the feasibility of implementing policy and/or diet interventions.
- (7) Systematic information about specific types of grains, their metabolic effects, health benefits/risks and possible substitutions.

Similarly, attendees shared ideas for practical skill building and training strategies regarding dietary interventions for diabetes prevention, particularly in international settings, such as:

- (1) Networking and fostering one-on-one discussions with diabetes and nutrition experts (researchers, policy-makers, etc) in each country.

- (2) Appropriate data collection, management, statistical analysis and interpretation, intrinsic of international intervention studies.
- (3) Workshops on quantitative and qualitative data analysis software.
- (4) 'Lessons-learned' sessions and practical perspectives on the design and implementation of a dietary intervention from investigators who have successfully conducted them.
- (5) Preparing protocols and obtaining approval for international Human Subjects Research.
- (6) Collaborative manuscript-writing skills.
- (7) Finding and preparing funding proposals within each country and globally.

In conclusion, the ongoing nutrition transition in developing countries, in particular the rapid changes in carbohydrate quality, plays a major role in the shift from infectious to chronic diseases. The alarming global trends of type 2 diabetes demand immediate action, and multiple approaches should be explored to tackle this global health issue. One strategy may be through community and population-based dietary interventions replacing foods of poor carbohydrate quality with whole grains, legumes or other high-quality carbohydrates. Such dietary interventions can be feasible and successful when properly designed and implemented. GNET investigators and the organisers of this symposium and workshop encourage researchers, health professionals, public health leaders and policy makers to seek opportunities for independent and collaborative international efforts to identify and disseminate the best evidence on nutritional risks factors and prevention of type 2 diabetes. Ultimately, this evidence will be translated into public health practice and messages, which will help shape global nutrition policies and food production.

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