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Healthy diet and lifestyle clustering and glucose intolerance

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Glucose intolerance represents a spectrum of abnormalities, including impaired fasting glucose, impaired glucose tolerance and type 2 diabetes. It is a major public health challenge worldwide, with rapidly increasing prevalence rates in both developed and developing countries. This global epidemic of diabetes is largely driven by the globalisation of Western culture and lifestyles. Specifically, there is now evidence from large-scale observational studies, and from intervention studies, of powerful synergistic interactions between diet, obesity, exercise, smoking and alcohol in the development of glucose intolerance. It is estimated that > 90 % of cases of type 2 diabetes in the population could be prevented with the adoption of a prudent diet (high in cereal fibre and polyunsaturated fatty acids and low in *trans*-fatty acids and glycaemic load), avoidance of overweight and obesity (BMI < 25 kg/m^2), engagement in moderate to vigorous physical activity for at least 0·5 h/d, non-smoking and moderate alcohol consumption. These findings are biologically plausible and have major public health implications. They form the basis for a clear, simple and coherent message for health promotion and public policy. However, to make progress on these issues health will need to be placed at the centre of public policy and relevant vested interests tackled, notably in the food, entertainment, tobacco and automobile industries.

Diet: Lifestyle: Type 2 diabetes: Glucose intolerance

Glucose intolerance is now considered one of the major threats to human health in the 21st century. The term glucose intolerance refers to a spectrum of abnormalities, including impaired fasting glucose, impaired glucose tolerance and type 2 diabetes. The World Health Organization (1999) criteria for the different categories of glucose intolerance have recently been revised and updated. Impaired fasting glucose is defined as a fasting plasma glucose of ≥ 6·1 and < 7 mmol/l, with a 2 h post-load glucose of < 7·8 mmol/l. A fasting plasma glucose of < 7·0 mmol/l and a 2 h post-load glucose of ≥ 7·8 mmol/l but < 11·1 mmol/l is regarded as consistent with impaired glucose tolerance. Type 2 diabetes is defined on the basis of a fasting plasma glucose of ≥ 7 mmol/l or a 2 h post-load glucose of ≥ 11·1 mmol/l. Glucose intolerance is a major public health challenge in both developed and developing countries (Zimmet *et al*. 2001). An estimated 135 million of the world population had diabetes in 1995, of which > 95 % is type 2 diabetes, and this number is expected to rise to at least 300 million by 2025. The major part of this increase will occur in developing countries, and it is estimated that by the year 2025 > 75 % of those with diabetes will reside in developing countries (King *et al*. 1998). For each case of diagnosed diabetes there is likely to be one additional undiagnosed case and two additional cases of abnormal glucose tolerance, either impaired fasting glucose or impaired glucose tolerance. For instance, in a recent Australian population-based screening study the estimated prevalence of diabetes in adults aged ≥ 25 years was 8 % in men and 6·8 % in women (of whom 50 % were undiagnosed) with an additional 17·4 % of men and 15·4 % of women having either impaired fasting glucose or impaired glucose tolerance (Dunstan *et al*. 2002). Thus, on the basis of current data it is estimated that almost one in four Australian adults have abnormal glucose tolerance. Both impaired fasting glucose and impaired glucose tolerance are associated with high rates of progression to type 2 diabetes (up to 40 % of subjects with impaired glucose tolerance will progress to diabetes over 5–10 years), and regardless of progression to diabetes both impaired fasting glucose and impaired glucose tolerance are associated with substantially-increased risk of cardiovascular disease (Zimmet *et al*. 2001).

The global pandemic of type 2 diabetes is largely driven by the globalisation of Western culture and lifestyles,

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specifically the interrelated issues of increasing obesity, decreasing physical activity levels and dietary change (Zimmet *et al*. 2001). The present paper will reflect briefly on current approaches in chronic disease and nutritional epidemiology to the problem of type 2 diabetes and related conditions. Major risk factors for type 2 diabetes will be reviewed briefly. Finally, the argument will be developed that the occurrence of type 2 diabetes and related conditions in the population can be largely explained on the basis of interactions between a small number of core lifestyle-related and dietary causal factors.

Chronic disease and nutritional epidemiology

Epidemiological research over the past 40 years has successfully delineated the scale of the global epidemic of type 2 diabetes, set diabetes and glucose intolerance within the broader spectrum of chronic non-communicable diseases, notably cardiovascular disease, and elucidated major causal factors in the development of type 2 diabetes. However, there are a number of problems with traditional approaches in chronic disease and nutritional epidemiology, and we need to consider how best to go forward.

In chronic disease and nutritional epidemiology there has been an excessive focus on individual risk factors, and in nutritional epidemiology on individual nutrients, and a tendency to ignore the extent to which lifestyle and dietary exposures are interrelated and interdependent. While work on estimating the independent effects of single exposures on the causes of disease is important in elucidating mechanisms, we need to consider potential interactions between exposures in assessing the impact of lifestyle and dietary factors on individuals and populations. For example, the extent to which physical inactivity increases risk of diabetes, independent of effects on obesity, is difficult to estimate and is of less relevance to individuals and populations than estimates of the combined effects of these factors. Similarly, disease end points are interrelated and interdependent, and there has been an excessive focus on individual diseases. Type 2 diabetes and CHD provide a classic example of interrelated conditions that share common causal factors (Stern, 1995), including common dietary causal factors, obesity, physical inactivity and smoking. Both diseases are related to economic, social and educational exclusion, exhibit a broadly similar relationship with alcohol intake, and share common intrauterine–early life causal factors, and possibly common genetic factors.

In our approach to risk factors for chronic disease we have tended to give equal weight to modifiable factors, such as obesity, and non-modifiable risk factors, such as age and gender. Moreover, it has not been sufficiently emphasised that not all risk factors are equal, i.e. that some risk factors are causal factors, others are mediators or markers of underlying causal factors, and some so-called risk factors are essentially early manifestations of the disease. Thus, in the context of type 2 diabetes physical inactivity may be considered as a fundamental causal factor, insulin resistance and hyperinsulinaemia as mediators and hyperglycaemia as an early manifestation of disease. We have also blurred the distinction between distal (macro level), intermediate (individual level) and proximal (micro level) causes of disease; for example, the distinction between poverty and social exclusion which operate at the distal or macro level, smoking and physical inactivity which operate at the individual level and factors acting at the micro level, e.g. genetic abnormalities, or indications of physiological derangements such as dyslipidaemia.

We have also permitted confusion on the differences between clinical and population health approaches to chronic disease epidemics. In the clinical approach to the control of chronic disease there has been a tendency to focus on measurements of biological variables such as blood pressure, blood glucose and blood lipids. These variables have reasonably high predictive power at the individual level, but are not readily amenable to monitoring and targeting at the population level. By contrast, in adopting a population health approach to chronic disease there is emphasis on lifestyle and behavioural causal factors for disease, such as obesity, dietary saturated fatty acid intake, smoking and physical inactivity, factors that can be monitored at the population level and which are susceptible to population level as well as individual level interventions.

A central argument of the present paper is that there are a small number of core causal factors for glucose intolerance and cardiovascular disease that are driven by macro level factors related to globalisation, including economic, social and educational exclusion. These factors operate at the individual level and display powerful synergistic interactions in the development of glucose intolerance and related conditions. In the present paper evidence will be presented of synergistic interactions between diet, obesity, exercise, smoking and alcohol in the development of glucose intolerance. Particular attention will be paid to disease occurrence in those individuals with low levels of exposure to these risk factors, i.e. the effect of protective factors on the occurrence of type 2 diabetes (the absence of obesity, regular exercise, non-smoking, moderate alcohol intake and a prudent dietary pattern). For each of these risk factors there is an extensive literature addressing their independent role in the development of type 2 diabetes. This literature will be briefly reviewed to consider the relative importance of the individual factors on risk of diabetes (as far as is possible) and to set in context recent findings on the effect of these interrelated factors acting in concert.

Obesity

Advancing age, obesity (both general and abdominal), family history of diabetes and physical inactivity are among the well-established risk factors for type 2 diabetes (Manson & Spelsberg, 1994).

The current epidemic of type 2 diabetes is largely driven by a worldwide epidemic of obesity which has gathered pace over the past two decades (Bray, 1998). This epidemic of obesity has been signalled by the rise in the percentage of the population with a BMI of $> 30\,kg/m^2$, e.g. in Britain from 8 % to 15 % between 1980 and 1995 (Wilding, 1997) and in the USA from 12·3 % to 20 % among men and from 16·5 % to 24·9 % among women between 1976–80 and 1988–94 (Flegal *et al*. 1998). In the 1997–9 Irish North/South Food Consumption Survey, involving a sample of 1379 adults aged 18–64 years, there was evidence of a marked increase

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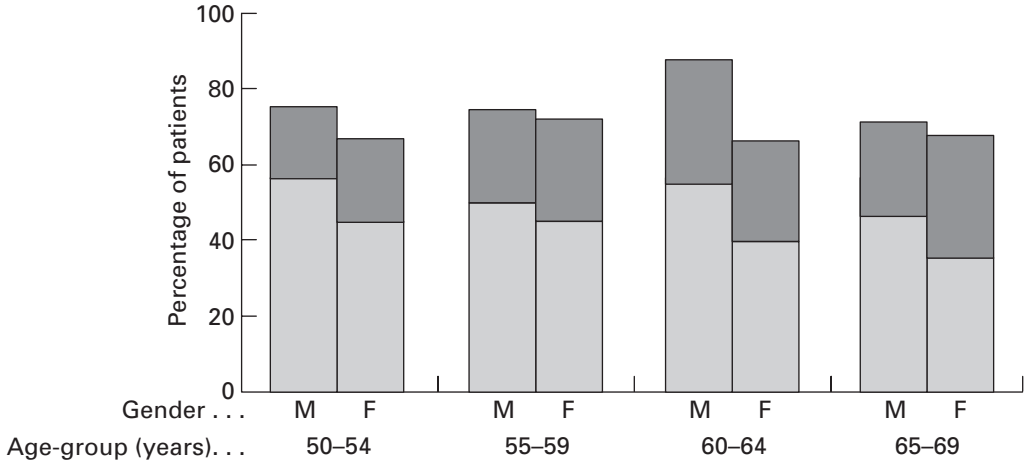

Fig. 1. The percentage of overweight (defined as a BMI of between 25 and 29·9 kg/m^2; ▨) and obese (a BMI > 30 kg/m^2; ■) by age-group in men (M) and women (F) aged 50–69 years participating in the Cork & Kerry Diabetes and Heart Disease Study. (From Creagh *et al*. 2002.)

in the prevalence of obesity over the preceding 10 years (McCarthy *et al*. 2002). In men the overall prevalence of obesity (BMI ≥ 30 kg/m^2) had more than doubled from 8 % to 20 %, with a prevalence of 24 % of men in the 36–64 year age-group. In women the increase in obesity prevalence was less marked. However, 16 % of women in the 1997 sample were obese, rising to 30 % in the 51–64-year age-group. Similarly, in the Cork & Kerry Diabetes and Heart Disease Study, involving a sample of > 1018 men and women aged 50–69 years drawn from general practitioner lists, approximately 50 % of the population were overweight (BMI 25·0–29·9 kg/m^2) and a further 25 % were obese (Fig. 1; Creagh *et al*. 2002). Of this population sample, 40 % reported minimal levels of physical activity. The obesity epidemic is also evident in childhood, with alarming implications for population health and health care expenditure over the next two to three decades. The definitions of overweight and obesity in children differ between epidemiological studies, making comparisons of cross-sectional prevalence data difficult. Nevertheless, data are now available from a number of studies that have examined changes in the distribution of BMI in childhood over time, and the findings suggest rapidly increasing rates of obesity among children in developed and developing countries. It is estimated that the prevalence of childhood obesity has increased between 2- and 3-fold over the last 25 years in the USA, approximately 2·5-fold over 10 years in England, and approximately 4-fold over 18 years in Egypt (Ebbeling *et al*. 2002).

Obesity and weight gain dramatically increase the risk of type 2 diabetes (Colditz *et al*. 1990, 1995). In the British Regional Heart Study Cohort the risk of type 2 diabetes was increased > 11-fold in men with a BMI of > 28 kg/m^2 relative to those with a BMI of < 23 kg/m^2 (Perry *et al*. 1995). In the US Nurses Health Study Cohort women with a BMI of 30–35 kg/m^2 had a 20-fold increased risk of diabetes, which was further increased in those women with a BMI of > 35 kg/m^2 (relative risk 38·8) compared with women with a BMI of < 23 kg/m^2, in analyses adjusted for age and family history of diabetes (Colditz *et al*. 1990; Hu *et al*. 2001*a*). It is noteworthy that the risk of diabetes increases across the normal range of BMI. In the US Nurses Health Study among women of average BMI (23–23·9 kg/m^2) the risk of diabetes was increased 3·6-fold relative to women with a BMI of < 22 kg/m^2 (Colditz *et al*. 1990). It is also clear that weight gain in adult life is associated with a substantially-increased risk of diabetes. In the British Regional Heart Study weight gain of ≥ 10 % over 5 years was associated with a 60 % increase in risk of type 2 diabetes during the subsequent 12 years follow-up in a cohort of > 6000 middle-aged men, in analyses adjusted for age, initial BMI and other risk factors (Wannamethee & Shaper, 1999).

Several biologically-plausible mechanisms link obesity with type 2 diabetes. All are linked with effects on insulin-mediated glucose uptake (the promotion of insulin resistance) that antedates the development of clinically-detectable glucose intolerance.

Physical activity

A protective effect of physical activity on the risk of developing type 2 diabetes is biologically plausible (Spelsberg & Manson, 1993). Skeletal muscle represents the predominant site of insulin resistance in diabetes, and exercise training has been shown to improve insulin sensitivity in these tissues (Chisholm *et al*. 1997). Exercise has a favourable effect on glucose tolerance and insulin sensitivity both in individuals with established type 2 diabetes and in non-diabetics. While early epidemiological studies on the role of exercise and type 2 diabetes were somewhat inconsistent (Jarrett *et al*. 1986), we now have clear evidence, from long-term prospective studies, of a strong and linear relationship between the frequency and intensity of exercise and risk of type 2 diabetes (Helmrich *et al*. 1991; Manson *et al*. 1991, 1992; Burchfiel *et al*. 1995; Perry *et al*. 1995). In the British Regional Heart Study Cohort a substantial fall in risk of diabetes was observed in men engaged in moderate levels of physical activity relative to physically-inactive men, after adjustment for age and BMI (relative risk 0·4, 95 % CI 0·2,

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0·7; Perry *et al*. 1995). In the US Nurses Health Study Cohort, in which physical activity data were available from 87 253 women who were followed for 8 years, the risk of developing type 2 diabetes was lower by one-third among those who engaged in vigorous exercise at least once weekly. This effect was independent of age, BMI, family history of diabetes and other potential confounding factors. Exercise was associated with a similar reduction in risk of diabetes among obese and non-obese women in this study (Manson *et al*. 1991).

Smoking and risk of diabetes

Cigarette smoking is well established as a causal factor in CHD and stroke. The role of smoking in the development of diabetes is less well documented, although as discussed earlier it is becoming increasingly clear that diabetes and cardiovascular disease share many common causal factors. Given the potential public health consequences of even a small increase in risk of type 2 diabetes (a common condition) associated with smoking (a common exposure), the potential role of smoking in the development of type 2 diabetes has received relatively little attention (Perry, 2001). However, there is now evidence from at least five prospective studies to suggest that smoking is associated with increased risk of type 2 diabetes in men and women (Rimm *et al*. 1993, 1995; Nakanishi *et al*. 2000; Wannamethee *et al*. 2001; Will *et al*. 2001), consistent with the evidence linking smoking and insulin resistance (Facchini *et al*. 1992; Attvall *et al*. 1993). In the British Regional Heart Study Cohort it was found that cigarette smoking was associated with a 70 % increased risk of type 2 diabetes in multivariate analyses with adjustment for age, BMI and other potential confounders. Evidence of benefit from smoking cessation on risk of diabetes was detectable after 5 years, but risk did not revert to that of never smokers until 20 years post cessation (Wannamethee *et al*. 2001).

Alcohol and diabetes

There are conflicting reports on the association between alcohol intake and type 2 diabetes. Longitudinal epidemiological studies relating alcohol consumption to the risk of type 2 diabetes are equivocal. A positive association between alcohol intake and the risk of type 2 diabetes was reported from the Rancho Bernardo Cohort (Holbrook *et al*. 1990), while inverse associations have been reported from the US Nurses Health Study (Stampfer *et al*. 1988) and from the US Male Health Professionals Cohort (Rimm *et al*. 1995). There is now considerable evidence that light to moderate alcohol consumption is associated with reduced risk of diabetes, with some studies suggesting a 'U'-shaped relationship between alcohol and risk of diabetes, similar to that between alcohol and CHD (Perry *et al*. 1995; Ajani *et al*. 2000; Wei *et al*. 2000; Wannamethee *et al*. 2002). In the British Regional Heart Study Cohort the relationship between alcohol consumption at baseline and risk of type 2 diabetes was examined during 16·8 years of follow-up. A non-linear relationship was observed between alcohol intake and age-adjusted risk of diabetes, with risk lowest in light and moderate drinkers and highest in heavy drinkers (Wannamethee *et al*. 2002). Further adjustment for BMI and other potential confounders attenuated the increased risk in heavy drinkers, but the reduced risk associated with moderate alcohol consumption was essentially unchanged, adjusted relative risk compared with occasional drinkers 0·66 (95 % CI 0·44, 0·99). As with most studies suggesting benefit from moderate alcohol consumption on health, there remains the possibility of unmeasured and residual confounding due to dietary exposures and other aspects of lifestyle associated with moderate drinking. While this issue is difficult to resolve (as discussed earlier), it is clear that the effect of alcohol on diabetes risk is relatively modest as compared with the effects of obesity, physical activity and possibly other dietary factors.

Diet and diabetes

Diet and nutrition are widely believed to play a critical role in the development of type 2 diabetes, and there is a substantial literature on the role of specific nutrients in the development of glucose intolerance, including type 2 diabetes. A detailed review of this literature is beyond the scope of the present paper. There has been considerable controversy about the relationship between the amount and type of dietary fat and carbohydrate and risk of diabetes. Currently-available evidence suggests that neither total fat nor total carbohydrate as proportions of total energy intake play a major part in the development of type 2 diabetes (Hu *et al*. 2001*b*). By contrast, it appears that different types of fat and carbohydrates may be more important (Hu *et al*. 2001*b*). In particular, a higher intake of polyunsaturated fatty acids, vegetable fat (Meyer *et al*. 2001; Salmeron *et al*. 2001) and possibly long-chain *n*-3 fatty acids (Feskens *et al*. 1995; Salmeron *et al*. 2001) may be beneficial. The data on saturated fatty acid intake are less consistent, with positive findings from the 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study (Feskens *et al*. 1995) and negative findings from the US Nurses Health Study cohort (Salmeron *et al*. 2001). There are also inconsistent data for *trans*-fatty acids. In the US Nurses Health Study there was an approximately 40 % increase in risk of diabetes associated with a 2 % increment in *trans*-fatty acid intakes in multivariate analyses (Salmeron *et al*. 2001), whereas no association with *trans*-fatty acid intake was observed in multivariate analyses in the Iowa Women's Health Study (Meyer *et al*. 2001). There is also accumulating evidence from both the US Health Professionals Follow-up Study and the US Nurses Health Study that a low-glycaemic-index diet with a greater amount of fibre and minimally-processed wholegrain products is associated with a reduced risk of glucose intolerance (Salmeron *et al*. 1997*a*,*b*).

Measurements of total intake of specific nutrients, as opposed to foods, provide powerful tests of specific nutritional hypotheses, particularly in situations where a number of foods each contribute only modestly to intake of a specific nutrient (Willet, 1990). However, the current data should be interpreted cautiously. We are heavily reliant on a small number of large US cohorts, in particular the Nurses Health Study and the Health Professionals Follow-up

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Study. Although the findings on specific nutrients have considerable biological plausibility from detailed metabolic studies (Hu *et al*. 2001*b*), the magnitude of the 'independent' effects observed in complex multivariate analyses with highly inter-correlated nutrient variables depends heavily on the underlying precision and reliability of measurement of different dietary exposures. Moreover, this approach does not allow the complexities of dietary intake of individuals or groups of individuals to be considered in terms of the overall dietary pattern. For these reasons there is increasing interest in addressing food and dietary pattern-based hypotheses in studies of the aetiology of type 2 diabetes and related chronic conditions. Both in the US Nurses Health Study (Liu *et al*. 2000) and the Iowa Women's Health Study (Meyer *et al*. 2000) increased intake of whole grain was associated with marked reductions in the incidence of type 2 diabetes. In the Iowa Women's Health Study the relative risk for diabetes when comparing women in the upper quintile *v*. women in the lower quintile was 0·79 (95 % CI 0·65, 0·96; $P<0·001$ for trend), independent of intakes of fibre and other constituents of whole grains. In the US Nurses Health Study the relative risk when comparing extreme quintiles of wholegrain intake was 0·73 (95 % CI 0·63, 0·85; $P<0·0001$ for trend). There is also limited evidence linking higher intakes of fish (Feskens *et al*. 1991, 1995) and vegetables (Colditz *et al*. 1992; Gittelsohn *et al*. 1998; Williams *et al*. 1999) with reduced risk of glucose intolerance, and meat intake with increased risk of this condition (van Dam *et al*. 2002*b*). Given that dietary recommendations for health promotion and public policy are largely food-based rather than nutrient-based, there is a clear need to address food-based hypotheses in studies of diet and disease (Williams *et al*. 1999). However, this approach is also problematical, given the large number of foods to be considered and the complex and often reciprocal interrelationships between foods that are largely due to individual behavioural patterns; for example, margarine users tend not to eat butter and skimmed-milk users tend not to use whole milk. This aspect raises the issue of the role of specific dietary patterns in the development of chronic disease, including glucose intolerance. It is essential to characterise eating behaviours that are associated with both beneficial and detrimental nutrient intakes and with specific health outcomes (Millen *et al*. 2001). In recent years there has been increasing interest in the identification of dietary patterns and interrelationships between foods consumed by free-living adults in the population. It is arguable that patterns of food consumption may be as important as specific foods or nutrients in the development of disease, given the complex and poorly-defined interrelationships and interactions between foods and nutrients in our diet. Statistical methods that facilitate work in this area are now available. Three main methods have been used to identify dietary patterns: principal component analysis (Schwerin *et al*. 1982); factor analysis (van Dam *et al*. 2002*a*); cluster analysis (Akin *et al*. 1986).

Dietary patterns and risk of type 2 diabetes

In a UK cross-sectional study, involving a random general population sample of 802 men and women aged 40–65 years, Williams *et al*. (2000) observed that a prudent dietary pattern high in fruit and vegetables, fish, pasta and rice, and low in processed meats and french fries was associated with lower fasting plasma glucose and a lower prevalence of previously-diagnosed diabetes. The risk for diabetes in participants >50 years of age following a prudent dietary pattern was 0·44 (95 % CI 0·22, 0·88) in analyses adjusted for age, gender, smoking and obesity. In a further cross-sectional study, involving a sample of native Canadians and using a thirty-four item food-frequency questionnaire, it was found that participants in the 'junk food' and 'bread and butter' dietary groups had a higher prevalence of glucose intolerance and type 2 diabetes (odds ratio 2·40 and 2·22, 95 % CI 1·13, 5·10 and 1·22, 4·41 respectively; Gittelsohn *et al*. 1998).

van Dam *et al*. (2002*a*) have examined the association between major dietary patterns and risk of type 2 diabetes in a prospective cohort study involving >42 000 US male health professionals aged 40–75 years (Health Professionals Follow-up Study). Using factor analyses based on data from food-frequency questionnaires they identified and validated two major dietary patterns, a 'prudent' pattern characterised by higher consumption of vegetables, fruit, fish, poultry and wholegrains, and a 'Western' pattern characterised by higher consumption of red meat, processed meat, French fries, high-fat dairy products, refined grains, sweets and desserts (van Dam *et al*. 2002*a*). During 12 years of follow-up 1321 cases of type 2 diabetes were documented in the cohort. The Western dietary pattern was associated with an increased risk of type 2 diabetes (relative risk 1·6, 95 % CI 1·3, 1·9). It was also noted that a high score for the Western dietary pattern combined with low physical activity was associated with a marked increase in risk, as was a high Western dietary score combined with obesity. Men with a Western dietary pattern and a BMI $\geq 30\,kg/m^2$ had a >11-fold increased risk of developing type 2 diabetes during follow-up (van Dam *et al*. 2002*a*).

These findings highlight the value of looking at dietary patterns in judging the role of diet in the development of type 2 diabetes and the need to consider interactions between dietary patterns and other behavioural and lifestyle factors. Essentially, it is becoming clear that work on the causes of chronic non-communicable diseases such as type 2 diabetes needs to address the clustering and interdependence of major dietary and lifestyle exposures.

Diet and lifestyle clustering and risk of type 2 diabetes

Using the US Nurses Health Study database, Hu *et al*. (2001*a*) have examined simultaneously a set of dietary and lifestyle factors in relation to the risk of type 2 diabetes and estimated the proportion of cases that could theoretically be avoided through the simultaneous adoption of a small number of core low-risk dietary, behavioural and lifestyle factors. The Harvard Group has presented data from 84 941 female nurses followed for 16 years during which 3300 new cases of type 2 diabetes were documented. In these analyses they confirmed the previously-documented significant independent effects of obesity, physical activity, smoking status and alcohol consumption on risk of type 2 diabetes (Table 1). They observed the expected smooth linear

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Table 1. Modifiable risk factors and relative risk of type 2 diabetes in the Nurses Health Study (from Hu *et al*. 2001*a*)

Factor	No. of cases	Percentage of person years	Relative risk	95 % CI
Quintile for dietary scores*				
1	670	15	1·0	
2	1032	27	0·86	0·78, 0·95
3	561	17	0·77	0·68, 0·86
4	746	26	0·67	0·60, 0·74
5	291	15	0·49	0·42, 0·56
Weekly exercise (h)				
< 0.5	263	5	1·0	
0.5–1.9	1055	29	0·89	0·77, 1·02
2.0–3.9	734	22	0·87	0·75, 1·00
4.0–6.9	668	26	0·83	0·71, 0·96
≥ 7.0	97	7	0·71	0·56, 0·90
BMI (kg/m^2)				
< 23.0	121	32	1·0	
23.0–24.9	202	18	2·67	2·13, 3·34
25.0–29.9	884	25	7·59	6·27, 9·19
30.0–34.9	885	9	20·1	16·6, 24·4
≥ 35.0	759	4	38·8	31·9, 47·2
Smoking status				
Never smoked	1446	43	1·0	
Former smoker	1217	35	1·15	1·07, 1·25
Current smoker				
1–14 cigarettes/d	181	7	1·20	1·03, 1·41
≥ 15 cigarettes/d	439	15	1·34	1·20, 1·50
Daily alcohol consumption (g)				
0	1715	34	1·0	
0.1–5.0	1034	33	0·78	0·72, 0·84
5.1–10.0	189	11	0·56	0·48, 0·65
< 10.0	358	21	0·59	0·52, 0·66

*The intakes of *trans*-fatty acids and cereal fibre, the glycaemic load and polyunsaturated fatty acid intake: saturated fatty acid intake were nscategorised into quintiles. Each woman was assigned a score for each nutrient on the basis of her quintile of intake (a higher score representing lower risk),the four nutrient scores were summed and the total score categorised into quintiles.

increase in risk of diabetes with increasing BMI and a linear inverse relationship with duration (h) of weekly exercise. Relative to those exercising for < 0·5 h/week, there was a 30 % reduction in risk for women exercising ≥ 7·0 h/week. Similarly, there was an approximately 30 % increased risk of diabetes among women smoking ≥ 15 cigarettes per d relative to never smokers, in analyses adjusted for age and family history of diabetes. Risk of diabetes fell with increasing alcohol consumption up to a > 10 g/d category (relative risk 0·59, 95 % CI 0·52, 0·66). No evidence of increased risk of diabetes at higher alcohol consumption was detected, but there were few heavy drinkers in the cohort. With regard to diet, the relative risk of diabetes was estimated for each quintile of a 'prudent' dietary score relative to the first quintile. The intakes of *trans*-fatty acids and cereal fibre, the glycaemic load and polyunsaturated fatty acid intake:saturated fatty acid intake were categorised in quintiles. Each woman was assigned a score for each nutrient on the basis of her quintile of intake (a higher score representing lower risk), the four nutrient scores were summed and the total score was categorised into quintiles. Risk of diabetes fell in a smooth linear fashion with increasing 'prudent' dietary score, with a relative risk in the fifth quintile relative to the first quintile of 0·49 (95 % CI 0·42, 0·56), adjusted for age and family history of diabetes (Table 1). To address the effects of clustering of diet and lifestyle on risk of diabetes in this cohort a low-risk group was defined according to a combination of the following five variables: a BMI < 25 kg/m^2; engagement in moderate to vigorous physical activity for at least 0·5 h/d; no current smoking; the consumption of an average of at least half a drink (5 g) of an alcoholic beverage per d; a composite dietary score in the upper 40 % of the distribution, i.e. a diet high in cereal fibre and polyunsaturated fatty acids and low in *trans*-fatty acids and glycaemic load. Only 3·4 % of the cohort of approximately 85 000 nurses had all five low-risk factors. Relative to the rest of the cohort women in this low-risk group (with all five factors) had a relative risk of diabetes of 0·09 (95 % CI 0·05, 0·17). A total of 91 % of the cases of diabetes in the cohort could be attributed to habits and forms of behaviour that did not conform to this low-risk pattern (Table 2). Of the cases of type 2 diabetes, 87 % could be attributed to non-conformity with three of the core low-risk factors, i.e. prudent diet, BMI < 25 kg/m^2 and regular moderate exercise. Remarkably these findings were unchanged in analyses confined to women with a family history of diabetes. Thus, despite the emphasis on genetic factors in the aetiology of type 2 diabetes, the clinical manifestation of the phenotype is almost entirely dependent on a small number of core interrelated dietary and lifestyle

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Table 2. Relative and population attributable risks of type 2 diabetes for groups defined by combinations of modifiable risk factors in the Nurses Health Study 1980–94 (from Hu *et al*. 2001*a*)

Group	Percentage of women	No. of cases	Relative risk	95 % CI	Population attributable risk	95 % CI
Three low-risk factors	9·5	34	0·12	0·08, 0·16	87	83, 91
Four low-risk factors	8	27	0·11	0·07, 0·16	88	83, 92
Five low-risk factors	3·4	10	0·09	0·05, 0·17	91	83, 95

factors. In further work based on this cohort women in the low-risk category (with five protective factors) had a relative risk of coronary events of 0·17 (95 % CI 0·07, 0·41) as compared with all other women. Of coronary events in the cohort, > 80 % could be attributed to lack of adherence to this low-risk pattern. This finding again emphasises the common causal factors linking type 2 diabetes and CHD, and the extent to which the causes of these two interrelated conditions are now well defined.

In a cross-sectional analysis based on the Cork & Kerry Diabetes and Heart Disease Study (Creagh *et al*. 2002), the role of six low-risk protective factors was examined, two obesity related (BMI < 25 kg/m^2 and normal waist:hip ratio < 0·85 for women and < 0·90 for men), combined with 'never smoking' status, participation in medium to high levels of physical activity, moderate alcohol consumption and membership of a 'prudent-eating cluster'. The effect of the number of low-risk protective factors (from none to all six) on insulin sensitivity and glucose intolerance was investigated. The findings from preliminary analyses are consistent with a marked increase in insulin sensitivity (estimated on the basis of fasting glucose and insulin, using the glucose homeostasis model; Matthews *et al*. 1985) and an equally marked fall in the prevalence of glucose intolerance with increasing numbers of low-risk protective factors.

Summary

There is now substantial evidence that the occurrence of glucose intolerance, including type 2 diabetes, can be explained on the basis of clustering of a small number of interrelated dietary and lifestyle factors. These findings are biologically plausible and are supported by emerging data from intervention studies (Eriksson & Lindgarde, 1991; Pan *et al*. 1997; Tuomilehto *et al*. 2001; Knowler *et al*. 2002). They form the basis for a clear, simple and coherent message for health promotion and public policy. They emphasise the need to avoid spurious controversy over minutiae and trivia in projecting our current understanding of the causes of type 2 diabetes and other major chronic non-communicable diseases. Traditionally, in population health monitoring and health promotion the control of major adverse factors linked with the development of cardiovascular disease and diabetes has been emphasised. We now have the opportunity to highlight the fact that adoption of one or two additional protective lifestyle factors, such as smoking cessation or increased levels of physical activity, can have profound effects on risk of glucose intolerance, including type 2 diabetes and risk of cardiovascular disease. We need to achieve a shift in the population distribution of low-risk factors to the upper tail, i.e. increase the proportion of the population with four and five protective factors and reduce the proportion with none or one protective factors. To this end we need ongoing population health monitoring data on the distribution of protective dietary and lifestyle factors in our population as an aid to target setting in the development of public health policy. In essence, the challenge we face is to effect the societal level changes required to reduce the quantity and change the composition of our diet in the global economy, increase levels of physical activity and reduce the prevalence of smoking. To make progress on these issues we will need to place health at the centre of public policy and tackle relevant vested interests, notably in the food, entertainment, tobacco and automobile industries.

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