Measuring the full economic costs of diet, physical activity and obesity-related chronic diseases

B. M. Popkin[1], S. Kim[2], E. R. Rusev[3], S. Du[4] and C. Zizza[5]

[1]Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]Department of Family and Community Medicine, University of California at San Francisco, CA, [3]Economics Department, University of North Carolina, Chapel Hill, NC, [4]Carolina Population Center, University of North Carolina, Chapel Hill, NC, [5]Department of Nutrition and Food Science, Auburn University, Auburn, AL, USA

Received 28 April 2005; revised 1 September 2005; accepted 5 September 2005

Address for correspondence: BM Popkin, Professor of Nutrition, Carolina Population Center, University of North Carolina, 123 W. Franklin St., Chapel Hill, NC 27516-3997, USA.
E-mail: popkin@unc.edu

Summary

Most studies that have focused on the costs of obesity have ignored the direct effects of obesity-related patterns of diet and physical activity. This study reviews the full effects of each component – poor dietary and physical activity patterns and obesity – on morbidity, mortality and productivity. The direct healthcare costs are based on a review of the effects of these factors on key diseases and the related medical care costs of each disease. The indirect costs on reduced disability, mortality and sickness during the period of active labour force participation prior to retirement are also examined. A case study is prepared for China to provide some guidance in the utilization of this review for economic analysis of obesity. The case study shows that the indirect costs are often far more important than the direct medical care costs. The Chinese case study found that the indirect effects of obesity and obesity-related dietary and physical activity patterns range between 3.58% and 8.73% of gross national product (GNP) in 2000 and 2025 respectively.

Keywords: Economic costs, obesity, obesity-related diets and activity patterns.

obesity reviews (2006) **7**, 271–293

Introduction

Rapidly changing diets and reduced physical activity levels have led to a marked increase in the prevalence of diet-related chronic diseases in both developed and developing countries. Considerable progress in the scientific study of this phenomenon has led to (i) a growing understanding of the responsible causal pathways, risk factors and mechanisms; and (ii) the development of effective risk reduction strategies and interventions. In particular, there is now strong evidence relating dietary factors and physical activity levels to the risk of obesity, hypertension, certain cancers, diabetes, stroke and other coronary heart diseases (CHD). The most recent cause of death estimates note that non-communicable diseases (NCDs) currently account for an estimated 59% of the 57 million deaths annually and 46% of the global disease burden (1,2).

The key risk factors related to this shift in the distribution of morbidity and mortality are described in the recently developed *Global Strategy on Diet, Physical Activity and Health*, discussed at the World Health Assembly in May 2004 (3). The promotion and implementation of this strategy at the public health level requires that policy-makers understand the economic benefits of undertaking such changes on a global and country level. To assist these policy-makers, we use existing epidemiological evidence to translate what is known about risk factors (diet, physical activity and obesity) into functional consequences in terms of disease, disability and death. These consequences including their economic impacts, such as healthcare costs and lost productivity, can now be quantified with some precision. This effort is very much in the spirit of work surrounding the global burden of disease project of World Health Organization (WHO) (4,5). That effort looked at some very limited effects of diet (only fruit and vegetable

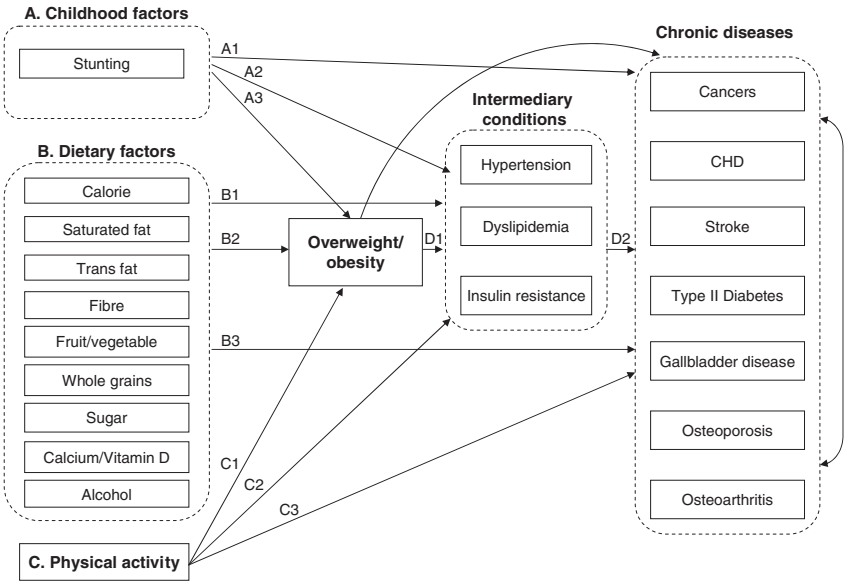

Figure 1 Key pathways for diet, physical activity and obesity on nutrition-related non-communicable diseases. CHD, coronary heart disease.

intake, body mass index [BMI] and physical inactivity) and did not examine the separate and total effects of each pathway (e.g. physical inactivity will directly affect adult onset diabetes but indirectly through its effects on obesity will have an additional effect).

In the past there have been direct estimates of the economic costs of obesity, either on society (6–11) or on US businesses (12). Colditz (8) has also examined some aspects of inactivity. Finkelstein and his collaborators have used more sophisticated, direct methods for some of their work but the focus has similarly been on obesity (13–15). A few have expanded their studies to address a few elements of inactivity (16,17). These studies focused on the United States or Canada and a related study focused on selected lower income countries (18,19).

The study reported here expands considerably on the limited economic analyses of diet and physical activity impacts on obesity and other NCDs (directly and indirectly via obesity) reported in the studies cited above. This is accomplished by drawing on epidemiological evidence concerning diet, physical activity and obesity-related chronic diseases to establish (i) the direct medical care costs of these diseases and (ii) the indirect costs that are seen via premature mortality, disability and lost economic productivity via sickness. Figure 1 displays the issues addressed. Essentially, the bulk of the research in this field has focused on pathways D1 and D2; however, there are other equally important ways that childhood factors, nutrition and physical activity may affect the costs of NCDs. These include the effects of diet directly on the NCDs (pathways B1 and B3), the effects of physical activity directly on these conditions (C2 and C3), and the effects of energy imbalance on obesity (via B2 and C1). The potential for some effects of fetal insults during the fetal and infant development period on either obesity (A3) or directly on these NCDs (A1 or A2) are included. Figure 1 clearly illustrates the additional ways that diet, physical activity and fetal insults could affect health, well-being and survival.

After a brief review of the methods and data used in this overall study, the literature concerning the impact of poor obesity and obesity-related poor dietary and activity patterns is summarized and tabulated in more detail. This includes the direct effects of these factors on healthcare costs and the indirect economic affects via the impact of these factors on mortality, disability free life and absenteeism. This is followed by a case study utilizing data from China on the measurement of (i) all the key diet, physical activity, obesity and other NCDs; and (ii) medical care costs, wage rates and gross national product (GNP). China is selected due to the availability of strong, existing data for all elements required, including more in-depth dietary and physical activity measures than are available for the United States or other higher income countries. It is important to note that there have been scholars and organizations that have promoted the use of lower BMI standards for China (1). While there is a growing literature that indicates larger adverse health effects of adiposity among Chinese with a BMI of 23 and even of 27, this study has taken a more conservative approach and used extant global BMI standards.

Methods

The various data sets and the methods used for creating the case study are presented. Essentially, the document reviews the literature that attempts to create estimates of the effects of overweight and obesity on the (i) costs of the healthcare system (i.e. costs of hospitalization, outpatient

visits, drugs, etc.) and (ii) costs of premature mortality, disability and sickness – in terms of lost work. For most countries, there are no major longitudinal data sets that allow for direct estimates of obesity effects on various components of medical care costs and productivity. Hence, we rely on a more indirect method that uses the best estimates of obesity effects on each disease and links those to disease-specific costs.

The relative risk (RR) for each condition associated with diet, physical activity or overweight/obesity was selected based on epidemiological review. To estimate this accurately would require meta-analyses for each of the postulated links, holding constant the other links, and carefully separating out the RRs for morbidity and mortality for men and women. However, this literature is still relatively underdeveloped. The best research available worldwide was selected as the basis for each condition; most of this research was performed in the United States. A summary of the effects of diet, physical activity and obesity-related conditions that provides the basis of our selection on the risk of NCD is presented. The RRs are presented by overweight/obesity, morbidity/mortality and gender wherever possible. Unless stated otherwise, the RRs for (i) morbidity of both genders are contained in the section on healthcare costs and for (ii) mortality in the section on lost working time prior to retirement. A comparison of our selected RRs related to obesity with those selected by Colditz *et al.* (8) indicates that our choices were quite conservative (lower).

Use of population attributable risks (PAR)

Direct costs

Direct costs – the costs to the healthcare system – such as costs of hospitalization, outpatient visits, drugs, etc. are calculated for each disease condition using the likelihood of each condition affecting the overall population. The likelihood (i.e. population attributable risks [PAR]) of each condition affecting the overall population can be calculated by combining RRs with prevalence data. This represents the proportion of the deaths or illnesses (in a specified time) in the whole population that may be preventable if a cause of mortality or sickness, such as obesity, were totally eliminated. The common epidemiological formula is:

$$\text{PAR}\ (\%) = 100z/(z + 1), \quad (1)$$

where z = (RR – 1) (prevalence of exposure to the factor).

The PARs should be interpreted as the per cent that the factor (z) contributes to the outcomes. For example, if 70% of CHD is attributable to obesity (i.e. z = 70%), we can reasonably attribute 70% of costs associated with CHD (direct, as well as indirect) to obesity. If the sum of the contributions of two or more factors, to the same disease, exceeds 100%, the effects are rescaled to equal 100%, keeping their relative magnitudes constant. This is because no analysis of the causes of death can explore jointly all factors related to that disease, as many of the dietary factors might be collinear and the funding and implementation of very large multiarm clinical trials that would allow us to jointly consider all these exposures is not feasible.

Indirect costs

We are also interested in the costs that society incurs indirectly from the same factors. Our pathways again include obesity. In the literature, it is established that obesity:

1. increases mortality before retirement;
2. decreases years of disability free life (YDFL) before retirement;
3. decreases time at work (i.e. increases absenteeism) before disability and death.

There are several ways to express these indirect costs. These include: (i) percentage of gross domestic product (GDP – examined yearly) and (ii) expected years lost for each group (by sex, race, BMI). Therefore, loss can be predicted for all individuals over their life time. Our requirements for each approach are noted below.

Mortality. Morality reduces working time as a percentage of GDP every year. If *A* denotes the expected working lifetime of a person with normal-weight and *A-a* is the expected working lifetime of an obese/overweight person, then an obese/overweight person would produce, on average in her lifetime: (1 – a/A) (yearly per capita GDP) of what a normal-weight person would produce. Therefore, the loss in income per person per year would be equal to a/A (per capita GDP) (prevalence of obesity in the population). Studies have examined the effect of obesity on mortality; however, this might be a poor proxy for our purposes. More specifically, we would not have a loss in GDP if a person died after retirement. The analysis is refined and an approximation included for the working years lost in one's life (below). As life expectancy and retirement age are quite different for men and women, it is logical to perform the analysis separately by sex. This is shown in Fig. 2. There is a 2% gap between genders for most of the loss distribution with respect to retirement age.

Economic costs are associated in this analysis with obesity-related deaths only when this death occurs prior to retirement age (e.g. if a person had a life expectancy of 88 years but died at the age of 80, this would be counted as zero costs to our analysis). Hence, a decrease in life expectancy would bias (upwards) our estimates for GDP lost (e.g. considering worker-years: one worker-year being a full year of work performed by one worker; one worker-year would produce a *per capita yearly GDP*. On the other hand, on average, the most obese people live much longer

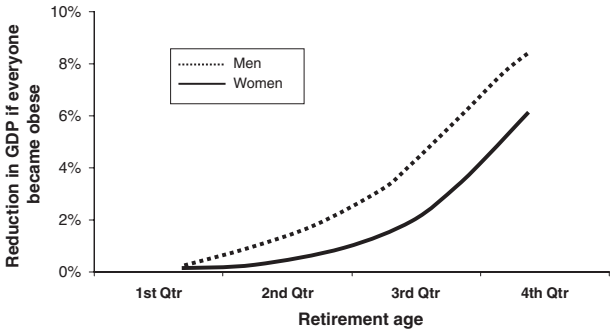

Figure 2 Loss of gross domestic product (GDP) as a result from obesity as a function of retirement age.

than retirement age; yet, an obese person is more likely to die than a normal-weight person at *any* age. This takes our analysis one step further; we need to analyse the distribution of the population and the probability of being alive for one more year, conditional on not having died earlier. These conditional probabilities are observed for the working population (18–55 years for women and 18–60 years for men). Our analysis divides the population into three groups: (i) normal (BMI = 21–25), (ii) overweight (BMI = 26–30), and (iii) obese (BMI > 30); each of these groups begins with a population (with current cohort distribution) and the fraction of individuals from each cohort that survive (work) every year is simulated.

Finally, 'work-years' is summed for all cohorts and all periods separately, by BMI. Therefore: the fraction of GDP that would be lost if all individuals were normal-weight and became

$$\text{obese} = (\text{SUM}_{\text{normal weight}} - \text{SUM}_{\text{obese}})/\text{SUM}_{\text{normal weight}}. \quad (2)$$

The computations are performed assuming different retirement ages. Results are shown in Fig. 2 and show that the effects of obesity are far from constant, being 2% at age 50 and 6% at age 70. Results are stronger for men than for women because men generally work longer and live shorter lives. Also, the fact that the labour force consists of more than 50% men must be taken into account. The overall reduction is a weighted average of the reductions in the subgroups:

$$\Sigma_{jjk}\ s_{jk}p_{jk}r_{jk} \quad (3)$$

where: r_{jk} = reduction; $j = 1_{[female]}$; $j = 2_{[male]}$; s_{jk} = shares of females and males in the labour force; p_{jk} = shares of weight groups within gender groups; and $k = 1_{[overweight]}$; and $k = 2_{[obese]}$.

Years of disability life lost (YDLL). Years of disability life lost (YDLL) applies the reasoning from years lost due to mortality. Keeping the same notation, *a/A* would be the years lost. Again, simply taking the difference between the YDLLs for normal-weight and overweight individuals would result in an overestimation of the relationship studied, because some people become disabled after retirement. (There is one more potential bias: some fraction of the population probably become disabled and later die before retirement, in which case they are 'counted' twice. To avoid this bias, disability and death data within the same data set would be needed.)

Unfortunately, there is not enough current data to compute this correctly and YDLL will be approximated before retirement with YDLL. One improvement that could be made is to assume that YDLL overestimates YDLL before retirement by the same factor that early death approximates early death before retirement. If the retirement age is 60, then this number would be approximately two for obese men (see Fig. 2). Another option is to assume that the age distribution for disability is similar to mortality (because obesity), but occurs *5* years earlier; this is the assumption made.

Days lost to sickness. Days lost to sickness also incorporates the reasoning related to mortality and disability, and applies this to the reduced number of workdays for overweight/obese people. If *B* is the number of yearly work days for a normal-weight person and *B-b* represents the figure for an overweight individual, then we can reasonably claim that the loss would be *b/B* for any time period.

1. *Data for China case study:* Case study data were obtained from large-scale surveys in China; the prevalence data are mainly from the China Health and Nutrition Survey (CHNS). The dietary and body composition data are derived from the 2000 CHNS. These data are based on 3 days of very detailed dietary intake measurements and high-quality clinic-based assessments of all body composition parameters for most adults except the very sick for whom home visits were made (20,21).

2. There are interesting issues related to estimating the patterns of dietary, physical activity and obesity exposures in 2025. The prevalence of high refined grains intake (>500 g d^{-1}) reduced rapidly from 38.9% in 1989 to 37% in 1991, 33.3% in 1993, 27.3% in 1997 and 22.8% in 2000. It was assumed this trend would increase and it would essentially be 0% in 2025. Grain intake has been considerably reduced in the Chinese diet because of the increased intake of edible oil and animal foods, even in rural areas. Of course, the decreased physical exertion by the occupational labour force is part of the reason for this.

The physical activity data on moderate physical activity indicated a decrease from 33.9% in 1989 to 17.8% in 1991 and then slowly increased to 18.6% in 1993, 19.4% in 1997 and 19% in 2000. The regression model built from this pattern retains moderate physical activity for approx-

imately 20% of the adult work force. If the initial reference year were changed (from 1989 to 1991), higher levels of physical activity would be noted; therefore, an average of different initial years and a predicted 26% moderate physical activity of the adult work force was used. Given the large increase that will occur in urban residence and the shift to the service sector jobs, we think moderate physical activity (e.g. driver, electrician, etc.) would not increase significantly more in 2025.

The predictions for overweight and obesity for China in 2025 indicate that by 2025, China would match the current overweight and obesity levels of Mexico, Egypt, South Africa and the United States. The CHNS results from monitoring the weight and height data of 16 000 Chinese every 2–3 years reveal that adult overweight has risen from 8.2% in 1989 to 20.5% in 2000 and obesity has risen from 0.6% to 3.4%. This results in 23.9% of adult Chinese being overweight and obese in 2000; an increase of 271% in 11 years. Moreover, the rate of increase has been accelerating and the increase from 1997 to 2000 was the largest 3-year increase in absolute percentage points. These results, however, reflect the pattern of change over the past decade. All previous predictions have been lower than the final outcomes, as the rates of change for diet and physical activity in China appear to be accelerating (20).

Health service cost data were obtained from the 1998 National Survey of Health Services for China. The data for China correspond to the total costs incurred by the institutions, whether they were reimbursed by the state or by private fees from patients or insurance plans. Although it is not possible to create any meaningful projection for these medical care costs for 2005, they likely will increase. Cancer and diabetes in China require hospital stays at least twice as long as the average for other diseases, and the costs per hospital stay are two to four times higher than for other diseases (18). In China, the cost of the average hospital stay for cancer is more than the annual per capita GDP.

A detailed breakdown of medical costs by type of cancer was not available in a manner that allowed us to allocate costs to each type. It was assumed that the deaths attributable to each type of cancer represent a reasonable allocation to each disease from the total cancer medical costs.

Furthermore, we do not have data from China on medical care costs for gallbladder disease, osteoporosis and osteoarthritis; therefore, the data under-represent total direct costs.

The mortality results, including the effect of being obese/overweight on life expectancy, are utilized for each age group. By having age-specific data with expected years left, we incorporate retirement age into the analysis (the reasoning is that if someone's life was shorter because of obesity, but he still died after retiring, there is no loss of GDP). Age-gender life expectancy values were obtained from the Department of Biostatistics, Section on Statistical Genetics (SSG), in the School of Public Health at the University of Alabama at Birmingham website (22).

The simulation of future costs, quantification and separation of the effects on medical costs – not only now, but into the future – were possible by predicting trends in growth of population, dietary habits and physical activity. The current official exchange rate of US $8.28 equal to one Chinese yuan Renminbi was used for all cost calculations.

Review of the effects of diet, physical activity and obesity-related conditions on the risk of non-communicable disease

Relative risks associated with the pathways shown in Fig. 1 are summarized in Tables 1–3. Most of the RRs of intermediary conditions and chronic diseases for diet, physical activity and obesity presented were adjusted so the total effect on morbidity or mortality was not greater than 1. Therefore, attributable risks should be largely independent, to the extent that the measures of diet, BMI and physical activity are accurate. This means that the attributable risk

Table 1 Pathways to overweight/obesity

Exposure	Exposure categories compared	Outcome	Relative risk (exposed vs. non-exposed)	References
Childhood factors				
Stunting		Overweight/obesity	1.5	(21–23)
Dietary factors				
Calorie	High vs. low	Overweight/obesity	1.22	(24)
Fibre	High vs. low	Obesity (BMI ≥ 30)	F: 0.7	(25)
Whole grain	High vs. low	Obesity (BMI ≥ 30)	F: 0.8	(25)
Refined grain	High vs. low	Obesity (BMI ≥ 30)	F: 1.2	(25)
Sugar		Overweight/obesity	NA	(26,27)
Physical activity				
Physical activity	Active vs. sedentary	Overweight/obesity	0.5	(28)

NA: studies present results with continuous outcome measures; therefore the relative risk measure is not available.

estimates for diet, BMI and physical activity can be approximately summed to express an estimate of their joint impact on risk – such as cancer.

In this summary, we first reviewed three sets of factors that may increase the risk of obesity: (i) childhood factors (stunting, low birth weight); (ii) dietary factors (various nutrients and foods), and (iii) physical activity (Table 1). Second, diet, childhood factors and physical activity were examined to determine their direct effects on the NCDs (Table 2) and in addition these way these factors affect obesity, and in turn the obesity effects on these other NCDs (Table 2). Third, pathways from intermediary conditions, such as hypertension to CHD, and other intermediate conditions to NCD pathways are summarized in Table 3. Each pathway (Fig. 1) is examined below; studies and results are presented in the tables. We do not review some other important effects of obesity on asthma, sleep apnea and other diseases and behaviours that have important effects (23).

Table 2 Pathways from childhood and dietary factors (A), physical activity (B), overweight/obesity (C)to intermediary conditions and chronic diseases

Exposure	Exposure categories compared	Outcome	Relative risk (exposed vs. non-exposed)	References
A. Childhood and dietary factors				
Childhood factors				
Low birth weight		Hypertension	2.0	(29,30)
		Type 2 diabetes	1.8	(31)
Dietary factors				
Saturated fat	High vs. low	Dyslipidaemia	NA	(32)
	High vs. low	CHD	NA	(33)
	High vs. low	Type 2 diabetes	NA	(33)
	High vs. low	Cancer, colon	2.0	(34)
Trans fat	High vs. low	Dyslipidaemia	NA	(35)
	High vs. low	Glucose intolerance	NA	(36)
	High vs. low	CHD	1.5	(35,37,38)
	High vs. low	Type 2 diabetes	F: 1.3	(39,40)
Fruits/vegetables	High vs. low	Hypertension	NA	(41)
	High vs. low	Cancer, larynx	0.4	(42)
	High vs. low	Cancer, oral cavity, pharynx	0.5	(42)
	High vs. low	Cancer, oesophagus	0.5	(42)
	High vs. low	Cancer, lung	0.5	(42)
	High vs. low	Cancer, stomach	0.4	(42)
	High vs. low	Cancer, colorectal	0.5	(42)
	High vs. low	Cancer, bladder	0.5	(42)
	High vs. low	Cancer, pancreas	0.4	(42)
	High vs. low	Cancer, cervix	0.5	(42)
	High vs. low	Cancer, ovary	0.6	(42)
	High vs. low	Cancer, breast	0.8	(42)
	High vs. low	Cancer, prostate	0.8	(42)
	Increase in intake of 100 g d^{-1}	Cancers	0.85	(43)
	High vs. low	CHD	0.8	(44)
	High vs. low	Stroke incidence	0.7	(45–47)
	High vs. low	Stroke mortality	0.6	(46)
Whole grains	High vs. low	Insulin resistance	NA	(48)
	High vs. low	Cancers	NA	(49)
	High vs. low	CHD	0.7	(50–52)
	High vs. low	CHD mortality	0.7	(53,54)
	High vs. low	Stroke	F: 0.7	(55)
	High vs. low	Type 2 diabetes	0.7	(56–59)
Calcium/vitamin D	High vs. low	Osteoporosis	NA	(60)
Alcohol	Heavy vs. light drinking	Cancers	1.5	(61,62)
	Moderate drinking (5–14 g d^{-1})	CHD	0.8	(52,64,65)
	Moderate drinking (≤2 drinks d^{-1})	Ischaemic stroke	0.5	(64–66)
	Heavy drinking (≥5 drinks d^{-1})	Ischaemic stroke	M: 1.3/F: 5.4	(64–66)
B. Physical activity	Active vs. sedentary	Hypertension	0.7	(28,67,68)
		Dyslipidaemia	NA	(69)
		Insulin resistance	NA	(5,69)
	Active vs. sedentary	Colon cancer	0.5	(28,49,70–74)
	Active vs. sedentary	Breast cancer	0.7	(63,70,75,76)

Table 2 *Continued*

Exposure	Exposure categories compared	Outcome	Relative risk (exposed vs. non-exposed)	References
	Active vs. sedentary	Endometrial cancer	0.7	(70)
	Active vs. sedentary	CHD	0.6	(28,77–79)
	Active vs. sedentary	CHD mortality	0.6	(28,67)
	Active vs. sedentary	Stroke	0.6	(80,81)
	Active vs. sedentary	Stroke mortality	0.5	(28)
	Active vs. sedentary	Type 2 diabetes	0.6	(28,82,83)
	Active vs. sedentary	Gallbladder disease	0.8	(84)
	Active vs. sedentary	Osteoporosis (hip fracture)	F: 0.6	(85–87)
		Osteoarthritis	NA	(86)
C. Overweight/obesity				
Overweight/obesity	Male (M): ≥29.7 vs. <24.1 Female (F): ≥29.2 vs. <22.3	Hypertension	M: 2.3/F: 1.8	(88)
Overweight/obesity		Dyslipidaemia	NA	(89)
Overweight/obesity		Insulin resistance	NA	(90)
Overweight	BMI ~ 25	Colon cancer	1.2	(70,91)
	BMI 25–29.9 vs. 18.5–24.9	Colorectal cancer mortality	M: 1.2/F: 1.1	(92)
Obesity	BMI > 30	Colon cancer	M: 1.5/F: 1.3	(70,73,91)
	BMI > 30	Colon cancer mortality	M: 1.7/F: 1.3	(92,93)
Overweight	25 ≤ BMI < 30	Breast cancer, post-menopausal	F: 1.1	(91)
	BMI 25–29.9 vs. 18.5–24.9	Breast cancer mortality	F: 1.3	(92)
Obesity	BMI ≥ 30.7 vs. ≤22.9	Breast cancer, post-menopausal	F: 1.5	(91,94)
	30–34.9 vs. 18.5–24.9	Breast cancer mortality	F: 1.6	(92)
	35–39.9 vs. 18.5–24.9		F: 1.7	
	≥40 vs. 18.5–24.9		F: 2.1	
Overweight/obesity	BMI > 25	Esophagus cancer	2.0	(70)
Overweight	25 ≤ BMI < 30	Endometrium cancer	1.6	(91)
Obesity	BMI > 30	Endometrium cancer	2.5	(70,91)
	25 ≤ BMI < 30	Kidney cancer	1.4	(91)
Overweight	25 ≤ BMI < 30	Kidney cancer	1.4	(91)
	BMI 25–29.9 vs. 18.5–24.9	Kidney cancer mortality	M: 1.2/F: 1.3	(92)
Obesity	BMI > 30	Kidney cancer	2.0	(70,91)
	30–34.9 vs. 18.5–24.9	Kidney cancer mortality	M: 1.4/F: 1.7	(92)
	≥40 vs. 18.5–24.9		F: 4.8	
Overweight	BMI 25–<29 vs. <21	CHD	2.6	(95,96)
Obesity	BMI ≥ 30 vs. <23	CHD	2.7	(34,79,95)
Obesity	BMI ≥ 30	CHD mortality	1.3	(67,97)
Obesity		Stroke	Through hypertension	
Overweight/obesity	BMI per unit	Type 2 diabetes	M: 1.2/F: 1.13	(90)
Overweight	25–26.9 vs. <22	Type 2 diabetes	F: 5.5	(98)
Obesity	25–29.9 vs. <23	Type 2 diabetes	F: 7.59	(98)
	30–34.9 vs. <23		F: 20.1	
	≥35 vs. <23		F: 38.8	
Obesity	BMI ≥ 30	Gallbladder disease	2.0	(5)
Obesity	Each increase in BMI above 27	Osteoarthritis	F: 1.15	(99)

NA means relative risk results are not available.
CHD, coronary heart disease; BMI, body mass index.

Pathways to overweight/obesity (Table 1)

Childhood factors (pathway A3)

Stunting to overweight/obesity. Children who are stunted (low-height-for-age caused by chronic and acute episodes of undernutrition during infancy; also by low birth weight) are more likely to be overweight later in life (24–32).

Dietary factors to overweight/obesity (pathway B2)

Calories to overweight/obesity. A higher energy intake compared with energy expenditure is a cause of obesity (33). There were no RRs published for calories for any population. These were examined for Chinese adults in 1989 and 2004. The likelihood that adults consuming the

Table 3 Pathways among intermediary conditions and chronic disease

Exposure	Exposure categories compared	Outcome	Relative risk (exposed vs. non-exposed)	References
Hypertension	Hypertensive vs. normotensive	Type 2 diabetes	M: 1.8	(100)
	Hypertensive vs. normotensive	CHD mortality	M: 1.7/F: 2.2	(97,101,102)
	Hypertensive vs. normotensive	Stroke mortality	M: 2.9/F: 3.8	(101)
Dyslipidaemia	Hypercholesterolaemia (unit increase)	CHD	F: 2.3	(103)
	Hypercholesterolaemia vs. non-hypercholesterolemia	CHD mortality	1.7	(997,102,104)
Insulin resistance	High vs. low 2-h glucose; high vs. low 2-h insulin	Cancer, colorectal	2.2	(105)
Type 2 diabetes	History of DM vs. no	Colorectal cancer	W: 1.4	(83)
	Type 2 diabetes vs. no	CHD	M: 2.5/F: 5.1	(106)

CHD, coronary heart disease; DM, diabetes mellitus.

highest quartiles and quintiles of total energy intake were more at risk of overweight status than the lowest quartile was examined. The results for energy intake quintiles and quartiles were identical (i.e. a RR of 1.22 for 1989).

Fibre to overweight/obesity. Diets rich in fibre are generally low in saturated fat (34) and low in energy density. This has an effect on reducing total caloric intake, and therefore, reducing the risk of overweight and obesity.

Whole grains to overweight/obesity. Intake of whole grains promotes satiety and slows starch digestion or absorption. This, in turn, leads to relatively lower insulin and glucose responses that favour the oxidation and lipolysis of fat, rather than its storage (34).

Refined grain to overweight/obesity. Refined grains have higher starch content and lower fibre content (i.e. greater energy density) than whole grains. Concentrations of vitamins, minerals, essential fatty acids and phytochemicals that are important in carbohydrate metabolism are also lower in refined grains (34).

Sugar to overweight/obesity. The major effect of sugar that has been shown relates excessive soft drink intake to weight gain, and to a lesser extent to other diseases – such as diabetes (35–38). A more highly controlled clinical study conducted in Denmark showed similar results – mainly that sweetened beverage intake was associated with considerable weight gain (35).

Fruits and vegetables to overweight/obesity. Emerging evidence suggests that consumption of fruits and vegetables imparts positive effects on satiety, overall caloric intake and weight regulation (39). Fruits and vegetables are low in energy density (kcal g^{-1}), in other words, they have a low number of calories per gram, because they are high in water and fibre. Therefore, consuming a diet high in fruits and vegetables results in a larger volume, or amount, of food that can be consumed at a given calorie level.

Physical activity to overweight/obesity (pathway C1) Physical activity comprises the other side of the energy balance equation. Energy expenditure less than energy consumption contributes to the development of obesity. The prevalence of obesity and the risk of becoming obese for active persons is one-half of that of sedentary persons (40). Physical activity not only increases non-resting energy expenditure but also develops and maintains lean body mass that determines the size of resting energy expenditure; resting energy expenditure uses approximately 60% of the total daily energy expenditure.

Pathways to intermediary conditions and chronic diseases (Table 2)

Childhood factors to intermediary conditions and chronic diseases (pathways A1, A2)

Low birth weight to hypertension (41,42). Low birth weight infants have been found to have a much greater risk of being hypertensive as adults.

Low birth weight to type 2 diabetes (43). Children born with a low birth weight have a much greater risk of having type 2 diabetes (or adult-onset diabetes) as an adult.

Dietary factors to intermediary conditions and chronic diseases (pathways B1, B3)

Saturated fat intake pattern to

1. *Dyslipidaemia:* Saturated fatty acids are the major serum cholesterol-raising fatty acids in the diet (44).
2. *Coronary heart disease:* Saturated fatty acids have a deleterious effect, not only on cardiovascular risk mediated by lipoproteins, but they also enhance thrombogenesis (45).

3. *Type 2 diabetes:* A high intake of saturated fatty acids has been associated with increased risk of developing impaired glucose tolerance (IGT), diabetes and progression from IGT to diabetes (45).

4. *Cancers:* Increased intake of total saturated fats was associated with nearly twice the risk of developing colon cancer (46).

Trans-fatty acids intake pattern to

1. *Dyslipidaemia*: Trans-fatty acids are shown to increase circulating low-density lipoprotein (LDL) cholesterol and reduce high-density lipoprotein (HDL) cholesterol (47).

2. *Glucose intolerance*: Trans-fatty acids have been shown to inhibit the activity of desaturase enzymes, and therefore, could also negatively affect insulin sensitivity (48).

3. *Coronary heart disease*: Trans-fatty acids can compete with natural fatty acids in enzymatic reactions involved in prostaglandin synthesis and can affect platelet activity and other critical functions. Intake of trans-fatty acids was directly related to the risk of myocardial infarction (47).

4. *Type 2 diabetes:* Metabolic studies have shown that trans-fatty acids, as compared with *cis* unsaturated fatty acids, increase concentrations of LDL cholesterol and decrease concentrations of HDL cholesterol. Inhibition of the activity of desaturase enzymes by trans-fatty acids could negatively affect insulin sensitivity, thus increasing the risk of type 2 diabetes (49).

Fruit and vegetable intake pattern to

1. *Hypertension*: High levels of fibre and minerals (e.g. potassium and magnesium) in fruits and vegetables are believed to reduce blood pressure (50).

2. *Cancers*: Diets with high levels of fruits and vegetables showed a protective effect for a wide range of cancers. For cancer sites, especially epithelial cancers of the respiratory and digestive tracts, persons with low fruit and vegetable intake had about twice the risk of cancer as those with high intake (51). Block *et al*. (51) undertook a very thorough review of over 200 studies. They presented median RRs (with their ranges) from all studies reported for each site. RRs for some of the cancer sites are based on numerous papers, while others are based on only a few studies; we used the RRs suggested by the authors. Whereas some other studies (52,53) have shown similar effect sizes, other recent studies (e.g. 54–56), provided more conservative estimates. It is possible that the estimates used here are overestimates.

3. *Coronary heart disease*: Consumption of fruits and vegetables, particularly green leafy vegetables and vitamin C-rich fruits and vegetables, appears to have a protective effect against CHD. The mechanisms are likely to be multiple. The postulated beneficial constituents in fruits and vegetables include antioxidant vitamins, folate, fibre and minerals such as potassium (57).

4. *Stroke*: Reduced risks of cardiovascular disease related to potassium, antioxidant and dietary fibre are also shown in the risk of stroke by fruits and vegetables, which are high in these nutrients and substances (58,59).

Whole grains intake pattern to

1. *Insulin resistance*: Whole grains slow glycemic response, while refining grains tend to increase glycemic response (60).

2. *Cancers*: Insulin is proposed as an important growth factor of colonic epithelial cells and is a mitogen of tumour cell growth *in vitro* (61). Therefore, improved insulin response mediated by whole grain intakes is thought to reduce the risk of colon cancer.

3. *Coronary heart disease*: Whole grains contain higher amounts of fibre; minerals; vitamins; and polyphenols, phytic acid and phytoestrogens – such as lignins. A significant inverse association of cereal fibre or whole grains with CHD has been observed (62–65). Improving plasma lipid, by cholesterol lowering effects of soluble fibre, explains only a minor part of this apparent protective effect of whole grains (66).

4. *Stroke*: Higher intake of whole grain foods are associated with a lower risk of ischaemic stroke, independent of known CHD risk factors (67). The protective effect of whole grains against ischaemic stroke may involve multiple biological pathways including active ingredients in whole grains such as antioxidants, minerals, phytochemicals and fibres (68).

5. *Type 2 diabetes*: Epidemiological studies repeatedly show that risk for type 2 diabetes mellitus is decreased with consumption of whole grains (68,69).

Calcium and vitamin D intake pattern to osteoporosis. Calcium is essentially required for the formation of bone and the maintenance of normal bone structure. Optimal utilization of calcium is dependent on adequate vitamin D status. Both of these nutrients are associated with a reduced risk of osteoporosis (70). People with osteoporosis are more prone to fractures in the event of fall, and higher dose (700–800 IU d^{-1}) of vitamin D supplementation has been shown to reduce the risk of hip and any non-vertebral fractures (71).

Alcohol intake pattern to

1. *Cancers*: Strongest associations with cancer risks are with oral, pharyngeal, esophageal and laryngeal cancers. Also, increased risk of breast cancer associated with drinking alcoholic beverages has been reported in epidemiological studies (72,73).

2. *Coronary heart disease*: The incidence of CHD is diminished in moderate drinkers (74).

3. *Stroke*: Moderate alcohol consumption (up to two drinks per day) has been associated with a reduced risk of ischaemic stroke in men and women, whereas heavy drinking (five or more drinks per day) has been associated with a significantly increased risk of the disease (75).

Physical activity patterns to (pathways C2 and C3/Table 2)

Hypertension. Regular moderate physical activity is shown to prevent the development of hypertension (76). The mechanisms include attenuation of adrenergic sympathetic activity, increased cellular insulin sensitivity and decreased level of circulation insulin, decreased peripheral resistance, increased baroreflex sensitivity, changes in renin-angiotensin-aldosterone system and reduction in body fat. The effects of physical activity and some dietary factors on blood pressure are additive (40).

Dyslipidaemia. At a physical activity volume that results in a weight loss of at least 4.5 kg, HDL-cholesterol is raised and triglycerides are lowered in men and post-menopausal women. Physical activity added to a low-energy, low-fat diet also reverses the HDL-lowering effect in overweight men and women and enhances the LDL-lowering effect of the diet in men and post-menopausal women (77).

Insulin resistance (impaired glucose tolerance). Inactivity is a major cause of IGT (8). Physical activity improves insulin action, and thus reduces insulin resistance in obese subjects (77).

Cancers

1. *Colon cancer*: Epidemiological studies are consistent in showing an inverse association between physical activity (occupational and leisure time) and colon cancer (78). Biologically plausible mechanisms underlying this association include: (i) increased intestinal mobility and decreased gastrointestinal transit time resulting in shorter contact between the colonic mucosa and potential carcinogens (79); (ii) reduced insulin resistance, thus avoiding colon cancer stimulation linked to hyperglycemia and hyperinsulinemia (80); (iii) changes in serum cholesterol and bile acid metabolism (or changes in levels and availability of sex hormones in women) (81); (iv) alterations in local prostaglandins synthesis (80) and (v) activation of the immune system response (82).

2. *Breast cancer:* The association between physical activity and breast cancer has been fairly consistent, showing on average, about 20–40% reduction in risk (78). Physical activity has an independent effect on breast cancer risk, aside from those of weight and weight gain.

3. *Other cancers:* Available evidence suggests that physical activity may protect against endometrial and prostate cancers. However, limited and inconsistent data make it difficult to draw definite conclusions (40,78).

Coronary heart disease. Physical inactivity is a well-established risk factor of CHD. Biological mechanisms by which physical activity may contribute to the prevention of CHD include maintaining or increasing myocardial oxygen supply, decreasing myocardial work and oxygen demand, increasing myocardial function and increasing electrical stability of myocardium (40).

Stroke. Two major causes of stroke are atherosclerosis of intracranial or extracranial vessels and high blood pressure (83). As physical activity has beneficial effects on the atherosclerotic process and blood pressure, promoting physical activity can be a promising strategy in the prevention of stroke. Physical activity has been included as a recommended measure in the prevention of a first stroke (84).

Type 2 diabetes. Regular physical activity lowers the risk of developing type 2 diabetes by 20–60% in a dose-related manner (40,85–87). Physical activity improves insulin sensitivity and glucose metabolism in skeletal muscle, adipose tissue and the liver. Physical activity also lowers the risk of diabetes by triggering favourable changes in lipid metabolism, blood lipids and weight control (40).

Gallbladder disease. Although limited, studies have shown protective effects of physical activity on gallstones. Regular exercise improves several metabolic abnormalities related to both obesity and cholesterol gallstones, such as hyperinsulinemia, high levels of plasma triglycerides and low levels of plasma high-density lipoprotein cholesterol (88).

Osteoporosis. Physical activity, combined with adequate diet, is essential for attaining and maintaining bone strength. High-intensity loading in relation to the strength of the bone causes an osteogenic response specifically at the loaded site if the internal milieu is adequate (89). Physical activities that maintain or improve co-ordination, balance, strength and other neuromuscular factors that influence risk of falling may also decrease the risk of bone fractures (90).

Osteoarthritis. Whereas a large amount of heavy physical activity for an extended period of time increases the risk of osteoarthritis of the loaded joints, light and moderate activities – even in large amounts – have not been shown to increase the risk (89). Regular physical activity is necessary for maintaining normal muscle strength, joint structure and joint function – which in turn helps to protect joints from injuries, abnormal movements and limited range of motion.

It also helps in maintaining a healthy weight. All of these effects contribute to maintenance of healthy joints (89).

Overweight/obesity pattern to (pathways D1 and D2/Table 2)

Hypertension. Epidemiological studies show a correlation between body weight and blood pressure, in both normotensive and hypertensive individuals. A main hypothesis for the pathogenesis of obesity-related hypertension is that leptin, free fatty acids and insulin – whose levels are increased in obesity – may act individually and synergistically to stimulate sympathetic activity and vasoconstriction. In addition, obesity-induced insulin resistance and endothelial dysfunction may act as amplifiers of the vasoconstrictor response. Increased renal tubular re-absorption of sodium may also occur, caused by an increased renal sympathetic nerve activity, direct effect of insulin, hyperactivity of rennin-angiotensin system, and possibly by an alteration of intrarenal physical forces (91). This pathway is an important public health concern, as recent epidemics of obesity may lead to epidemics of hypertension, both of which predispose to cardiovascular morbidity and mortality (92).

Dyslipidaemia. Obesity has been associated with increased levels of triglycerides and decreased high-density lipoprotein cholesterol. Both of these are recognized as independent risk factors for cardiovascular disease (93).

Insulin resistance (glucose intolerance). Insulin resistance (IGT) has been strongly associated with overweight and obesity in many epidemiological studies (94).

Cancers. It is clear from epidemiological studies that obesity is associated with some cancers. However, it has been difficult to separate the role of overweight and obesity *per se* from the effect of the macronutrient composition of the diet or of total calories (93).

1. *Colon cancer:* Higher BMI is associated with increased risk for colon cancer, with the association stronger for larger adenomas and for men. These may suggest an effect of factors related to adiposity on the promotion of cancer and a possible counteracting effect on these factors by oestrogens (78).
2. *Breast cancer*: A contrasting pattern has been shown by menopausal status. Higher body weight, especially higher adult weight, is associated with increased breast cancer risk among post-menopausal women (78).
3. *Esophagus cancer*: An increased incidence of gastric reflux in persons with high BMI has been proposed as the underlying cause of more than a twofold increase in the risk of esophageal cancer (78).
4. *Endometrium cancer*: Convincing evidence from epidemiologic studies shows a linear increase in the risk of endometrial cancer with increasing adult obesity (78,95).
5. *Kidney cancer*: Studies conducted across nations consistently show a more than twofold increase in renal-cell cancer risk among obese (both men and women), compared with those of normal weight (78).

Coronary heart disease. As described above, obesity increases the risk of hypertension, dyslipidaemia and diabetes mellitus – all of which are risk factors for CHD. However, obesity has been shown to be an independent risk factor for CHD in both men and women (96,97).

Stroke. The pathway from obesity to stroke is thought of as being developed through hypertension.

Type 2 diabetes. Whereas a relationship between obesity and type 2 diabetes is not completely clear, it is well established that excess body fat leads to increasing insulin resistance, and insulin resistance predisposes to diabetes (93). As obesity is characterized by a reduced number of insulin receptors and insulin resistance, the combination of epidemiologic and metabolic data leaves little doubt that obesity is causally related to type 2 diabetes (98).

Gallbladder disease. Epidemiological studies have reported an association between gallbladder disease, overweight and obesity (93).

Osteoarthritis. The well-recognized association between obesity and knee osteoarthritis is more marked in women than in men (99). Proposed mechanisms include being overweight, as being overweight increases the amount of force across a weight-bearing joint (100). In addition, adipose tissue may produce atypical hormone or growth factor concentrations that affect cartilage or underlying bone, predisposing them to osteoarthritis development (101).

Pathways linking the selected intermediary conditions and the chronic diseases (pathway D2/Table 3)

Hypertension to

Type 2 diabetes. A history of hypertension is shown to increase the risk of type 2 diabetes independently of other known risk factors, including obesity (102).

Coronary heart disease. Elevated blood pressure is a powerful risk factor for CHD (103).

Stroke. High blood pressure is a significant predictor of mortality from stroke – for men and women (103).

Dyslipidaemia (imbalance in total, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides) to

Coronary heart disease. Elevated levels of total cholesterol, LDL-cholesterol, triglycerides and lipoproteins are major risk factors for CHD in both men and women (104,105), whereas HDL levels are correlated inversely with the risk of CHD (106).

Insulin resistance (glucose tolerance and hyperinsulinemia) to

Colorectal cancer. Hyperinsulinemia is believed to increase the risk of colon cancer by directly promoting colon carcinogenesis and stimulating insulin-like growth factor-I receptors (61,107).

Type 2 diabetes to

Colorectal cancer. The remarkable similarity of risk factors for type 2 diabetes and colon cancer, coupled with a general hypothesis that hyperinsulinemia increases the risk of colon cancer, has led to a theory that type 2 diabetes, itself, is a risk factor for colon cancer; this association has been observed in epidemiological studies (87).

Coronary heart disease. Diabetes is a risk factor for CHD and CHD accounts for much of the serious morbidity and a high proportion of the premature deaths in type 2 diabetes (45). Diabetic men and women have a two to threefold and three to sevenfold increase in risk of CHD respectively, compared with their non-diabetic counterparts (108,109).

Review of the effects on morality, disability and sickness/absenteeism

Obesity and mortality before retirement

As noted earlier, our focus is on the development of a measure of the effect of obesity and overweight on mortality. The measurement needs to provide this by age grouping in order to only count mortality that reduces the working period prior to retirement.

Several reviews have been written regarding the relationship between obesity and all-cause mortality (110–116). Manson and colleagues (117), in a landmark methodological paper, highlighted many potential biases that could occur in studying the effect of body weight on mortality. The authors contend that adjustment for hypertension and dyslipidaemia could lead to underestimation of the effect of obesity on mortality. Because BMI is related to hypertension and dyslipidaemia, one should not adjust for these intermediaries in statistical models. They also argued that the first 5 years of mortality should be eliminated from such analyses to account for possible weight loss, which would be a consequence of preclinical disease among individuals who died early in the follow-up period. Lastly, they contend smoking status needs to be considered in any analysis of BMI–mortality association because smoking is associated with lower body weight. Because of these methodological issues as well as others, comparisons across studies can be problematic. Nonetheless, they feel there is a general consensus that a J- or U-shaped relationship between BMI and all-cause mortality exists; more specifically, mortality risk is increased in underweight, overweight and obese individuals.

Another approach to evaluating the influence of obesity on longevity is by estimating the number of years of life lost (YLL) associated with being obese (Table 4, part A). Few studies have examined the effect of obesity on an individual's expected number of YLL (118–120). YLL in this context is defined as the difference between (i) the number of years an obese individual would be expected to live and (ii) the number of years a normal-weight individual would be expected to live (121). Using several sources of US national data (National Health and Nutrition Examination Survey [NHANES] III, NHANES I Epidemiologic Follow-up Study [NHEFS], NHANES II Mortality Study, US Life Tables), Fontaine and colleagues (118) found differences between blacks and whites in the relationship between BMI and YLL. In order to derive estimates of YLL, Fontaine and colleagues used a BMI of 24 as the reference category. Using this as a reference point, 40-year-old white men having a BMI $\geq$ 45, BMI = 40 and BMI = 30 would result in YLLs of 10, 4 and 1 respectively. Again, using this as a reference point for 40-year-old white women, having a BMI $\geq$ 45, BMI = 40 and BMI = 30 resulted in YLLs of 7, 4 and 1 respectively. Similarly, among all black men, estimated YLLs due to obesity did not begin for any age group until a BMI = 32 was reached. Consequently, for 40-year-old black men having a BMI $\geq$ 45, BMI = 40 and BMI = 30 resulted in YLLs of 7, 3 and 0 respectively. For 40-year-old black women having a BMI $\geq$ 45, BMI = 40 and BMI = 30 resulted in YLLs of 3, 1 and –1 (indicating an increased life expectancy).

The Framingham Heart Study was used by Peeters to estimate YLL for 40-year-old smokers and non-smokers (119). Among non-smokers, 40-year-old obese women and obese men (BMI $\geq$ 30) lost 7.1 and 5.8 years of life respectively, compared with normal-weight ($18.5 <$ BMI < 25) women and men. Overweight ($25 \leq$ BMI < 30) men and women lost 3.3 and 3.1 years of life compared with normal-weight women and men; however, the differences for overweight individuals were not significant. Among smokers, obese women and men lost 7.2 and 6.7 years of life when compared with normal-weight

women and men. Among overweight smokers, neither men nor women had statistically significant decreases in life expectancy. Stevens found that 40–49-year-old overweight and obese men lost 0.12 and 0.73 years of life respectively, when compared with normal-weight men (120). Among women 40–49 years old, overweight and obesity was associated with 0.10 and 0.43 YLL respectively. These last estimates by Stevens were restricted to a 12-year period rather than the subjects' remaining life span and consequently may have led to underestimation of the YLL.

We utilize the YLL from the Fontaine (118) study for our effects of overweight and obesity on mortality. This study provides an estimation, by year of life and BMI level, for all effects – providing a much more precise, but quite conservative approach.

Obesity and years of disability free life (Table 4, part B)

Using the Original and Offspring Framingham Heart Study, Peeters and colleagues (122) have again used the Years of Life concept to estimate the life expectancy for individuals, free of disability, and classified by weight status. Disability was defined as limited mobility (i.e. limited walking on a level surface and walking up/downstairs) and limited activities of daily living (ADL) (i.e. limited dressing, grooming/bathing, feeding/eating, getting in and out of chairs). Among non-smokers, obese men had 5.70 (95% confidence interval [CI]; 4.11, 7.35) and obese women had 5.02 (95% CI; 3.36, 6.61) fewer years free of ADL limitations than normal-weight counterparts. Simi-

Table 4 Indirect effects of obesity on years of life lost (YLL), disability and absenteeism

A. Years of life lost

Author	Year	Population	Years of life lost – Findings
Peeters	2003	Framingham Heart Study	Among non-smokers, 40-year-old obese (BMI ≥ 30) women and obese men lost 7.1 and 5.8 years of life respectively, compared with normal-weight (18.5 < BMI < 25) women and men. Overweight (25 ≤ BMI < 30) men and women lost 3.3 and 3.1 years of life compared with normal-weight women and men; however, the differences for overweight individuals were not significant. Among smokers, obese women and men lost 7.2 and 6.7 years of life when compared with normal-weight women and men. Among overweight smokers, neither men nor women had statistically significant decreases in life expectancy.
Fontaine	2003	NHANES III, NHEFS, NHANES II Mortality Study, US Life Tables	Differences between blacks and whites in the relationship between BMI and YLL. BMI of 24 as the reference category. For 40-year-old white men having a BMI ≥ 45 resulted in 10 YLL whereas a BMI of 30 resulted in 1 YLL and a BMI of 40 resulted in 4 YLL. For 40-year-old white women having a BMI ≥ 45 resulted in 7 YLL whereas a BMI of 30 resulted in 1 YLL and a BMI of 40 resulted in 4 YLL. Among all black men, estimated YLL because of obesity did not begin for any age group until a BMI of 32 was reached. Consequently, for 40-year-old black men having a BMI ≥ 45 resulted in 11 YLL whereas a BMI of 30 resulted in 0 YLL and a BMI of 40 resulted in 3 YLL. For 40-year-old black women having a BMI ≥ 45 resulted in 3 YLL whereas a BMI of 30 resulted in –1 YLL (indicating an increased life expectancy) and a BMI of 40 resulted in 1 YLL.
Stevens	1999		Among men 40–49 years old, overweight and obese lost 0.12 and 0.73 years respectively, when compared with normal-weight men. Among women 40–49 years old, overweight and obesity was associated with 0.10 and 0.43 YLL respectively. These estimates were restricted to a 12-year period rather than the subjects' remaining life span and consequently this may have led to an underestimation of YLL.

B. Disability free years, early pension and retirement, and sick leave

Author	Year	Population	Disability free years/early pension/retirement/sick leave	Findings
Peeters	2004	Original and offspring Framingham Heart Study	Disability free years Mobility only (walking on a level surface and walking up/down stairs) and activities of daily living (ADL) (dressing, grooming/bathing, feeding/eating, getting in and out of chairs)	Among non-smokers, obese men had 5.70 (4.11, 7.35) and obese women had 5.02 (3.36, 6.61) fewer years free of ADL limitation than normal-weight counterparts. Among non-smokers, overweight men had 2.48 (1.18, 3.65) and overweight women had 2.13 (0.90, 3.23) fewer years of ADL limitation than normal-weight counterparts. Regarding any mobility or ADL limitation, obese men had 6.02 (4.35, 7.61) and obese women had 5.53 (3.76, 7.34) fewer years free of limitation than normal-weight counterparts. Overweight men had 2.00 (0.80, 3.16) and overweight women had 1.54 (0.35, 2.65) fewer years free of any limitation than normal-weight counterparts.

Table 4 *Continued*

Ostermann & Sloan	2001	Health and Retirement Study	(1) Any kind of limitation Do you have any impairment or health problem that limits the kind or amount of paid work you can do? Does any impairment or health problems limit the kind or amount of work you can do around the house? Are you limited in any way in activities because of an impairment or problem?	Odds ratios (Wave 4) Compared with normal-weight 18.5 to <25 Any kind of limitation BMI < 18.5 2.13 (1.30, 3.49) BMI 25 to <30 1.05 (0.92, 1.19) BMI 30 to <35 1.31 (1.12, 1.54) BMI ≥ 35 2.51 (2.00, 3.15)
			(2) Social Security Disability Insurance/Supplemental Security Income (SSDI/SSI)	(SSDI/SSI) BMI < 18.5 1.62 (0.71, 3.68) BMI 25 to <30 0.95 (0.74, 1.21) BMI 30 to <35 0.98 (0.73, 1.32) BMI ≥ 35 2.17 (1.54, 3.06)
			(3) SSDI/SSI given any limitation	SSDI/SSI given any limitation BMI < 18.5 1.09 (0.45, 2.62) BMI 25 to <30 0.90 (0.69, 1.18) BMI 30 to <35 0.75 (0.55, 1.04) BMI ≥ 35 1.33 (0.91, 1.95)

BMI, body mass index; NHANES, National Health and Nutrition Examination Survey; NHEFS, NHANES I Epidemiologic Follow-up Study.

larly, among non-smokers, overweight men had 2.48 (95% CI; 1.18, 3.65) and overweight women had 2.13 (95% CI; 0.90, 3.23) fewer years of ADL limitation than normal-weight counterparts. Regarding any mobility or ADL limitation, obese men had 6.02 (95% CI; 4.35, 7.61) and obese women had 5.53 (95% CI; 3.76, 7.34) fewer years free of limitation than normal-weight counterparts. Overweight men had 2.00 (95% CI; 0.80, 3.16) and overweight women had 1.54 (95% CI; 0.35, 2.65) fewer years free of any limitation than normal-weight counterparts. These researchers concluded, however, due to the higher mortality in the obese and overweight groups, there was no significant difference in the years lived with disability (mobility or ADL limitation) between those overweight or obese and those with normal weight at baseline.

Obesity and loss of productivity

Minimal research has been conducted regarding the effect of obesity on the loss of productivity (123–129). The research has examined loss of productivity in terms of disability or early retirement and days absent from work. The majority of this work was conducted in Scandinavian countries: Finland, Denmark and Sweden (123–127). Most of these studies (six of seven) have found obesity to be associated with disability or early retirement. One study examined sick leave histories and found an increased BMI to be associated with long-term sick leave (125). Another study conducted in the United States found obesity to be associated with the combined outcome of limitations in the kind or amount of paid work, kind or amount of housework, and kind or amount of any activity (128). Finally, another study found obesity to be associated with days spent ill in bed; however, this association may vary depending on age (129).

The results of the China case study

Table 5 presents the current patterns of diet, physical activity, obesity and NCD prevalence in China; all sources are noted. These data, combined with the direct and indirect cost RR results, allow us to measure the costs of inadequate nutritional patterns.

Table 5 Measurement of dietary, nutritional status and morbidity exposures in China, 2000 and 2025

Exposure	Exposure definition	Prevalence 2000	Prevalence 2025	References
Low fibre	<24 g d^{-1}	92.7%	92.7%	(151–153)
High added sugar intake	>10% energy	0%	0%	(154)
Calorie imbalance	Unbalanced (>100% RDA)	34.4%	45.5%	(151,152)
Calorie imbalance		0.86 lb^{-1} weight gain/ year is 1.12%/year overweight prevalence increase & 0.25/ year obesity increase	0.86 lb^{-1} weight gain/year is 1.12%/year overweight prevalence increase & 0.25/ year obesity increase	
Low fruit/vegetables	<300 g d^{-1}	65.9%	66.0%	(151,152)
Low whole grains	<100 g d^{-1}	93.4%	100%	(151,152)
High refined grains	≥500 g d^{-1}	22.8%	0%	(151,152)
Trans fat		NA	NA	
Low calcium	<400 mg d^{-1}	80.8%	62.3%	(151,152)
Alcohol	5–7 times/week	15.8%	35%	(61)
	1–4 times/week	20.3%	40%	
	≥40 g d^{-1}	3.0%	13.3%	(64,65)
	1–40 g d^{-1}	4.9%	6.7%	
High saturated fat	>10% energy from saturated fat	59.7%	80%	(155)
Physical activity	Heavy	47.4%	23%	(156)
	Moderate	19.0%	26%	
Stunting (1970)	% height/age –2 Z-scores	45%	17%	(157)
Overweight	BMI ≥ 25 and <30			(156)
Male		19.6%	50%	
Female		21.3%	47%	
Total		20.5%	48%	
Obesity	BMI ≥ 30			(156)
Male		3.1%	9%	
Female		3.7%	10%	
Total		3.4%	10%	
Overweight & obesity	BMI ≥ 25			(156)
Male		22.7%	59%	
Female		25.0%	58%	
Total		23.9%	58%	
Hypertension	Diastolic pressure ≥90 mmHg or systolic pressure ≥130 mmHg			(156)
Male		31.1%	50%	
Female		21.8%	38%	
Total		26.3%	44%	
Dyslipidaemia	Triglycerides >150 mg dL^{-1} or serum cholesterol >200 mg dL^{-1}	27.4%	54%	(158,159)
Insulin resistance	Fasting plasma glucose levels between 100 and 125 mg dL^{-1} or blood glucose between 140 and 199 mg dL^{-1} 2 h after oral glucose tolerance test.	7.3%	24.8%	(160–162)
Diabetes	Fasting plasma glucose levels over 126 mg dL^{-1} or blood glucose over 200 mg dL^{-1} 2 h after oral glucose tolerance test.			(163)
Male		5.2%		
Female		5.8%		
Total		5.5%	10%	

NA means relative risk results are not available.
RDA, recommended dietary allowance.

Measurement of direct costs

The direct costs are calculated based on the RRs and PARs noted in Fig. 1 and Tables 1–3. These total results are presented below (Table 6). We also present the costs by disease.

As shown in Table 5, dietary intake data for China are limited to a set of foods and nutrients. The Chinese food

Table 6 Costs of dietary and activity factors and obesity in US dollars (in millions) for China*

	Direct dietary effects			Dietary cost effect via overweight/obesity		
	Inpatient costs	Outpatient costs	Total cost	Inpatient cost	Outpatient cost	Total cost
A. Year 2000						
Dietary factors						
Low fibre	0	0	0	104.4	295.5	400
Calories	0	0	0	25.8	72.9	98.7
No fruit/vegetables	643.8	920.2	1564	0	0	0
Whole grains	569.6	1070.3	1639.8	69.3	196.2	265.6
Refined grain	0	0	0	16	45.2	61.2
Alcohol – moderate drinking	29.7	71.7	101.4	0	0	0
Saturated fat	15.6	15.6	31.3	0	0	0
Activity						
Low physical activity	424.2	923.4	1347.3	92.2	260.7	352.9
Total	1682.9	3000.9	4683.8	307.8	870.6	1178.3
B. Year 2025						
Dietary factors						
Low fibre	0	0	0	138.2	410.9	549.1
Calories	0	0	0	44.1	131.2	175.3
No fruit/vegetables	563.5	771.8	1335.3	0	0	0
Whole grains	457.2	837.6	1294.8	96.2	286.0	382.2
Alcohol – moderate drinking	40.2	96.9	137.1	0	0	0
Saturated fat	13.4	13.4	26.9	0	0	0
Activity						
Low physical activity	469.2	1046.8	1516	163.8	486.9	650.7
Total	1543.5	2766.6	4310.1	442.4	1314.9	1757.3

*An exchange rate of US $8.2765 equal to one Chinese yuan Renminbi was used.

composition table does not contain data on trans-fatty acid composition. Further, in a forthcoming study we could not find evidence of trans-fatty acid composition in edible oils in China. The data for other toxic oils noted in that paper have not been studied adequately in humans and a cost cannot be ascribed to their intake. In addition, as osteoporosis and related data are unavailable in China, we cannot provide medical costs for these items, and thus do not measure the effects of calcium and vitamin D. In addition, the conditions of excessive sugar intake and very heavy drinking (of alcohol) do not exist in China and there is no evidence of high sedentary behaviour (i.e. high inactivity levels).

Table 6 provides the data for each of the dietary and physical activity factors. The year 2000 costs for the direct dietary and physical activity effects are more than US $4.7 billion. Similarly the diet and physical activity effects via obesity are approximately an added US $1.2 billion. Table 7 presents these same costs for each disease. The stroke and the CHD costs are both more than US $2 billion while the cancers (oesophagus, lung, stomach), diabetes and hypertension costs are all less. Hypertension is a very prevalent condition; however, the costs are much lower, as currently this condition is mainly an undiagnosed and untreated disease. If this trend changed, medical costs for hypertension would rise dramatically (130).

Figure 3 displays how these direct costs are divided as a per cent of the total for 2000. Essentially, we find that stroke and CHD represent the largest direct health costs. This is expected, because the prevalence of these conditions is now very large in the Chinese population. The relatively higher stroke costs in China is unique. This relates to the higher likelihood of hypertension and stroke than diabetes, as Chinese BMI and inactivity levels rise (131). Observing these same factors in 2025, we find that the total direct costs do not increase considerably.

Measurement of the indirect costs

Table 8 presents results on indirect cost losses – from overweight and obesity – as they relate to effects on mortality and disability prior to retirement and absenteeism from work. The estimation method was described above. Similar to the problem with early death before retirement, we needed to develop a reasonable estimate for the effect of obesity on early disability before retirement. Again, the years of disability free life lost (YDFL) were calculated prior to retirement. Unfortunately, there is not a sophisticated life table for YDFL by age of life as exists for obesity and mortality; therefore, it must be assumed that the disability before retirement is overestimated by the same proportion as was the death before retirement. The results in

Table 7 Dietary/activity costs by disease in US dollars (in millions) for China

	Dietary factors		Activity factors		Dietary/activity through obesity		Total
	Inpatient	Outpatient	Inpatient	Outpatient	Inpatient	Outpatient	
A. Year 2000							
Breast cancer	4.9	5.1	4.3	4.5	1.3	1.3	21.4
Colon cancer	32.3	32.3	10.5	10.5	2.3	2.4	90.3
Esophagus cancer	67.9	70.5	0	0	27.1	28.1	193.5
Endometrial cancer	0	0	2.4	2.5	2.5	2.6	9.8
Lung cancer	68.3	70.9	0	0	0	0	139.2
Stomach cancer	123.1	127.7	0	0	0	0	250.8
Bladder cancer	3.9	4.1	0	0	0	0	7.6
Coronary heart disease	333.2	803.6	130.3	314.2	168.1	405.4	2154.8
Type 2 diabetes	30.1	82.6	19.6	53	54.6	147.6	387.9
Hypertension	0	0	41.8	219.2	54.5	285.8	601.2
Stroke	594.6	881.2	215.4	319.2	0	0	2010.3
Total	1258.3	2078	424.3	923.1	310.4	873.2	5866.8
B. Year 2025							
Breast cancer	4.9	5.1	6.2	6.4	3.2	3.3	29.1
Colon cancer	25.5	25.5	10.2	10.2	4	4.2	79.5
Esophagus cancer	68.4	71	0	0	56.2	58.3	253
Endometrial cancer	0	0	3.4	3.5	5.3	5.5	17.6
Lung cancer	68.4	71	0	0	0	0	139.3
Stomach cancer	123.2	127.8	0	0	0	0	251
Bladder cancer	3.9	4	0	0	0	0	8
Coronary heart disease	246.6	594.7	119.4	288	208.3	502.4	1959.5
Type 2 diabetes	24.4	66.1	20.8	56.4	58.6	158.6	385
Hypertension	0	0	59.5	312.3	112.1	588.1	1072
Stroke	509.5	755.1	249.7	370	0	0	1884.3
Total	1074.8	1720.3	469.2	1046.8	447.7	1320.4	6078.3

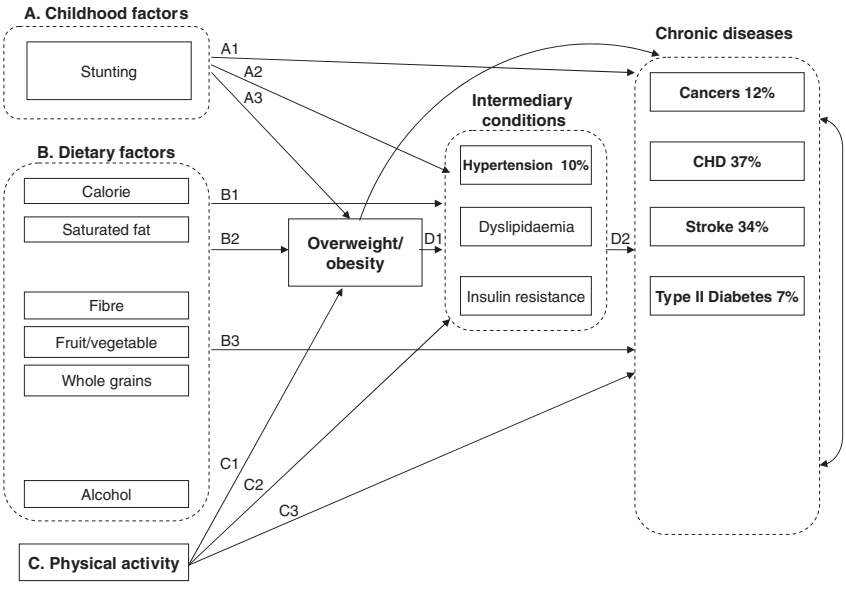

Figure 3 Pathways measured for China case study for the economic effects of diet, physical activity and obesity on nutrition-related non-communicable diseases in 2000. CHD, coronary heart disease.

Table 8 Indirect costs from obesity/overweight – as a fraction of GDP per period and US dollars (in millions) for China

Women	Obesity – >Mortality		Obesity – >YDFL before		Sick leave	Grand total
	Men	Women	Men	Women		
A. Indirect costs from obesity/overweight – as fraction of GDP per period						
2000						
Obese	0.01%	0.00%	0.07%	0.06%		
Overweight	0.01%	0.00%	0.20%	0.16%		
Overweight/obese	0.00%	0.00%	0.00%	0.00%	3.06%	
Total	0.02%	0.01%	0.27%	0.22%	3.06%	3.58%
2025						
Obese	0.04%	0.01%	0.22%	0.18%		
Overweight	0.02%	0.01%	0.46%	0.37%		
Overweight/obese	0.00%	0.00%	0.00%	0.00%	7.43%	
Total	0.05%	0.02%	0.68%	0.54%	7.43%	8.73%
B. Indirect costs from obesity/overweight – yearly amount						
2000						
Obese	158	51	907	742		
Overweight	86	48	2380	1898		
Overweight/obese					37 284	
Total	244	99	3288	2640	37 284	43 555
2025						
Obese	466	151	2669	2182		
Overweight	201	112	5573	4445		
Overweight/obese					90 480	
Total	667	263	8242	6627	90 480	106 278

GDP, gross domestic product; YDFL, years of disability free life.

Table 8 were based on these YDFL results. Clearly, these adjustments were very conservative, because disability would always occur before death. So, the figures for the pathway, *Obesity leading to YDFL before retirement*, should be perceived as the lower bounds for the parameters of interest. If no adjustments were made (i.e. assume there is no retirement), the totals would increase the estimate to 0.53%. Realistically, the true values should be in the interval enclosed by the adjusted and unadjusted values – probably closer to the high bounds. Obesity gradually makes people become sick more often and disables them, leading to chronic NCDs. Disability time is required before terminal outcomes occur. This was also confirmed by the higher average sick days taken by overweight and obese people every year relative to normal-weight people; sick leave losses accounted for more than 75% of the indirect costs.

From the results in Table 8 (parts A and B), overweight and obesity can be seen to become more and more prevalent in the population, indirect cost figures rose dramatically, and each component more than doubled in the years from 2000 to 2025. In each of these cases, the most significant factor was sick leave (i.e. loss of productivity was permanent for obese and overweight people because they were much more likely to use sick leave). What is important to note is that these indirect costs equalled 3.58% of GNP in 2000 but more than 8.7% in 2025. More than US $4.3 billion, in terms of total dollars, were expended on these productivity losses in 2000 and they rose dramatically to US $10.6 billion in 2025.

Table 9 Total direct and indirect costs from overweight and obesity for Chinese adults, US dollars (in millions) and percentage of gross national product (GNP)

	2000		2025	
	US Dollars	Portion of China's GNP (%)	US Dollars	Portion of China's GNP (%)
Direct costs	5 862	0.48	6 067	0.50
Indirect costs	43 555	3.58	106 278	8.73
Total	49 417	4.06	112 345	9.23

The total costs are summarized in Table 9. Again, the growth in the costs attributable to overweight and obesity in China rose from about US $49 billion in 2000 to about US $112 billion in 2025.

Discussion

Rapid changes in dietary, physical activity and obesity patterns are occurring on a worldwide level. Except for very

limited subpopulations, most of the world's populations – in urban or rural areas – are becoming increasingly overweight and less underweight (132). Elsewhere, we have examined the economic consequences of this shift from underweight to overweight in India and China and shown that already in China, the economic costs of overweight far exceed those of underweight – and the same shift is occurring in India during the 2000–2025 period (19).

This review and case study expands the previous work on the economic consequences of obesity much further than other work. First, it attempts to encompass the full range of obesity and obesity-related behaviours – poor diets and physical activity patterns. Most studies have only examined pieces of the overall pattern of diet, physical activity and obesity (6,7,13–15,119). The prior work omitted physical activity costs completely and examined only a few components of diet; estimates of the effects of obesity and diet on cancer were very inexact. Conversely, the current study examines *all* the consequences of nutrition-related factors linked with NCDs. Second, our review of the effects of physical activity, diets and obesity are quite exhaustive and examine both the direct and indirect economic effects. The main direct effects are medical care costs. The indirect costs include the effects of overweight and obesity status on mortality, disability and sickness that occur during the active work period of each adult. The RRs selected were based on a much more complete review of the literature than previously seen in other economic cost studies as they relate to poor diets, obesity and physical activity (6,7,13–15,119). These strengths are important as they show that the combined effects of all diet and physical activity related behaviours that affect health directly and via their effects on obesity have a much larger total effect than any separate pathway, the approach used by Ezzati *et al*. in their *Lancet* papers and in the overall global burden of disease project (4,5).

There are some weaknesses in this review. This is particularly true in the use of literature on how physical activity affects morbidity and mortality. Uncertainties in assessing and differentiating occupational and leisure-time physical activity may result in inconsistent results. Occupational activity tends to decrease for most people in developed societies, and leisure-time and recreational activities are felt to become a greater part of overall physical activity variation, although there is limited research on this point. Therefore, it is likely that occupational activity is becoming a less sensitive discriminator of risk. Inconsistencies in the measurement of physical activity (type, dose and time period of activity) may have resulted in discrepancies in study results. Measurement errors also result from underestimation of the strength of associations (133).

The China case study utilizes data on the prevalence of most of the key nutritional, physical activity and mortality patterns – as well as available retirement age and medical care costs for China. As shown, the current 2000 level overweight and obesity levels for China are 23.9% of all adults aged 20–45 years. The rate of change in overweight and obesity in China has accelerated over the past decade. Conservative assumptions for the predicted prevalence in 2025 utilized linear regression to predict future obesity. In other words, an increasing rate of change for overweight and obesity was not assumed – as the CHNS and other data from China seem to indicate. The same approach was used for the other prevalence measures, in particular the prediction of their 2025 values. Thus, if anything, the direct medical costs are underestimated, in particular because costs from 1995 were used and the rate of inflation in medical care costs was assumed to be no greater than the rate of overall inflation.

The indirect costs, on the other hand, might be slightly overestimated if a smaller effect on productivity and sickness rates is found in China than in the United States, or because it is possible that overweight Chinese – because of their work ethic and culture – might not use sick leave as often. The increasing role of the service sector and modern manufacturing in China would indicate that effects on lost work time in China are similar to those in the United States in terms of days of sickness. The latter is possibly conservative because we know that for a lower BMI level in China, there appear to be higher rates of hypertension and other health effects (1,130).

Overall, however, this review does represent important steps forward. The total impact of these nutrition-related components of poor diets, inactivity and obesity on NCD medical costs and on labour productivity and national production are very large. In the Chinese case study, the indirect effects of obesity and obesity-related dietary and physical activity patterns, range between 3.58% and 8.73% of GNP in 2000 and 2025 respectively. The total direct and indirect costs are even greater. Clearly, these results present a clear rationale for action in China.

Much more work needs to be accomplished and understood on the economic impact of obesity and its related behaviours. At some point, longitudinal studies of the actual impacts of all these factors on large representative studies are needed. Unfortunately, there are as yet, no data bases that encompass data adequate for such explorations. In the interim, we are forced to utilize reviews and studies such as those represented in this manuscript.

Conflict of Interest Statement

No conflict of interest was declared.

Acknowledgements

We wish to thank Tom Swasey for preparing the graphics, Frances Dancy for her administrative help and Bill Shapbell

for his editing assistance. This report and the related software were developed by the Consortium for the Primary Prevention and Treatment of Obesity. The consortia is headed by Professor Shlomo Ben-Haim, Hobart Holdings Ltd., POB 3562, Caesarea, 38900 Israel.

References

1. International Obesity Task Force World Health Organization. *The Asian-Pacific Perspective: Redefining Obesity and Its Treatment*. International Diabetes Institute: Caulfield, Victoria, 2000.
2. Organization WH. Report of the Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases. WHO Technical Report Series No. 916. Geneva, Switzerland, 2002.
3. World Health Assembly Resolution WHA57.17. Global strategy on diet, physical activity and health. Geneva, Switzerland, 2004.
4. Ezzati M, Lopez AD. Estimates of global mortality attributable to smoking in 2000. *Lancet* 2003; **362**: 847–852.
5. Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; **360**: 1347–1360.
6. Allison DB, Zannolli R, Narayan KM. The direct health care costs of obesity in the United States. *Am J Public Health* 1999; **89**: 1194–1199.
7. Colditz GA. Economic costs of obesity. *Am J Clin Nutr* 1992; **55**: 503S–507S.
8. Colditz GA. Economic costs of obesity and inactivity. *Med Sci Sports Exerc* 1999; **31**: S663–S667.
9. Wolf AM, Colditz GA. Social and economic effects of body weight in the United States. *Am J Clin Nutr* 1996; **63**: 466S–469S.
10. Wolf AM, Colditz GA. Current estimates of the economic cost of obesity in the United States. *Obes Res* 1998; **6**: 97–106.
11. Thompson D, Edelsberg J, Colditz GA, Bird AP, Oster G. Lifetime health and economic consequences of obesity. *Arch Intern Med* 1999; **159**: 2177–2183.
12. Thompson D, Edelsberg J, Kinsey KL, Oster G. Estimated economic costs of obesity to U.S. business. *Am J Health Promot* 1998; **13**: 120–127.
13. Finkelstein E, Ruhm CJ, Kosa KM. Economic causes and consequences of obesity. *Ann Rev Public Health* 2004; **26**: 239–257.
14. Finkelstein EA, Fiebelkorn IC, Wang G. National medical spending attributable to overweight and obesity: how much, and who's paying? *Health Aff (Millwood)* 2003; Suppl Web Exclusives: W3-219-226.
15. Finkelstein EA, Fiebelkorn IC, Wang G. State-level estimates of annual medical expenditures attributable to obesity. *Obes Res* 2004; **12**: 18–24.
16. Wang G, Brown DR. Impact of physical activity on medical expenditures among adults downhearted and blue. *Am J Health Behav* 2004; **28**: 208–217.
17. Katzmarzyk PT, Janssen I. The economic costs associated with physical inactivity and obesity in Canada: an update. *Can J Appl Physiol* 2004; **29**: 90–115.
18. Popkin B, Horton S, Kim S. The nutrition transition and prevention of diet-related chronic diseases in Asia and the Pacific. *Food Nutr Bull* 2001; **22**: 1–58.
19. Popkin BM, Horton S, Kim S, Mahal A, Shuigao J. Trends in diet, nutritional status, and diet-related noncommunicable diseases in China and India: the economic costs of the nutrition transition. *Nutr Rev* 2001; **59**: 379–390.
20. Du S, Mroz TA, Zhai F, Popkin BM. Rapid income growth adversely affects diet quality in China – particularly for the poor! *Soc Sci Med* 2004; **59**: 1505–1515.
21. Popkin BM, Du S. Dynamics of the nutrition transition toward the animal foods sector in China and its implications: a worried perspective. *J Nutr* 2003; **133**: 3898S–3906S.
22. Department of Biostatistics in the School of Public Health at the University of Alabama at Birmingham. URL http://www.soph.uab.edu//statgenetics/Research/Tables/YLL.htmAccessed January 2005.
23. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW, Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 1999; **341**: 1097–1105.
24. Popkin BM, Richards MK, Montiero CA. Stunting is associated with overweight in children of four nations that are undergoing the nutrition transition. *J Nutr* 1996; **126**: 3009–3016.
25. Sawaya AL, Martins P, Hoffman D, Roberts SB. The link between childhood undernutrition and risk of chronic diseases in adulthood: a case study of Brazil. *Nutr Rev* 2003; **61**: 168–175.
26. Sawaya AL, Roberts S. Stunting and future risk of obesity: principal physiological mechanisms. *Cad Saude Publica* 2003; **19**: S21–S28.
27. Forrester TE, Wilks RJ, Bennett FI, Simeon D, Osmond C, Allen M, Chung AP, Scott P. Fetal growth and cardiovascular risk factors in Jamaican schoolchildren. *BMJ* 1996; **312**: 156–160.
28. Hoffman DJ, Sawaya AL, Verreschi I, Tucker KL, Roberts SB. Why are nutritionally stunted children at increased risk of obesity? Studies of metabolic rate and fat oxidation in shantytown children from Sao Paulo, Brazil. *Am J Clin Nutr* 2000; **72**: 702–707.
29. Sawaya AL, Dallal G, Solymos G, de Sousa MH, Ventura ML, Roberts SB, Sigulem DM. Obesity and malnutrition in a Shantytown population in the city of Sao Paulo, Brazil. *Obes Res* 1995; **3**: 107s–115s.
30. Schroeder DG, Martorell R, Flores R. Infant and child growth and fatness and fat distribution in Guatemalan adults. *Am J Epidemiol* 1999; **149**: 177–185.
31. Sichieri R, Siqueira KS, Moura AS. Obesity and abdominal fatness associated with undernutrition early in life in a survey in Rio de Janeiro. *Int J Obes Relat Metab Disord* 2000; **24**: 614–618.
32. Yajnik CS, Fall CH, Vaidya U, Pandit AN, Bavdekar A, Bhat DS, Osmond C, Hales CN, Barker DJ. Fetal growth and glucose and insulin metabolism in four-year-old Indian children. *Diabet Med* 1995; **12**: 330–336.
33. Hill JO, Melanson EL. Overview of the determinants of overweight and obesity: current evidence and research issues. *Med Sci Sports Exerc* 1999; **31**: S515–S521.
34. Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. *Am J Clin Nutr* 2003; **78**: 920–927.
35. Raben A, Vasilaras TH, Moller AC, Astrup A. Sucrose compared with artificial sweeteners: different effects on ad libitum food intake and body weight after 10 wk of supplementation in overweight subjects. *Am J Clin Nutr* 2002; **76**: 721–729.
36. Schulze MB, Manson JE, Ludwig DS, Colditz GA, Stampfer MJ, Willett WC, Hu FB. Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women. *JAMA* 2004; **292**: 927–934.
37. Bray GA, Nielsen SJ, Popkin BM. Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. *Am J Clin Nutr* 2004; **79**: 537–543.
38. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective, observational analysis. *Lancet* 2001; **357**: 505–508.

39. Rolls BJ, Roe LS, Meengs JS. Salad and satiety: energy density and portion size of a first-course salad affect energy intake at lunch. *J Am Diet Assoc* 2004; **104**: 1570–1576.
40. Vuori IM. Health benefits of physical activity with special reference to interaction with diet. *Public Health Nutr* 2001; **4**: 517–528.
41. Curhan GC, Chertow GM, Willett WC, Spiegelman D, Colditz GA, Manson JE, Speizer FE, Stampfer MJ. Birth weight and adult hypertension and obesity in women. *Circulation* 1996; **94**: 1310–1315.
42. Zhao M, Shu XO, Jin F, Yang G, Li HL, Liu DK, Wen W, Gao YT, Zheng W. Birthweight, childhood growth and hypertension in adulthood. *Int J Epidemiol* 2002; **31**: 1043–1051.
43. Rich-Edwards JW, Colditz GA, Stampfer MJ, Willett WC, Gillman MW, Hennekens CH, Speizer FE, Manson JE. Birthweight and the risk for type 2 diabetes mellitus in adult women. *Ann Intern Med* 1999; **130**: 278–284.
44. Schaefer EJ, Lichtenstein AH, Lamon-Fava S, McNamara JR, Ordovas JM. Lipoproteins, nutrition, aging, and atherosclerosis. *Am J Clin Nutr* 1995; **61**: 726S–740S.
45. Mann JI. Diet and risk of coronary heart disease and type 2 diabetes. *Lancet* 2002; **360**: 783–789.
46. Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *N Engl J Med* 1990; **323**: 1664–1672.
47. Ascherio A, Hennekens CH, Buring JE, Master C, Stampfer MJ, Willet WC. Acute myocardial infarction/antiplatelet and thrombolytic therapy: trans-fatty acids intake and risk of myocardial infarction. *Circulation* 1994; **89**: 94–101.
48. Hu FB, van Dam RM, Liu S. Diet and risk of Type II diabetes: the role of types of fat and carbohydrate. *Diabetologia* 2001; **44**: 805–817.
49. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 2001; **345**: 790–797.
50. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin P-H, Karanja N, Simons-Morton D, McCullough M, Swain J, Steele P, Evans MA, Miller ER, Harsha DW. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997; **336**: 1117–1124.
51. Block G, Patterson B, Subar A. Fruit, vegetables, and cancer prevention: a review of the epidemiological evidence. *Nutr Cancer* 1992; **18**: 1–29.
52. Vecchia CLAA, Tavani A. Vegetables, fruit, antioxidants and cancer: a review of Italian Studies. *Eur J Nutr* 2001; **40**: 261–267.
53. Miller ABAH, Bueno-de-Mesquita B, Boshuizen HC, Agudo A, Berrino F, Gram IT, Janson L, Linseisen J, Overvad K, Rasmuson T, Vineis P, Lukanova A, Allen N, Amiano P, Barricarte A, Berglund G, Boeing H, Clavel-Chapelon F, Day NE, Hallmans G, Lund E, Martinez C, Navarro C, Palli D, Panico S, Peeters PH, Quiros JR, Tjonneland A, Tumino R, Trichopoulou A, Trichopoulos D, Slimani N, Riboli E. Fruits and vegetables and lung cancer: findings from the European Prospective Investigation into Cancer and Nutrition. *Int J Cancer* 2004; **108**: 269–276.
54. Riboli E, Norat T. Epidemiologic evidence of the protective effect of fruit and vegetables on cancer risk. *Am J Clin Nutr* 2003; **78**: 559S–569S.
55. Hung HC, Joshipura KJ, Jiang R, Hu FB, Hunter D, Smith-Warner SA, Colditz GA, Rosner B, Spiegelman D, Willett WC. Fruit and vegetable intake and risk of major chronic disease. *J Natl Cancer Inst* 2004; **96**: 1577–1584.
56. Jansen MC, Bueno-de-Mesquita HB, Feskens EJ, Streppel MT, Kok FJ, Kromhout D. Quantity and variety of fruit and vegetable consumption and cancer risk. *Nutr Cancer* 2004; **48**: 142–148.
57. Joshipura KJ, Hu FB, Manson JE, Stampfer MJ, Rimm EB, Speizer FE, Colditz G, Ascherio A, Rosner B, Spiegelman D, Willett WC. The effect of fruit and vegetable intake on risk for coronary heart disease. *Ann Intern Med* 2001; **134**: 1106–1114.
58. Gillman MW, Cupples LA, Gagnon D, Posner BM, Ellison RC, Castelli WP, Wolf PA. Protective effect of fruits and vegetables on development of stroke in men. *JAMA* 1995; **273**: 1113–1117.
59. Joshipura KJ, Ascherio A, Manson JE, Stampfer MJ, Rimm EB, Speizer FE, Hennekens CH, Spiegelman D, Willett WC. Fruit and vegetable intake in relation to risk of ischemic stroke. *JAMA* 1999; **282**: 1233–1239.
60. Jenkins DJ, Wolever TM, Jenkins AL, Giordano C, Giudici S, Thompson LU, Kalmusky J, Josse RG, Wong GS. Low glycemic response to traditionally processed wheat and rye products: bulgur and pumpernickel bread. *Am J Clin Nutr* 1986; **43**: 516–520.
61. Giovannucci E. Insulin and colon cancer. *Cancer Causes Control* 1995; **6**: 164–179.
62. Rimm EB, Ascherio A, Giovannucci E, Spiegelman D, Stampfer MJ, Willett WC. Vegetable, fruit, and cereal fiber intake and risk of coronary heart disease among men. *JAMA* 1996; **275**: 447–451.
63. Liu S, Stampfer MJ, Hu FB, Giovannucci E, Rimm E, Manson JE, Hennekens CH, Willett WC. Whole-grain consumption and risk of coronary heart disease: results from the Nurses' Health Study. *Am J Clin Nutr* 1999; **70**: 412–419.
64. Wolk A, Manson JE, Stampfer MJ, Colditz GA, Hu FB, Speizer FE, Hennekens CH, Willett WC. Long-term intake of dietary fiber and decreased risk of coronary heart disease among women. *JAMA* 1999; **281**: 1998–2004.
65. Pietinen P, Rimm EB, Korhonen P, Hartman AM, Willett WC, Albanes D, Virtamo J. Intake of dietary fiber and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Circulation* 1996; **94**: 2720–2727.
66. Truswell AS. Cereal grains and coronary heart disease. *Eur J Clin Nutr* 2002; **56**: 1–14.
67. Liu S, Manson JE, Stampfer MJ, Rexrode KM, Hu FB, Rimm EB, Willett WC. Whole grain consumption and risk of ischemic stroke in women: a prospective study. *JAMA* 2000; **284**: 1534–1540.
68. Slavin J. Why whole grains are protective: biological mechanisms. *Proc Nutr Soc* 2003; **62**: 129–134.
69. van Dam RM, Rimm EB, Willett WC, Stampfer MJ, Hu FB. Dietary patterns and risk for type 2 diabetes mellitus in U.S. men. *Ann Intern Med* 2002; **136**: 201–209.
70. Shikany JM, White GL, Jr. Dietary guidelines for chronic disease prevention. *South Med J* 2000; **93**: 1138–1151.
71. Bischoff-Ferrari HA, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. *JAMA* 2005; **293**: 2257–2264.
72. Colditz GA. A prospective assessment of moderate alcohol intake and major chronic diseases. *Ann Epidemiol* 1990; **1**: 167–177.
73. Collaborative Group on Hormonal Factors in Breast Cancer. Alcohol, tobacco and breast cancer-collaborative reanalysis of individual data from 53 epidemiological studies, including 58515 women with breast cancer and 95067 women without the disease. *Br J Cancer* 2002; **87**: 1234–1245.

74. Rimm EB, Giovannucci EL, Willett WC, Colditz GA, Ascherio A, Rosner B, Stampfer MJ. Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet* 1991; **338**: 464–468.
75. Sacco RL, Elkind M, Boden-Albala B, Lin IF, Kargman DE, Hauser WA, Shea S, Paik MC. The protective effect of moderate alcohol consumption on ischemic stroke. *JAMA* 1999; **281**: 53–60.
76. World Health Organization International Society of Hypertension. Guidelines for the management of hypertension. *J Hypertens* 1999; **17**: 151–183.
77. Grundy SM, Blackburn G, Higgins M, Lauer R, Perri MG, Ryan D. Physical activity in the prevention and treatment of obesity and its comorbidities. *Med Sci Sports Exerc* 1999; **31**: S502–S508.
78. IARC Working Group on the Evaluation of Cancer-Preventive Strategies. *Weight Control and Physical Activity*. IARC Press: Lyon, 2002.
79. Thune I, Lund E. Physical activity and risk of colorectal cancer in men and women. *Br J Cancer* 1996; **73**: 1134–1140.
80. Colditz GA, Cannuscio CC, Frazier AL. Physical activity and reduced risk of colon cancer: implications for prevention. *Cancer Causes Control* 1997; **8**: 649–667.
81. Potter JD. Risk factors for colon neoplasia – epidemiology and biology. *Eur J Cancer* 1995; **31A**: 1033–1038.
82. Simon HB. The immunology of exercise. A brief review. *JAMA* 1984; **252**: 2735–2738.
83. Lee I, Paffenbarger R, Jr. Physical activity and stroke incidence: the Harvard Alumni Health Study. *Stroke* 1998; **29**: 2049–2054.
84. Gorelick PBSR, Smith DB, Alberts M, Mustone-Alexander L, Rader D, Ross JL, Raps E, Ozer MN, Brass LM, Malone ME, Goldberg S, Booss J, Hanley DF, Toole JF, Greengold NL, Gregg E, Cauley J, Seeley D, Ensrud K, Bauer D. Physical activity and osteoporotic fracture risk in older women. *Ann Intern Med* 1998; **129**: 81–89.
85. Manson JE, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Krolewski AS, Rosner B, Hennekens CH, Speizer FE. Physical activity and incidence of noninsulin-dependent diabetes mellitus in women. *Lancet* 1991; **338**: 774–778.
86. Lewis CE, Raczynski JM, Heath GW, Levinson R, Hilyer JC, Jr, Cutter GR. Promoting physical activity in low-income African-American communities: the PARR project. *Ethn Dis* 1993; **3**: 106–118.
87. Hu FB, Manson JE, Liu S, Hunter D, Colditz GA, Michels KB, Speizer FE, Giovannucci E. Prospective study of adult onset diabetes mellitus (type 2) and risk of colorectal cancer in women. *J Natl Cancer Inst* 1999; **91**: 542–547.
88. Leitzmann MF, Rimm EB, Willett WC, Spiegelman D, Grodstein F, Stampfer MJ, Colditz GA, Giovannucci E. Recreational physical activity and the risk of cholecystectomy in women. *N Engl J Med* 1999; **341**: 777–784.
89. Vuori IM. Dose-response of physical activity and low back pain, osteoarthritis, and osteoporosis. *Med Sci Sports Exerc* 2001; **33**: S551–S586; discussion 609– 610.
90. Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, Cauley J, Black D, Vogt TM. Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group. *N Engl J Med* 1995; **332**: 767–773.
91. Montani JP, Antic V, Yang Z, Dulloo A. Pathways from obesity to hypertension: from the perspective of a vicious triangle. *Int J Obes Relat Metab Disord* 2002; **26**: S28–S38.
92. Wolk R, Shamsuzzaman AS, Somers VK. Obesity, sleep apnea, and hypertension. *Hypertension* 2003; **42**: 1067–1074.
93. Pi-Sunyer FX. Comorbidities of overweight and obesity: current evidence and research issues. *Med Sci Sports Exerc* 1999; **31**: S602–S608.
94. Lipton RB, Liao Y, Cao G, Cooper RS, McGee D. Determinants of incident non-insulin-dependent diabetes mellitus among blacks and whites in a national sample. The NHANES I Epidemiologic Follow-up Study. *Am J Epidemiol* 1993; **138**: 826–839.
95. Bergstrom A, Pisani P, Tenet V, Wolk A, Adami HO. Overweight as an avoidable cause of cancer in Europe. *Int J Cancer* 2001; **91**: 421–430.
96. Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, Hennekens CH. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. *JAMA* 1995; **273**: 461–465.
97. Manson JE, Colditz GA, Stampfer MJ, Willett WC, Rosner B, Monson RR, Speizer FE, Hennekens CH. A prospective study of obesity and risk of coronary heart disease in women. *N Engl J Med* 1990; **322**: 882–889.
98. Colditz GA, Willett WC, Stampfer MJ, Manson JE, Hennekens CH, Arky RA, Speizer FE. Weight as a risk factor for clinical diabetes in women. *Am J Epidemiol* 1990; **132**: 501–513.
99. Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. *Am J Epidemiol* 1988; **128**: 179–189.
100. Syed IY, Davis BL. Obesity and osteoarthritis of the knee: hypotheses concerning the relationship between ground reaction forces and quadriceps fatigue in long-duration walking. *Med Hypotheses* 2000; **54**: 182–185.
101. Sowers M. Epidemiology of risk factors for osteoarthritis: systemic factors. *Curr Opin Rheumatol* 2001; **13**: 447–451.
102. Helmrich S, Ragland D, Leung R, Paffenbarger R, Jr. Physical activity and reduced occurrence of noninsulin-dependent diabetes mellitus. *N Engl J Med* 1991; **325**: 147–152.
103. Antikainen R, Jousilahti P, Tuomilehto J. Systolic blood pressure, isolated systolic hypertension and risk of coronary heart disease, strokes, cardiovascular disease and all-cause mortality in the middle-aged population. *J Hypertens* 1998; **16**: 577–583.
104. Coleman MP, Key TJ, Wang DY, Hermon C, Fentiman IS, Allen DS, Jarvis M, Pike MC, Sanders TA. A prospective study of obesity, lipids, apolipoproteins and ischaemic heart disease in women. *Atherosclerosis* 1992; **92**: 177–185.
105. Stamler J, Dyer AR, Shekelle RB, Neaton J, Stamler R. Relationship of baseline major risk factors to coronary and all-cause mortality, and to longevity: findings from long-term follow-up of Chicago cohorts. *Cardiology* 1993; **82**: 191–222.
106. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, Jacobs DR, Jr, Bangdiwala S, Tyroler HA. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation* 1989; **79**: 8–15.
107. Schoen RE, Tangen CM, Kuller LH, Burke GL, Cushman M, Tracy RP, Dobs A, Savage PJ. Increased blood glucose and insulin, body size, and incident colorectal cancer. *J Natl Cancer Inst* 1999; **91**: 1147–1154.
108. Bonow RO, Bohannon N, Hazzard W. Risk stratification in coronary artery disease and special populations. *Am J Med* 1996; **101**: 4A17S–22S; discussion 22S–24S.
109. Seeman T, Mendes de Leon C, Berkman L, Ostfeld A. Risk factors for coronary heart disease among older men and women: a prospective study of community-dwelling elderly. *Am J Epidemiol* 1993; **138**: 1037–1049.

110. Katzmarzyk PT, Janssen I, Ardern CI. Physical inactivity, excess adiposity and premature mortality. *Obes Rev* 2003; **4**: 257–290.
111. Troiano RP, Frongillo E, Jr, Sobal J, Levitsky DA. The relationship between body weight and mortality: a quantitative analysis of combined information from existing studies. *Int J Obes* 1996; **20**: 63–75.
112. Kushner RF. Body weight and mortality. *Nutr Rev* 1993; **51**: 127–136.
113. Seidell JC, Visscher TL, Hoogeveen RT. Overweight and obesity in the mortality rate data: current evidence and research issues. *Med Sci Sports Exerc* 1999; **31**: S597–S601.
114. Stevens J. Obesity and mortality in African-Americans. *Nutr Rev* 2000; **58**: 346–353.
115. Manson J, Stampfer M, Hennekens C, Willett W. Body weight and longevity. *JAMA* 1987; **257**: 353–358.
116. Andres R. Effect of obesity on total mortality. *Int J Obes* 1980; **4**: 381–386.
117. Manson JE, Stampfer MJ, Hennekens C, Willet WC. Body-weight and longevity – a reassesment. *JAMA* 1987; **257**: 187–193.
118. Fontaine KR, Redden DT, Wang C, Westfall AO, Allison DB. Years of life lost due to obesity. *JAMA* 2003; **289**: 187–193.
119. Peeters A, Bonneux L, Barendregt J, Nusselder W. Methods of estimating years of life lost due to obesity. *JAMA* 2003; **289**: 2941; author reply 2941–2.
120. Stevens J, Cai J, Juhaeri, Thun MJ, Williamson DF, Wood J. Consequences of the use of different measures of effect to determine the impact of age on the association between obesity and mortality. *Am J Epidemiol* 1999; **150**: 399–407.
121. Manson JE Bassuk SS. Obesity in the United States – a fresh look at its high toll. *JAMA* 2003; **289**: 229–230.
122. Peeters A Bonneux L Nusselder WJ De Laet C Barendregt JJ. Adult obesity and the burden of disability throughout life. *Obes Res* 2004; **12**: 1145–1151.
123. Rissanen A Heliovaara M Knekt P Reunanen A Aromaa A Maatela J. Risk of disability and mortality due to overweight in a Finnish population. *BMJ* 1990; **301**: 835–837.
124. Krause N Lynch J Kaplan GA Cohen RD Goldberg DE Salonen JT. Predictors of disability retirement. *Scand J Work Environ Health* 1997; **23**: 403–413.
125. Narbro K Jonsson E Larsson B Waaler H Wedel H Sjostrom L. Economic consequences of sick-leave and early retirement in obese Swedish women. *Int J Obes Relat Metab Disord* 1996; **20**: 895–903.
126. Biering-Sorensen F Lund J Hoydalsmo OJ Darre EM Deis A Kryger P Muller CF. Risk indicators of disability pension. A 15 year follow-up study. *Dan Med Bull* 1999; **46**: 258–262.
127. Mansson NO Eriksson KF Israelsson B Ranstam J Melander A Rastam L. Body mass index and disability pension in middle-aged men – non-linear relations. *Int J Epidemiol* 1996; **25**: 80–85.
128. Ostermann J Sloan FA. Effects of alcohol consumption on disability among the near elderly: a longitudinal analysis. *Milbank Q* 2001; **79**: 487–515, iii.
129. Ferraro KF Booth TL. Age, body mass index, and functional illness. *J Gerontol B Psychol Sci Soc Sci* 1999; **54**: S339–S348.
130. Bell A Adair LS Popkin BM. Ethnic differences in the association between body mass index and hypertension. *Am J Epidemiol* 2002; **155**: 346–353.
131. Eastern Stroke and Coronary Heart Disease Collaborative Research Group. Blood pressure, cholesterol, and stroke in eastern Asia. *Lancet* 1998; **352**: 1801–1807.
132. Mendez MA, Monteiro CA, Popkin BM. Overweight exceeds underweight among women in most developing countries. *Am J Clin Nutr* 2005; **81**: 714–721.
133. IARC Working Group. *IARC Working Group on the Evaluation of Cancer-Preventive Strategies*. IARC Press: Lyon, 2002.