PAPERS AND SHORT REPORTS

Weight and mortality in the Whitehall Study

R J JARRETT, M J SHIPLEY, G ROSE

Abstract

Ten-year mortality rates in men aged 40-64 years in the Whitehall Study were analysed in relation to weight and height at the initial examination. At ages 40-49 "all-causes" mortality increased with increasing body mass index; but this simple relation disappeared at older ages, where there was an increased mortality in the lowest quintile of body mass index. The "all-ages" relation was "J"-shaped, and this could not be explained by the confounding effects of blood pressure, cholesterol values, and cigarette smoking. Some, but not all, of the J shape was due to a high short-term mortality in thin men from cancers (presumably already present at examination). At younger ages mortality from coronary heart disease was positively related to body mass index, but this depended on its association with other risk factors. Mortality from causes other than cancers or coronary heart disease was highest in the lowest quintile of body mass index.

Introduction

There is general agreement that severe obesity is associated with increased mortality rates, in particular from coronary heart disease. Evidence concerning lesser degrees of obesity is conflicting, however, one study[1] reporting a graded increase in risk from the very thin to the very fat, while several others report a more complex relation.[2-5] British studies have been few and small. We present the results of a large study of male civil servants (the Whitehall Study)[6 7] relating baseline measurements of weight to 10-year mortality.

Department of Community Medicine, Guy's Hospital Medical School, London SE1
R J JARRETT, MD, MFCM, reader

Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine, London WC1
M J SHIPLEY, BA, MSC, research fellow
G ROSE, DM, FRCP, professor

Subjects and methods

In the Whitehall Study 18 403 male civil servants aged 40-64 years were examined between 1967 and 1969[7]; because of missing data our analysis is based on 18 393 men. Procedures included measurement of height and weight (without shoes and jackets), from which an index of relative weight was calculated—namely, the body mass index (weight in kg/(height in m)^2). Participants' records were identified in the NHS Central Registry and a coded copy of the death certificate provided for each subsequent death.

Results

Body mass index increased slightly with age, from a mean of 24·32 ± SD 2·9 kg/m^2 at ages 40-44 up to 25·01 ± 3·1 kg/m^2 at ages 60-64. Age-standardised and age-specific mortality rates were therefore calculated after first dividing the population into quintiles of body mass index (≤22·4, −24·0, −25·4, −27·0, >27·0 kg/m^2). Mortality ratios for each of the higher quintiles were relative to mortality in the lowest quintile.

"All-causes" age-standardised mortality (table I) followed overall a "J"-shaped distribution, being highest in the top quintile of body mass index and lowest in the second quintile; the departure from linearity was highly significant ($p < 0.01$). The patterns at different ages, however, were distinctive. In the 40-49-year age group mortality increased from the lowest to the highest quintile of body mass index; the excess mortality in the thinnest men became apparent only after the age of 50, and the excess in the most overweight men dis-

TABLE I—*Ten-year "all-causes" mortality by quintile of body mass index and age*

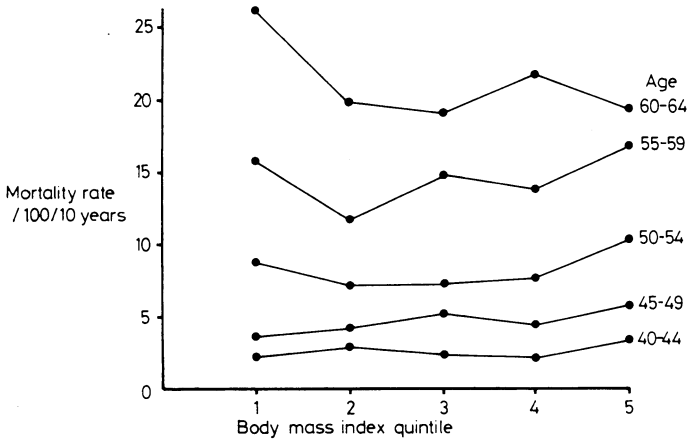
Quintile of body mass index	No of deaths/population (mortality ratio)			
	Age 40-49	Age 50-59	Age 60-64	All ages (standardised)
1	52/1755 (1·00)	196/1617 (1·00)	123/474 (1·00)	371/3846 (1·00)
2	57/1597 (1·20)	148/1617 (0·76)	77/393 (0·75)	282/3607 (0·82)
3	66/1602 (1·39)	179/1679 (0·88)	87/464 (0·72)	332/3745 (0·90)
4	53/1411 (1·27)	168/1592 (0·87)	105/491 (0·82)	326/3494 (0·90)
5	67/1362 (1·66)	236/1775 (1·10)	108/564 (0·74)	411/3701 (1·04)
Total	295/7727	927/8280	500/2386	1722/18393
χ^2_1 (linear trend)	7·06**	2·73	4·38*	1·27
χ^2_3 (departures from linearity)	1·61	14·47**	5·72	11·72**

* $p < 0.05$. ** $p < 0.01$.

appeared after the age of 60. The figure illustrates how advancing age was accompanied by an increasing relative risk for the thinnest men but a disappearance of the excess risk for the heaviest quintile.

Table II shows mortality rates for coronary heart disease (ICD 410-414, eighth revision). The "all-ages" rates rose with increasing overweight, mortality in the highest quintile being 36% higher than in the lowest. The gradient was steepest in the youngest age group, and by age 60 it had disappeared.

As we have shown for low plasma cholesterol concentrations,[8] in some people a low body mass index also might be a result rather than an antecedent of disease, particularly cancer. We therefore analysed mortality according to the interval from examination (table III). In the first two years all-causes mortality rates were highest in quintiles 1-3; a J-shaped relation persisted in years 2-10, when only quintile 5 had a higher rate than quintile 1. Most of this J-shaped relation seen for total mortality was due to causes other than coronary heart disease and cancer. A higher early mortality in the first two years was seen, particularly for cancer mortality.



"All-causes" mortality analysed by body mass index quintile and five-year age group.

TABLE II—*Ten-year coronary heart disease mortality by quintile of body mass index and age*

Quintile of body mass index	No of deaths (mortality ratio)			
	Age 40-49	Age 50-59	Age 60-64	All ages (standardised)
1	20 (1·00)	70 (1·00)	39 (1·00)	129 (1·00)
2	24 (1·32)	66 (0·94)	31 (0·96)	121 (1·00)
3	27 (1·48)	78 (1·07)	39 (1·02)	144 (1·12)
4	24 (1·49)	77 (1·12)	45 (1·11)	146 (1·16)
5	24 (1·55)	116 (1·51)	47 (1·01)	187 (1·36)
Total	119	407	201	727
χ^2_1 (linear trend)	2·26	10·04**	0·11	8·80**
χ^2_3 (departures from linearity)	0·51	3·80	0·41	1·58

** $p < 0.01$.

TABLE III—*Mortality (expressed as annual rates) by quintile of body mass index (Q) and interval to death*

Cause of death	Interval (years)	Deaths/1000/year				
		Q1	Q2	Q3	Q4	Q5
All causes	<2	5·8	5·9	5·5	4·3	4·8
	2–10	11·3	8·9	10·0	10·3	12·1
Total		10·0	8·2	9·0	9·0	10·5
Coronary heart disease	<2	1·6	2·4	2·3	2·3	2·5
	2–10	4·0	3·8	4·4	4·5	5·4
Total		3·5	3·5	3·9	4·0	4·7
Cancers	<2	2·4	1·7	2·0	1·0	0·7
	2–10	3·5	2·8	3·3	3·5	3·6
Total		3·2	2·6	3·0	3·0	3·0
Remainder	<2	1·8	1·8	1·2	1·0	1·6
	2–10	3·8	2·3	2·3	2·3	3·1
Total		3·3	2·1	2·1	2·0	2·8

TABLE IV—*Ten-year coronary heart disease mortality by quintile of body mass index and age, controlling for age, systolic blood pressure, cholesterol, and smoking habit*

Quintile of body mass index	Relative risk			
	Age 40-49	Age 50-59	Age 60-64	All ages
1	1·00	1·00	1·00	1·00
2	1·23	0·98	0·83	0·99
3	1·25	0·98	0·86	1·00
4	1·16	1·02	0·98	1·06
5	0.94	1·33	0·83	1·14
χ^2_1 (linear trend)	0·01	2·67	0·25	1·24
χ^2_3 (departures from linearity)	1·41	2·98	0·89	0.65

For $p = 0.05$, $\chi^2_1 = 3.84$ and $\chi^2_3 = 7.81$.

Since body mass index is related to blood pressure, cholesterol concentration, and cigarette smoking its independent relation with mortality was assessed using multiple logistic analyses.[9] Table IV shows the effect of body mass index on mortality from coronary heart disease after controlling for these other factors. The independent effect of body mass index was seen to be slight, mortality from coronary heart disease in the highest body mass index quintile of the whole population being only 14% higher than in the lowest. The effect of the adjustment was seen most in the 40-49 age group, where the relation of body mass index to mortality from coronary heart disease was completely removed.

A similar analysis for all-causes mortality made only slight differences to the mortality ratios shown in table I, except in the youngest age group, where the mortality ratios were roughly halved.

Discussion

In the Build and Blood Pressure Study,[1] reporting the experience of United States insurance companies, the five-year all-causes mortality rates showed some increase among the thinnest men, although this was not emphasised in the report. The American Cancer Society study[3] also detected an increased mortality in men of below average weight. The same finding was later repeated in the Framingham[5] and other studies.[10] In a survey of 8006 Japanese in Hawaii[11] this phenomenon was found to be confined to men who had lost weight since the age of 25; and the excess mortality in the top body mass index quintile was greatest in those who had also been heavy at age 25. In the Seven Countries Study[4] all-causes mortality was not related to either body mass index or obesity (the sum of three skinfold thicknesses).

The Whitehall Study extended these analyses to middle-aged men in Britain, where distributions of build and weight differ from those in North America. The overall relation was again J-shaped, though the gradients were shallow; but within narrower age bands this was seen to be due to a positive association between mortality and obesity in younger men, giving way at later ages to an excess mortality in thinner men.

All studies seem to agree on the risks of severe obesity. In the American Cancer Society study,[3] at ages 40-69 the mortality ratio was 1·7 among the 2% of men who were more than 30% above average weight for their age and height. In our study this would correspond to a body mass index of >30 kg/m²: 4·2% of men were in this category, and their mortality ratio (age standardised) was 1·3.

With regard to coronary heart disease our results initially supported those studies[10] which suggested that obesity is a risk factor in younger but not in older men. Obesity, however, is related to blood pressure, hyperlipidaemia, and diabetes, and an association with coronary heart disease is therefore to be expected. When controlling for these confounding variables together with smoking habits we found that the independent

effect of obesity was negligible. It is surprising that the earlier reports from the Framingham Study[5] (based on two-year incidence estimates) as well as the 10-year results from the Seven Countries Study[4] failed to show a convincing relation between obesity and coronary heart disease. A recent report from Framingham,[12] however, based on 26-year incidence data, identified obesity as an important and independent risk factor (especially in women).

In the Whitehall Study mortality from causes other than coronary heart disease and cancer was increased by about 50% in the lowest quintile of body mass index, relative to the middle quintiles. This unexplained finding merits further study.

We are grateful for the co-operation of the Civil Service and their medical advisory service. The work was supported in part by a grant from the British Heart Foundation.

References

1 Society of Actuaries. *Build and Blood Pressure Study, 1959.* Chicago: Society of Actuaries, 1959.

2 Dyer AR, Stamler J, Berkson DM, Lindberg HA. Relationship of relative body weight and body mass index to 14-year mortality in the Chicago People's Gas Company Study. *J Chronic Dis* 1975;**28**:108-23.

3 Lew EA, Garfinkel L. Variations in mortality by weight among 750,000 men and women. *J Chronic Dis* 1979;**32**:563-76.

4 Keys A. *Seven countries: a multivariate analysis of death and coronary heart disease.* Cambridge, Massachusetts, and London, England: Harvard University Press, 1980.

5 Sorlie P, Gordon T, Kannel WB. Body build and mortality: the Framingham Study. *JAMA* 1980;**243**:1828-31.

6 Reid DD, Hamilton PJS, McCartney P, Rose G, Jarrett RJ, Keen H. Smoking and other risk factors for coronary heart disease in British civil servants. *Lancet* 1976;ii:979-84.

7 Reid DD, Brett GZ, Hamilton PJS, Jarrett RJ, Keen H, Rose G. Cardio-respiratory disease and diabetes among middle-aged male civil servants. *Lancet* 1974;i:469-73.

8 Rose G, Shipley MJ. Plasma lipids and mortality: a source of error. *Lancet* 1980;i:523-6.

9 Walker SH, Duncan DB. Estimation of the probability of an event as a function of several independent variables. *Biometrika* 1967;**54**:167-79.

10 Larsson B, Björntorp P, Tibblin G. The health consequences of moderate obesity. *Int J Obes* 1981;**5**:97-116.

11 Kagan A, Rhoads G. The relation of mortality to adiposity in youth and middle age. In: Shekelle RB, ed. *CVD epidemiology newsletter No 31 of Council of Epidemiology of American Heart Association.* New York: AHA, 1982.

12 Hubert HB, Feinlieb M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease. In: Shekelle RB, ed. *CVD epidemiology newsletter No 31 of Council of Epidemiology of American Heart Association.* New York: AHA, 1982.

(*Accepted 24 June 1982*)

Randomised controlled trial of nicotine chewing-gum

M J JARVIS, MARTIN RAW, M A H RUSSELL, C FEYERABEND

Abstract

The effectiveness of 2 mg nicotine chewing-gum as an aid to stopping smoking was compared with a placebo containing 1 mg nicotine, but unbuffered, in a double-blind randomised trial. Of 58 subjects given the active gum, 27 (47%) were not smoking at one-year follow-up compared with 12 (21%) of the 58 subjects treated with placebo ($p < 0.025$). By the most stringent criterion of outcome, 18 (31%) subjects in the active treatment group and eight (14%) in the placebo group had not smoked at all from the start of treatment to follow-up at one year ($p < 0.05$).

Subjects receiving the active gum experienced less severe withdrawal symptoms and rated their gum as more helpful than did the placebo group. Minor side effects were common but only gastric symptoms were more frequent with the active gum. Subjects receiving active gum used it for longer than those receiving placebo but most stopped using it within six months and only four (7%) developed longer-term dependence. The number of gums used daily correlated significantly with pretreatment blood nicotine concentrations in the active treatment group and with pretreatment cigarette consumption in the placebo group. A lower pretreatment blood nicotine value was the best predictor of success at one year ($p < 0.001$) but there was no significant relation to cigarette consumption, sex, and social class.

The results clearly confirm the usefulness of nicotine chewing-gum as an aid to stopping smoking and imply a definite role for nicotine in cigarette dependence and withdrawal. Successful use of the gum requires careful attention to subjects' expectations and clear instructions on how to use it.

Addiction Research Unit, Institute of Psychiatry, Maudsley Hospital, London SE5

M J JARVIS, BSC, MPHIL, clinical psychologist

MARTIN RAW, BA, MPHIL, clinical psychologist (now at St George's Hospital Medical School, London)

M A H RUSSELL, FRCP, FRCPSYCH, senior lecturer and consultant psychiatrist

Poisons Unit, New Cross Hospital, London SE14

C FEYERABEND, BSC, senior biochemist

Introduction

Many smokers give up smoking without any special help or treatment, but others have great difficulty and fail many times. The first smoking-cessation clinic was started in Stockholm in 1955.[1] Since then there has been an intensive search for an effective treatment for dependent smokers. Simple support and encouragement, given individually or in groups, has a success rate of around 15-25% abstinent at one-year follow-up.[2] Numerous other methods have been tried, including tranquillisers,[3] lobeline,[4] electric aversion therapy,[5] rapid smoking,[6] hypnosis,[7] and, more recently, acupuncture.[8] None of these methods, however, has been found to have a specific effect over and above the attention-placebo element inherent in any treatment.

We have reported encouraging results from the use of nicotine chewing-gum (Nicorette) in our smokers' clinic. In a comparative study the success rate of smokers who received the gum was 38% abstinent at one year of follow-up compared with only 14% of those who had had intensive psychological treatment.[9] We now report the results of a randomised double-blind placebo-controlled trial of the gum with one-year follow-up and biochemical validation of reported abstinence from smoking.