...but does it increase lifespan in the others?

EDITOR,—M R Law and colleagues' findings[1,2] are encouraging for those engaged in health promotion.

Their findings do not, however, necessarily solve the real concerns of the public. Many people ask their doctor how to reduce the risk of heart attacks, but their real concern is how to live a longer and healthier life. If these major reductions in heart disease were matched by an equally impressive lengthening of the lifespan we could wholeheartedly advocate the measures recommended. There have been suggestions that the gain in healthy years may be more modest. Several years ago I tried to solve this problem by computer modelling.[3] I used age specific mortality for Australia for 1984 and assumed that (*a*) lowering the serum cholesterol concentration would reduce the cardiac mortality to that of men naturally at this lower level; (*b*) the relative risks for cholesterol concentrations were the same at all ages; and (*c*) lowering the serum cholesterol concentration did not affect mortality from other causes.

There were two main results from this modelling exercise. The first was a dramatic change in the causes of death. With the present range of serum cholesterol concentrations the model predicted that 47% of deaths would be due to heart disease, 27% to cancer, and 26% to other causes. This is close to the actual figures at the time. If all cholesterol concentrations were reduced by 10% the model predicted that 42% of deaths would be due to heart disease, 30% to cancer, and 28% to other causes while the median lifespan would be increased by one year. Reducing the cholesterol concentration of all people to within the range of the present lowest fifth of concentrations would result in 33% of deaths being due to heart disease, 34% to cancer, and 33% to other causes while the median lifespan would be increased by three years. A reduction in the mean cholesterol concentration by 10% is an achievable goal, but the gain is only one extra year of life. The major reduction in cholesterol concentrations is not a practical goal.

Computer modelling is inferior to analysis of data and should be used to generate hypotheses rather than test them. Law and colleagues have used their data to find the changes in the causes of death with changes in cholesterol concentrations. With little extra analysis their data could also be used to show the effect of reduced cholesterol concentrations on lifespan. Could I persuade them to do the analyses to answer questions about changes in lifespan, which are important (dare I say vital) for practising clinicians and health educators?

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1 Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? *BMJ* 1994;308:367-72. (5 February.)
2 Law MR, Thompson SG, Wald NJ. Assessing possible hazards of reducing serum cholesterol. *BMJ* 1994;308:373-9. (5 February.)
3 Dugdale AE. Serum cholesterol and mortality rates. *Lancet* 1987;i:155-6.

Authors' reply

EDITOR,—Limited space compels us to be brief in replying to comments on our papers.[1-3]

In reply to Bonneux and Barendregt, cholesterol is not the only factor in ischaemic heart disease but it is an important one. Death rates were higher in the Whitehall study than the BUPA study because the men were older.

In reply to Ravnskov, cholesterol is not a "weak risk factor of ischaemic heart disease" in old age.[2] In elderly people, as in middle aged people, the larger reduction in ischaemic heart disease will outweigh the small increase in stroke. Appropriate analysis of the trials confirms a dose-response relation between cholesterol reduction and lower rates of ischaemic heart disease.[4,5] Ravnskov's estimates of the reduction in ischaemic heart disease in relation to duration of treatment (0·51%, 1·64%, and 0·75% after <2, 2-5, and >5 years, are a fraction of ours (7%, 22%, and 25%). Table IV in our paper[2] presents the raw data and readers can draw their own conclusions.

In reply to Ramsay *et al*, studies documenting changes in serum cholesterol over time in the same communities showed average serum cholesterol reductions of 0·5 mmol/l in four American communities between 1960 and 1970 and in five Nordic communities between 1970 and 1980.[6] There is no reason why Britain could not achieve the same.

In reply to Sheldon and Song, the numbers of deaths from ischaemic heart disease in treated and control subjects in the Helsinki trial (17 and eight) were transposed in table I in our paper, but the correct figures were used in the calculations.[3] Data from the Helsinki study were not "ignored." We did not tabulate deaths occurring years after the termination of treatment because of the expected dilution of effect, but made an exception with respect to cancer because this was a particular concern and deaths can occur many years after exposure to a carcinogen. The cited publication from Helsinki did not specify cancer deaths. Selecting "nearly significant" ($P=0·14$) all cause mortality data from this one study out of many is unhelpful.

In reply to Millo, the effect of the mean fall of 0·15 mmol/l in serum cholesterol in the 5696 men in the BUPA study with repeat measurements is trivial. The estimate for the correction factor for regression dilution bias was also 1·4 in studies in which the mean did not fall—an earlier unpublished series of 1440 BUPA men and the median estimate of five published studies.[1]

In reply to Sudlow and MacLeod, our analysis showed that the risk of ischaemic heart disease was almost completely reversed five years after treatment to lower serum cholesterol. The expected long term reduction in ischaemic heart disease from the observational studies was 27% for a cholesterol reduction of 0·6 mmol/l; the estimate from the trials after five years was 25%.

In reply to Heady *et al*, the statement cited would be incorrect if directed at the WHO trial specifically, but it was not. It was a summary of all the trials together and as such it is correct. In stating that the higher mortality in treated men was not statistically significant in any one trial we were referring to the four groups of deaths defined in our paper (discussed on pages 376-7).[2] The WHO trial is exceptional in many respects; this should not override the collective evidence from all the trials.

In reply to Vine and Hastings, the reductions in risk of 54%, 39%, 27%, and 20% at ages 40, 50, 60, and 70 correspond to absolute reductions in the risk of dying of ischaemic heart disease over the next 10 years in British men of 0·3%, 0·9%, 1·9%, and 3·6%.

In reply to Dugdale, expressing the impact of the serum cholesterol reduction of 0·6 mmol/l as the average life gained by a whole population conceals the benefit to those who would otherwise die from ischaemic heart disease. This is about four years on average and about eight years in those dying at younger ages (under 50)—a significant gain in middle age.

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1 Law MR, Wald NJ, Wu T, Hackshaw A, Bailey A. Systematic underestimation of association between serum cholesterol concentration and ischaemic heart disease in observational studies: data from the BUPA study. *BMJ* 1994;308:363-6. (5 February.)
2 Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? *BMJ* 1994;308:367-72. (5 February.)
3 Law MR, Thompson SG, Wald NJ. Asessing possible hazards of reducing serum cholesterol. *BMJ* 1994;308:373-9. (5 February.)
4 Thompson SG. Controversies in meta-analysis: the case of the trials of serum cholesterol reduction. *Statistical Methods in Medical Research* 1993;2:173-92.
5 Holme I. An analysis of randomized trials evaluating the effect of cholesterol reduction on total mortality and coronary heart disease incidence. *Circulation* 1990;82:1916-24.
6 Law MR, Wald NJ. An ecological study of serum cholesterol and ischaemic heart disease between 1950 and 1990. *Eur J Clin Nutr* (in press).

Gender identity in testicular feminisation

Phenotypically, anatomically, legally, and socially female

EDITOR,—The personal view on testicular feminisation expresses poignantly the difficulties facing someone who has to come to terms with the condition.[1] The author was clearly distressed to learn that she was "chromosomally male, a pseudohermaphrodite," and highlights the essence of the problem in asking "What makes a person female?" Doctors make a fundamental mistake in cases of testicular feminisation if they concentrate on the chromosomal definition of sex—a definition that is unhelpful to the patient.

There are many definitions of a person's gender: genotypic (chromosomal pattern); gonadal (testis or ovary); phenotypic (including body habitus and genital anatomy); hormonal (oestrogen or androgen effects in the target tissues); legal (birth certificate, passport, etc); and, most importantly, social, which includes how we see ourselves, how others see us, the approach to sexual relationships, and everyday matters such as which changing room to use and which schools we may go to. Discordance among these definitions of gender may lead to problems in sexual identity. But patients with testicular feminisation have a high degree of concordance in their sexual identity: they are phenotypically, anatomically, hormonally, legally, and socially female.

To explain the diagnosis by telling the patient that she is fundamentally male but with abnormal sexual development may, to the purist, be embryologically correct but does nothing to help: it simply destroys a most fundamental part of a person's identity—gender. That is unnecessary. The explanation offered should begin from the understanding that the patient is female, and it should build on that assumption. The need for gonadectomy will ultimately require that the gonadal and chromosomal sex be explained, but care must be taken to do this in a way that does not disturb the overall gender identity. There are conditions in which gender assignment is sometimes difficult (for example, congenital adrenal hyperplasia), but testicular feminisation is not one of them.

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1 Once a dark secret. *BMJ* 1994;308:542. (19 February.)

Be open and honest with sufferers

EDITOR,—I should like to endorse the recommendations of the writer of "Once a dark secret" concerning the androgen insensitivity syndrome