Letters

Outcomes of screening to prevent cancer

Think of screening as insurance

Editor—Raffle et al provide interesting new data on the outcome of cervical screening.[1] It is particularly useful to be able to tell women that over 20 years of five yearly screening, around 16% will have an abnormal smear test result, 8% will have a biopsy, and 4% will be treated for high grade disease.

The authors also estimate the number of cancers and deaths that might be prevented over 30 years in such a cohort. How they obtained their estimates is unclear, but numbers are surprisingly low. When estimating the number of premature deaths avoided in screened women, they apply the factor 60%, obtained from a population in which approximately one in five eligible women are not screened regularly. In screened women the figure should be closer to 75%, which is more in keeping with the results from case-control studies.[2 3]

Fitting an age cohort model to mortality data from England and Wales for 1950-87 and extrapolating to 2011, we estimate the cumulative number of deaths in an unscreened cohort to be some 50% greater than do Raffle et al. Assuming that 75% of the deaths after 1996 would be prevented in a screened cohort, the number of premature deaths avoided is 2.4 times greater than in the paper. Over the next 30 years, the effect of screening in women born in the early 1960s will be much greater—some 2% of those screened will be prevented from developing cervical cancer.

Describing the benefits of screening in terms of the number needed to be screened to prevent one death equates screening with treatment. Screening is not treatment. It is perhaps better to think of it as insurance. The issue is not how many need to be insured for one person to avoid bankruptcy. It is not even simply a question of whether the cost of an insurance premium is more or less than the expected pay out (it will always be more).

Insurance is put in place to avoid catastrophic consequences of an unlikely event. Women need to be aware of the common negative consequences of regular screening, but they should perhaps think of it as a costly and imperfect insurance policy that may save them from the horrors of invasive cervical cancer.

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Authors' reply

Editor—We agree that screening can be thought of like insurance. It is not the likelihood of a house fire that makes you pay your premiums, it is the seriousness.

We believe numbers screened are valuable. Policy about screening is unsatisfactory in that support for, or dismissal of, the worth of screening programmes is dominated by advocacy rather than scientific debate.[1] Part of the reason this situation persists is that the literature is so hard to understand. It is full of statistical jargon, opaque terminology, and flawed concepts. We need to present complete information about all consequences of screening in an easily understandable way. People understand numbers and explanations in plain English, far better than probabilities, percentages, or sensitivity and specificity.[2]

Sasieni questions our estimates of cases and deaths. Our adjustment for "without screening" is as shown in figures 6.6 and 6.8 of page 51 of the reference we gave.[3] We are happy to share our calculations, and without access to the age breakdown of our cohort we are unsure how alternative estimates can be derived.

We tested varying assumptions for mortality reduction after 1996. Even if 75% of deaths in our study population are prevented after 1996, our conclusion is still that screening is very labour intensive, with 790 women screened for 35 years to prevent one death, involving 6098 tests. We view case-control studies with caution.[4]

We can all hope that future benefits will be substantial, but we cannot let this divert us from the sobering finding that before 1996 there were 57 000 tests and 1955 women with abnormal results for each death prevented. Misguided media campaigns are already causing a repetition of this situation with prostate cancer screening. Invasive investigations and treatments for 2000, in the hope of possibly helping one, will seriously damage men's health.

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Effectiveness of lipid lowering drugs in general practice

Article illustrates major problem

Editor—The article by Hippisley-Cox et al illustrates a major problem of describing a recommended cholesterol concentration as a target value—scatter around a bullseye will always ensure at least 50% of values above the target.[1] What was most interesting about their data was the dispersion of last recorded serum cholesterol concentrations about the means. This was small for simvastatin and atorvastatin, indicating that cholesterol values were close to recommended values even for those >5 mmol/l, and as Marshall has implied,[2] many of these patients may have concentrations $\leqslant 5$ mmol/l on remeasurement.

Although only one trial has compared five statins in a single study,[3] several paired comparisons of the efficacy of the statins[4] and of statins versus fibrates[5] have been undertaken. The data of Hippisley-Cox et al are consistent with these.

However, the statement "Statins reduce lipid levels better than fibrates" is at best misleading. Fibrates are often used in diabetic patients and other patients with an atherogenic lipoprotein phenotype (raised triglyceride, low high density lipoprotein, and mildly raised low density lipoprotein cholesterol concentrations), in whom chol-

esterol lowering is not the only consideration. Fibrates are also often used in combination treatment or in patients intolerant or poorly responsive to statins. Hence Marshall may be wrong to dismiss selection bias as a confounding problem. It was unclear whether patients receiving combined treatment were excluded from the analysis, and if included, which starting cholesterol concentrations were chosen. The lack of dosing data also makes it difficult to assess the validity of the statement that a target value of ≤5 mmol/l is unrealistic.

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1 Hippisley-Cox J, Cater R, Pringle M, Coupland C. Cross sectional survey of effectiveness of lipid lowering drugs in reducing serum cholesterol concentration in patients in 17 general practices. *BMJ* 2003;325:689-92. (29 March.)
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Study had two major flaws

EDITOR—The paper by Hippisley-Cox et al is a large study of how prescribed drugs are used in the community and gives a useful picture of the lipid lowering drugs used and their effectiveness.[1] It has two major flaws, however.

The first is the omission to report the characteristics of patients receiving different drugs. The pretreatment cholesterol concentrations in patients prescribed different statins differed, implying non-random selection of drug. In non-randomised studies differences among treatment groups may be systematic, substantial, and consequential. Extreme differences might require matching of subpopulations for comparisons.

The second problem is the omission of drug dosage in the analysis, although the data were collected. The authors probably assumed that the clinician could adjust the dose to achieve target and therefore failure to reach target implied lack of efficacy. Although statins have pertinent differences in potency and efficacy,[2] "recommended dosage" could be another confounding factor. In the *British National Formulary*, the highest recommended daily dose for pravastatin is only 40 mg whereas atorvastatin is licensed for use at 80 mg. The lipid lowering efficacy of 40 mg of the former is equivalent to only 10 mg of the latter.[2]

Under these circumstances, failure to reveal and discuss the dosages of the various drugs in the study seriously undermines the conclusions drawn. A blanket endorsement of atorvastatin and simvastatin as the more effective statins oversimplifies an important subject and might inadvertently provide a pseudoscientific basis for misleading advertisements.

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1 Hippisley-Cox J, Cater R, Pringle M, Coupland C. Cross sectional survey of effectiveness of lipid lowering drugs in reducing serum cholesterol concentration in patients in 17 general practices. *BMJ* 2003;325:689-92. (29 March.)
2 Jones P, Kafonek S, Laurora I, Hunninghake D, for the CURVES Investigators. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia. The CURVES Study. *Am J Cardiol* 1998;81:582-7.

Authors' reply

EDITOR—Wang et al, and Kumana and Cheung are concerned by the omission of data on drug dosage. We included an analysis of drug dosage in the original paper submitted to the *BMJ* and removed it at the request of the editorial board. Of the 1116 patients whose serum cholesterol value was above 5 mmol/l, 209 (18.7%) were receiving maximum doses compared with 96 (7.1%) of the 1353 patients who did achieve the target range. In addition, in those patients receiving the maximum dose only 32% (96) achieved the target cholesterol value.

The table shows the number of patients taking each drug who reached target cholesterol values according to whether the maximum dose recommended in the *British National Formulary* had been prescribed. However, we have not looked at equivalent doses when these are submaximal for one drug, but maximal for another.

We did not write the statement "Statins reduce lipid levels better than fibrates"—this appeared in This week in the *BMJ* rather than in our paper. The text was different from the version we submitted, and we had no opportunity to comment on it before publication.

Kumana and Cheung raise the issue of differences between patients taking different statins. As we described in our paper, we took account of potential confounders by including the following variables in the multivariate analysis: sex, age, obesity, smoking status, pretreatment cholesterol values, comorbidity (ischaemic heart disease, diabetes, hypertension, and stroke), and registered general practices. We discussed the potential effect on the results in our discussion.

We think that the "dispersion" mentioned by Wang et al refers to the 95% confidence intervals (which are not standard deviations), and naturally these are narrower for atorvastain and simvastatin because of the larger sample sizes in those groups.

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Achievement of serum cholesterol value of ≤5 mmol/l and use of maximum dose of individual lipid agents

Agent	Maximum dosage	No (%) with cholesterol >5mmol/l	No (%) with cholesterol ≤5 mmol/l	Total	P value (χ^2 or Fisher's exact test)
Simvastatin	No	362 (40.7)	528 (59.3)	890	0.233
	Yes	4 (66.7)	2 (33.3)	6	
	Total	366 (40.8)	530 (59.2)	896	
Pravastatin	No	58 (51.8)	54 (48.2)	112	0.18
	Yes	16 (66.7)	8 (33.3)	24	
	Total	74 (54.4)	62 (45.6)	136	
Cerivastatin	No	63 (41.2)	90 (58.8)	153	0.004
	Yes	53 (60.2)	35 (39.8)	88	
	Total	116 (48.1)	125 (51.9)	241	
Fluvastatin	No	36 (61.0)	23 (39.0)	59	0.06
	Yes	6 (100)	0	6	
	Total	42 (64.6)	23 (35.4)	65	
Atorvastatin	No	377 (40.3)	558 (59.7)	935	0.78
	Yes	7 (43.8)	9 (56.3)	16	
	Total	384 (40.4)	567 (59.6)	951	
Fibrates and others	No	11 (73.3)	4 (26.7)	15	0.92
	Yes	123 (74.5)	42 (25.5)	165	
	Total	134 (74.4)	46 (25.6)	180	

Assisted suicide and euthanasia in Switzerland

Doctors occupy special position

EDITOR—I agree with Hurst and Mauron that the Swiss penal code illustrates how important it is to separate the issue of whether assisting death should be allowed in some circumstances from that of whether doctors should do it.[1] Assistance in dying raises questions that cannot be answered from the perspective of medicine alone.

We should not, however, be misled into denying that doctors inevitably occupy a special position in this issue,[2] and not just