

Ironically, the recognised healthiness of vegetarians in terms of reduced mortality and morbidity^{1,2} may have biased the results in the direction of a spurious health risk. If, for instance, out of the 400 original vegetarian and non-vegetarian tuberculosis cases between 1982 and 1993 the vegetarians amongst them survived in greater numbers and were more represented in the 56 cases in the study, then we are left with a false impression that vegetarian diet is more common amongst cases of tuberculosis.

In the clinic control group there could have been an abnormally low proportion of vegetarians resulting from their better health and lower clinic attendance.³ Then, even with a normal proportion of vegetarians in the cases of tuberculosis, this figure would have appeared higher than the proportion in the controls and would therefore have created a spuriously elevated risk. The same selection mechanisms may have produced a spurious correlation between the level of vegetarianism and risk of tuberculosis.

The postal questionnaire study of Chanarin⁴ quoted by the authors, purporting to show a 2.8 fold increased incidence of tuberculosis in Hindu Asian strict vegetarians, should be discounted since it does not take account of the fact that there were many more vegetarians in the older age groups where the risk of having had tuberculosis is higher.

Finally, stricter Hindu vegetarians may also be more inclined to follow the traditional habit of avoidance of sunlight exposure, which might give rise to a surrogate mistaken association of vegetarian diet with tuberculosis since, as the authors point out, vitamin D deficiency from lack of sunlight may weaken the immune system. While the data have been presented quite strongly as indicating a potential weakening effect of vegetarian diet on the immune system, they may also reflect the selection effects of a health-promoting influence of vegetarian diet consistent with a strengthening of the immune system.

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- 1 Thorogood M, Mann J, Appleby P, McPherson K. Risk of death from cancer and ischaemic heart disease in meat and non-meat eaters. *BMJ* 1994;**308**:1667-70.
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- 4 Chanarin I, Stephenson E. Vegetarian diet and cobalamin deficiency: their association with tuberculosis. *J Clin Pathol* 1988;**41**:759-62.

AUTHORS' REPLY We recognise that British vegetarians have somewhat lower mortality rates than non-vegetarians, but this difference is not large enough to introduce substantial bias as suggested by Dr Davis. In the study by Thorogood *et al*¹ adjusted mortality rates from ischaemic heart disease and cancer among vegetarians were, respectively, 72% and 61% of the corresponding mortality rates for non-vegetarians. If all-cause mortality is reduced by about one third among vegetarians, who accounted for about half of our case group, then, on the most extreme assumption that 15% of non-vegetarian cases died over the follow up period, we would expect 10% of vegetarian cases to die also. This difference in survival would increase the

proportion of vegetarians among survivors by no more than 1-2%, generating a spurious elevation in odds ratio of about 6%. This is far too small to account for the observed odds ratios of 2.5 or greater.

Our suggestion of an increased risk of tuberculosis among vegetarian Asians is not a recommendation against adherence to a vegetarian diet. Dietary advice needs to take account of the balance of risks and benefits across a wide range of major disease outcomes. The importance of our findings is that they may be pointing to a hitherto unrecognised risk associated with vegetarianism which, if our nutritional hypothesis is correct, may be remediable by vitamin supplementation without the need for major dietary change. Indeed, prevention of vitamin D deficiency may be particularly important for the stricter Hindu vegetarians with reduced sunlight exposure who are already recognised as a group at risk of osteomalacia.²

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Control and prevention of tuberculosis in the UK

Recent guidelines on the control and prevention of tuberculosis (December 1994;¹ 1193-200) recommend chemoprophylaxis for children (<16 years) with grade 2-4 Heaf reactions who are close contacts of cases of pulmonary tuberculosis or newly arrived immigrants from high prevalence countries. Chemoprophylaxis, they advise, should also be considered for grade 3-4 Heaf positive young adult immigrants.

The evidence from randomised controlled trials of prophylactic isoniazid underpinning this policy was summarised by Ferebee in 1970¹ and data abstracted from this review for populations comparable to those for whom chemoprophylaxis is recommended are shown in table 1.

Table 1

Trial	Tuberculosis morbidity		Difference in numbers/1000 (95% CI)
	Control	Isoniazid	
Trial 1: US children (1955-7) with "asymptomatic primary TB" and normal chest radiograph	5/495	3/556	4.7 (0 to 12.2)
Trial 2: Household contacts of new "active" cases (1957-9) in the USA, Puerto Rico, and Mexico			
All ages	147/4992	57/4852	17.7 (13.7 to 21.6)
Tuberculin reaction >10 mm			
All ages	31/1616	18/1716	8.7 (2.9 to 14.5)
Tuberculin reaction 5-9 mm			
All ages			
Initial negative tuberculin reaction but 5 mm+ at 12 months (recent converters)	32/867	10/694	22.5 (16.9 to 28.1)
<15 years			
Tuberculin reaction >4 mm	52/3132	17/3022	11.1 (7.3 to 14.7)

Data in the third column show the likely benefit per 1000 people treated; it may be substantially less than expected. US children in the first trial are comparable to non-immunised UK children undergoing testing before BCG vaccination. The end point of this trial was symptomatic disease: two of the five children in the placebo arm developed tuberculous meningitis compared with none of those given chemoprophylaxis, although the difference is not statistically significant. The benefit (five symptomatic cases prevented per 1000 children treated) is small and raises questions about a policy of routine chemoprophylaxis for low risk/low benefit groups.

The end point of the second trial was new cases of tuberculosis in a population of mixed exposure risk (37 US centres, 19 Puerto Rican, and one Mexican). Extrapolation from these data to the UK suggests that nationwide compliance with the guidelines might result in about 980 people per 1000 receiving treatment without expectation of benefit. In view of this evidence, should the benefit of chemoprophylaxis be measured in the UK subgroups at highest risk to justify future policy recommendations?

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- 1 Ferebee SH. Controlled chemoprophylaxis trials in tuberculosis: a general review. *Adv Tuberc Res* 1970;**17**:28-106.

AUTHOR'S REPLY A UK study to establish the benefits of chemoprophylaxis would be very difficult in view of the number of subjects needed, coordination required, and ethical difficulties. However, such a study is unnecessary because the effectiveness of chemoprophylaxis is known. It depends on two factors: firstly, the efficacy of chemoprophylaxis and, secondly, the risk of tuberculosis in the population treated. Efficacy is known to be around 60% from the studies Dr Harding quotes, and others. If we assume 60% efficacy and include a "knock on" factor (1/33) for secondary cases prevented as a result of cases prevented by chemoprophylaxis, we arrive at estimates of effectiveness for a range of at-risk populations as shown in table 2.

The 10 year risk of disease in infected children (most of which is in the first two years) is 8.1%,¹ giving an NNT of 15. The two year risk of disease in contacts of smear