EDITORIAL

An epidemic averted through medical screening

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It is generally recognized that screening for cervical cancer considerably reduces mortality from the disease. This belief holds despite the fact that a randomized clinical trial of cervical cancer screening has never been done and probably never will be done because most would judge it to be unethical to withhold screening in a clinical trial. So epidemiologists must be ingenious in their use of observational data on screening and mortality to show that screening prevents deaths. To their credit, they have made a persuasive case. For example, in one analysis of data from England and Wales it was estimated that by 1978 about 40% of cervical cancer was prevented by screening.[1] An inferred benefit also has been made from the observation of a decline in cervical cancer mortality since the widespread uptake of screening in Europe.[2]

In a recent paper in the *Lancet*, Peto *et al.* continued the tradition of making use of trends in mortality rates to argue that screening saves lives.[3] The authors conclude that screening for cervical cancer has prevented an epidemic that otherwise would have resulted in one death in every 65 British women born since 1950. In doing so, they assume that there is an established screening effect and then estimate the number of cervical cancer deaths that would have occurred in the absence of screening. Specifically, Peto *et al.* use the age-specific cervical cancer mortality rates for five-year time periods between 1953 and 1987 to construct birth cohorts starting from 1882 through to about 1952. Women born in 1882 are observed only at ages 70–85 between 1953 and 1987, while women born in 1952 are observed only until age 35 in this period. The authors sought to estimate the unobserved age-specific rates at older ages among a cohort of young women born in about 1952. This analytical problem is complicated by the fact that cervical cancer mortality rates have been falling in older British women since the 1960s, independent of screening. Their solution was elegant. They noted that the shape of the age distribution of the mortality rates was about the same for each of the birth cohorts. Then they filled in the missing rates for the 1952 birth cohort using a Poisson regression model and demonstrated that the fitted rates for the period between 1953 and 1987 agreed very well with the observed rates.

Thus, they obtain the fitted age-specific mortality rates for the cohort of women born in about 1952. Since approximately a quarter of young women were screened each year in the 1980s,[3] they then inflate these fitted rates by as much as 40% for some of the younger age groups to accommodate the effect of non-systematic screening before the introduction of the national screening programme in 1988. With this inflation factor, these age-specific rates pertain to the counterfactual experience reflecting the ‘absence of screening’ for the 1952 birth cohort. Assuming that these rates would stay constant for future generations, the authors projected that the number of deaths in England and Wales would have reached about 3000 per year by the end of 2002 (1003 cervical cancer deaths occurred in England and Wales in 2002) and may have reached 5500 per year by 2030.[3]

These estimates are defensible, although, as noted by the authors, they are probably imprecise. It is important to remember that it was assumed from the outset that 40% of deaths from cervical cancer in young women were being prevented by screening. That is, the exercise assumes that there is a screening effect, it does not establish one. A limitation of the paper is that the authors are a little zealous in their defense of the national screening programme. The last sentence of the paper mentions ‘unjustified’ criticism of the UK cervical screening programme. What criticism and why was it unjustified? The authors comment that one individual opined that the cost of screening was too expensive and suggested that screening should be restricted to sexually promiscuous women without providing a plan for screening such women, even if ‘promiscuous’ could be defined. Although it is undoubtedly socially unacceptable to identify and label a subset of women in the general population as sexually promiscuous, it probably is defensible to increase the interval between screening examinations in older women involved in a mutually monogamous relationship. Since resources are always limited and screening costs can be prohibitive, consideration of such strategies may be warranted.

Table 1 Number of cervical cancer deaths, the actual to fitted mortality rate, and the estimated number of deaths prevented since the introduction of the National Screening Program by age and calendar year

	Age (years)							
	20–34		35–49		50–64		65–84	
	Deaths	Obs/Fit*	Deaths	Obs/Fit*	Deaths	Obs/Fit*	Deaths	Obs/Fit*
1988–1992	516	0.86	1816	0.70	2067	0.90	3890	0.94
1993–1997	410	0.63	1411	0.41	1495	0.65	2877	0.78
1998–2002	278	0.44	1100	0.28	1262	0.40	2252	0.73
Number of prevented deaths†								
1988–1992	84		778		230		248	
1993–1997	241		2030		805		811	
1998–2002	354		2829		1893		833	

*Observed (actual) mortality rate divided by the fitted rate from the Poisson model:

†$\text{Deaths} * \left(\frac{1-\text{Obs/Fit}}{\text{Obs/Fit}}\right)$

The important point is that cervical cancer screening saves lives, and because of innovative analyses such as that in the Peto paper we can quantify the number of deaths prevented. Furthermore, the data presented in that paper provide additional evidence that screening is beneficial. Table 1 displays the ratio of the actual mortality rate to the fitted rate obtained from the Poisson model for the period 1988–2002. I have added my estimate of the number of deaths prevented since the introduction of the national screening programme in 1988 to Table 1.

In the 15-year period from 1988 to 2002, I estimate the total number of prevented cervical cancer deaths as 11,136, to be compared with 19,374 deaths actually observed. Thus, the proportion prevented is:

$$\frac{11,136}{(11,136 + 19,374)} = 0.36.$$

These prevented deaths are attributable to the national screening programme *per se*, rather than to screening in general. If you combine this prevented fraction to the 0.4 attributed by the authors to non-systematic screening, the total is about 75%. Given the considerable uncertainty associated with such estimates, this figure agrees reasonably well with their statement that 80% or more of cervical cancer deaths are preventable by screening. Thus, screening for cervical cancer was already preventing deaths and the introduction of the national screening programme has accelerated the process.

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REFERENCES

1 Parkin DM, Nguyen-Dinh X, Day NE. The impact of screening on the incidence of cervical cancer in England and Wales. *Br J Obstetr Gynaecol* 1985;**92**:150–7
2 Levi F, Lucchini F, Negri E, Franceschi S, la Vecchia C. Cervical cancer mortality in young women in Europe: patterns and trends. *Eur J Cancer* 2000;**36**:2266–71
3 Peto J, Gilham C, Fletcher O, Matthews FE. The cervical cancer epidemic that screening has prevented in the UK. *Lancet* 2004;**364**:249–56

Obituary

It is with great sadness that we notify readers of the death from prostate cancer of Professor David Brock, FRSE, on 25 November 2004. David was a Founding member of the Editorial Board of the *Journal* and worked with us for thirteen years until illness necessitated his resignation. He made outstanding contributions in biochemical and molecular genetics, much of which had with major implications for medical screening. He will long be remembered.