Letters

Withdrawing low risk women from cervical screening programmes

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Conclusions cannot yet be drawn

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EDITOR—Sherlaw-Johnson et al evaluated policies for withdrawing women from the cervical cancer screening programmes before the recommended age of 64, using a mathematical model.1 Their results were obtained with specific and uncertain model assumptions, which were insufficiently subjected to validation and sensitivity analysis.

From the description of the model in cited earlier papers, most new cases of cervical intraepithelial neoplasia seem to originate at younger ages. The duration is assumed to be independent of age and very long on average (50 years for cervical intraepithelial neoplasia grade III). This implies that most invasive cancers occurring over age 50 started as cervical intraepithelial neoplasia before age 50, which could thus be detected by screening before age 50. Hence this model is bound to predict only small increases in incidence when women are withdrawn from screening before the recommended age of 64.

The sensitivity analysis considers only small adaptations of this basic assumption. Other models, for which detailed analysis of screening data and data on the incidence of cancer was used, resulted in much lower estimates of the mean duration of cervical intraepithelial neoplasia.2–4 These models would predict less favourable effects of withdrawal policies.

Present data on human papillomavirus allow for widely different models, some of which are and some of which are not favourable for use in screening.5 Given this uncertainty, it is not yet possible to come to conclusions about the impact of withdrawing women from cervical screening programmes if results of their smear test and a simultaneous test for high risk types of human papillomavirus are negative.

References

1.Sherlaw-Johnson C, Gallivan S, Jenkins D. Withdrawing low risk women from cervical screening

programmes: mathematical modelling study. *BMJ* 1999; **318**: 356–361.

2.Brookmeyer R, Day NE. Two-stage models for the analysis of cancer screening data. *Biometrics* 1987; **43**: 657–669.

3.Gustafsson L, Adami HO. Natural history of cervical neoplasia: consistent results obtained by an identification technique. *Br J Cancer* 1989; **60**: 132–141.

4.Van Oortmarssen GJ, Habbema JD. Epidemiological evidence for age-dependent regression of pre-invasive cervical cancer. *Br J Cancer* 1991; **64**: 559–565.

5.Van Ballegooijen M, van den Akker-van Marle ME, Warmerdam PG, Meijer CJ, Walboomers JM, Habbema JD. Present evidence on the value of HPV testing for cervical cancer screening: a model-based exploration of the (cost-) effectiveness. *Br J Cancer* 1997; **76**: 651–657.

Authors' reply

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EDITOR—The authors of this letter criticise our assumptions about mean durations of cervical intraepithelial neoplasia, yet our paper makes no mention of such quantities; indeed, there is mathematical ambiguity about what this “mean” represents in the context of disease progression, which is why we have found it wise to avoid the term. Certainly, readers should not be given the impression that our paper is based on the nonsensical assumption that those who develop malignancy have had cervical intraepithelial neoplasia grade III for an average of 50 years. It is not. Our analysis uses assumptions about rates of progression of premalignancy. We have tried to tease out fact from opinion in the authors' letter, and the core criticism seems to be that the progression rates that we assumed are too low.

Ethics preclude direct observation of the rate at which cervical intraepithelial neoplasia grade III progresses when left untreated, and thus inference about transition rates relies on indirect methods. Notwithstanding the authors' high opinion of work investigating such rates, the fact is that little is known with precision, as we point out.

Given this, as reported, we carried out extensive sensitivity analysis to judge the robustness of the conclusions, and assumptions about progression rates were tested over a wide range of values. We have even considered the possibility of regression from cervical intraepithelial neoplasia grade III—an assumption some may find barely credible from a clinical viewpoint. This allowed us to investigate the effects of assuming increased rates of progression from cervical intraepithelial neoplasia grade III (with compensating increases in regression rates to maintain compatibility with United Kingdom data). The effects of this sensitivity analysis on the results reported in our paper are small.

The authors imply that our results favour a policy of early withdrawal. This is an inappropriate value judgment. We predict an increased risk of invasive cancer among women who are withdrawn early. As we have pointed out, the size of the predicted increase depends on several factors, such as the clinical course of disease in older women and the natural course of human papillomavirus infection, for which

complete information is not available. The important question is whether these increases are justified by the resource savings and any other favourable effects of early withdrawal. This touches on ethical and pragmatic issues that are beyond the scope of our study.