Oral contraception and health

IT is now 30 years since two large cohort studies of the benefits and risks of oral contraceptive use were launched in Great Britain. The Royal College of General Practitioners' (RCGP) Oral Contraception Study involved 1400 general practitioners who recruited 46 000 women, half of whom were users of the pill and half of whom were not.[1] The Oxford Family Planning Association (Oxford FPA) contraceptive study involved the staff of 17 family planning clinics and recruited 17 000 women of whom rather more than half were oral contraceptive users while the remainder were users of a diaphragm or an intrauterine device.[2] Both studies have received major financial support from the Medical Research Council and both are still collecting follow-up information.

The two studies differ from each other in a number of important respects. The RCGP study was large in size, was organized around information provided by general practitioners (including diagnostic information about all illnesses), was concerned with a reasonably representative sample of the general population, did not have a lower age limit for recruitment, collected information only about oral contraceptive use, and has had high levels of loss to follow-up over the years (mainly because many women have moved away from participating practices). The Oxford FPA study, on the other hand, was only moderate in size, was organized around information provided by the participating women (including diagnostic information only for illnesses requiring referral to hospital), was concerned with fairly health-conscious clinic attenders with a tendency to come from the middle classes, did not include any women below the age of 25, collected information about all contraceptive methods, and has had high levels of follow-up over the years. Given these major differences, it is reassuring that the findings in the two studies, with regard to the effects of oral contraceptives, have been closely comparable from the very first. Communication between those responsible for running the two studies has, of course, always been close, and many joint papers have been published.

Taken together with the results of numerous case-control studies, it is fair to say that the findings in the two British cohort studies have played a major role in determining what is currently known about the benefits and risks of oral contraceptives. In addition to their high efficacy and acceptability, oral contraceptives suppress menstrual disorders and reduce the risk of iron-deficiency anaemia, suppress benign breast disease, reduce the risk of pelvic inflammatory disease, suppress functional ovarian cysts, and, most importantly, decrease the incidence of ovarian cancer and endometrial cancer by at least 50% — furthermore, these beneficial effects on malignant disease seem to persist for many years in ex-users.

There are several other possible beneficial effects of the pill on the risk of disease, however, for which the evidence is somewhat contradictory or incomplete. These conditions include thyroid disease, rheumatoid arthritis, uterine fibroids, and endometriosis. On the negative side, oral contraceptives are well known to increase the risk of venous thromboembolism, stroke (especially thrombotic stroke), and myocardial infarction. All these effects seem to be limited to current users, while in addition, the arterial (but not the venous) events are concentrated in pill users who smoke. Furthermore, recent work reported by the World Health Organization indicates that measuring blood pressure, both before starting oral contraceptive use and subsequently (and avoiding use in those with elevated levels), can considerably reduce the risk of arterial events attributable to the pill.[3,4]

In addition to the vascular effects of oral contraceptives, there is now strong evidence that current pill users experience a small increase in the risk of breast cancer (about 25%), but this effect wanes in ex-users and is not detectable 10 years after discontinuation.[5] The evidence that pill users experience an increased risk of cervical cancer is also fairly strong, but this effect has not been subjected to such close scrutiny as breast cancer. The effects of any increased risk should be mitigated in any event by routine cervical cytological screening. Oral contraceptive users also experience a slight impairment in fertility after discontinuing use, but this is only a temporary effect. Possible adverse effects of oral contraceptive use include an increase in the risk of gallbladder disease, chronic inflammatory bowel disease, and (extremely rarely) liver tumours. A careful watch is also being kept on any possible relationship between oral contraceptive use and HIV infection.

Clearly, the balance of benefits and risks is of major importance, and a number of reports have been published taking mortality as the relevant endpoint. Some of these reports are based on computer modelling,[6] but the overall patterns of mortality in the RCGP study, the Oxford FPA study, and the Nurses' Health Study have also been published.[7,8,9] In general, the findings have been reassuring.

In this month's *Journal*, Hannaford and Kay have taken a somewhat different approach using the *morbidity* data collected in the RCGP study.[10] They have focused on serious diseases (defined as those which are life-threatening and/or associated with long-term disability) that have been found, or postulated, to be associated with oral contraceptive use. As expected, the findings for individual diseases fit in well with what is already known. In aggregate, the relative risk of serious disease for ever-users of oral contraceptives in comparison with never-users was 1.17 (95% confidence interval = 1.09–1.25). This small increase in overall risk was concentrated in younger women and in current or very recent pill users. By age 50, ever-users had the same risk as never-users while the increased risk seemed to affect only those women using older oral contraceptives containing 50 μg or more of oestrogen.

The analysis presented by Hannaford and Kay is subject to a number of important limitations (which are considered with exemplary care in the discussion section of the report). Nonetheless, the findings add to the reassurance that can be given to women about the effects of oral contraceptives, especially those women in the older age groups who used the pill in the past.

An important limitation of the available epidemiological information from the two cohort studies (and from most case-control studies as well) is that it very largely concerns the use of pills containing 50 μg oestrogen, which are no longer in general use. The relatively small amount of information about pills containing less than 50 μg oestrogen, while reassuring as far as it goes, is insufficient for clear conclusions to be drawn. Hannaford has cautioned against direct extrapolation of data about older, higher-dose pills to newer, lower-dose pills both with respect to benefits and risks.[11] Furthermore, the recent publication of results from epidemiological studies concerned with venous thromboembolism and the pill has suggested that the type of progestogen may be of importance as well as the dose of oestrogen.[12] Sadly,

neither of the two British cohort studies includes a significant amount of information about pills containing gestodene, desogestrel, or norgestimate.

It seems unlikely that any new *ad hoc* large-scale cohort studies of the RCGP type will be set up in this country to monitor the long-term effects of current and future oral contraceptives, although a new Nurses' Health Study is in progress in the United States. One problem that any study of this type will have to deal with is that almost all women now use oral contraceptives at some stage of their reproductive life, so an unexposed control group is not likely to be available.

In the absence of an *ad hoc* cohort study in this country, the General Practice Research Database (GPRD) offers opportunities to fill some of the gaps in knowledge. The GPRD covers a population of about 3.5 million subjects enrolled in 500 general practices, and includes detailed clinical and drug prescription data. The methods used by Jick *et al*[13] in examining the relationship between venous thromboembolism and type of pill could readily be exploited for other diseases, and it is to be hoped that this will be done.

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Evaluating primary care groups

KENNETH Clarke famously precluded the piloting of fundholding on the grounds that this would obstruct its implementation. The same sense of policy imperatives surrounds the introduction of primary care groups (PCGs), but those who ignore the lessons of history are often condemned to repeat them. Academics are not alone in questioning the wisdom of policy divorced from an evidence base. It will be important to ensure that the evaluation of PCGs goes beyond the mechanics of implementation.

How should success criteria for PCGs be defined? The key issue is whether this major organizational upheaval will lead to better and more cost-effective patient care. Answering this question will not be easy. The universal nature of this latest stage in the evolution of primary care-led commissioning excludes the possibility of controlled comparison groups. Those PCGs that elect to enter at level three or four will, by definition, be better organized and more developed than others. It will be difficult to generalize from their experience but it could nevertheless provide useful learning. In these circumstances evaluation is necessarily formative rather than summative. In the short term, any changes will be limited to activity or process and attributing causation will be problematic. Longer term health impact assessment is likely to prove difficult, but the hard questions about the effects on equity, efficiency and quality of care must not be ducked.

The government attaches a high priority to raising standards across the board and avoiding 'two-tierism',[1] but inequities are inevitable if self-selected innovators move swiftly up the ladder. It will be important to monitor the 'inverse care' effect, whereby PCGs servicing the neediest populations struggle to establish themselves. Involvement in well-functioning PCGs could do much to raise standards in poorly performing practices. The advent of clinical governance places new professional responsibilities on general practitioners for the quality of care provided by colleagues as well as themselves, but will create new tensions between practices. PCGs will bring together practices that were ideologically divided, for example over fundholding. Practices with low referral rates or with efficient prescribing policies will be reluctant to share risks with practices perceived as less developed. Ironically, while least likely to want to participate, the latter may have most to contribute to improving the quality of primary care in the locality.

Despite enthusiastic reports of the achievements of those involved in fundholding and other types of primary care commissioning, it has been hard to detect real improvements in the quality of patient care.[2] The Audit Commission found that few fundholders were making full use of the increasing body of knowledge about clinical effectiveness.[3] Clinical governance leads in PCGs will presumably shoulder the burden of promoting and monitoring audit and continuing professional development among the practices they relate to. Existing audit groups will need to be aligned to support this process. Attempts to promote

clinical effectiveness across practices will offer fertile ground for learning about change management in primary care.

The new NHS White Paper promised patient involvement in PCGs.[4] It may be difficult for larger groups to secure consumer involvement. Patients may more easily identify with their own practice and much will depend on the extent to which localities coincide with 'natural communities'. The issue of identity links to the wider question of accountability. In practice, accountability arrangements for fundholders have tended to be based almost exclusively on financial management with little emphasis on accountability to patients and the local public. It will be important to examine the ways in which PCGs make themselves accountable to the people they serve.

Much of the current debate centres on the size of PCGs and whether they will be efficient and effective purchasers. Fundholders fear that the new groups will be too large and that they will lose the leverage they once enjoyed. Others feel that groups covering populations of 100 000 will be too small to counter the power of providers.[5] Financial risk resulting from unpredicted demand is greater when the population pool is small. Received wisdom, based on the experience of health maintenance organizations, suggests that purchasing for populations of less than 50 000 involves punitive transaction costs and unmanageable risks,[6] but this view has been challenged.[7] Models have been devised for spreading the risk over three to five years but these need to be tested.[8]

Effective purchasing requires a wide range of skills, including needs assessment, contracting, performance monitoring, accounting and budget management and specialist knowledge to make strategically coherent decisions. These skills are scarce and expensive. Most of the highest achieving multi-practice total purchasing pilots were in the top quartile of direct costs and they did not necessarily reduce bureaucracy.[9] In theory, larger purchasers should have greater leverage but this is only likely to be true if the PCGs can agree common goals and access the relevant skills. Commissioning for population groups of 100 000, particularly where budgetary control remains with the health authority, ought to reduce transaction costs, but these efficiency gains must be balanced against the reduced incentives for individual practices to control demand by restricting referrals or investing in practice-based facilities as a substitute for more expensive secondary services.

The downside of budgetary control is the uncomfortable fact of having to live within cash limited budgets. Many general practitioners abhor the role of rationer, as it conflicts with their preferred role as patients' advocate,[10,11] and patients may share these concerns.[12] Experience of non-fundholding commissioning groups shows that it is possible to involve primary care staff in setting priorities without delegating budgetary control, but will their commitment endure? Real rather than notional budget setting offers greater incentives for general practitioner involvement, and may be associated with greater success in the achievement of commissioning objectives.

The current policy concern to shift the balance of care from secondary to primary care settings is partly driven by a desire to contain rising health care costs. To date, there are few signs that giving secondary care budgets to general practitioners achieves the desired shift;[13] hence the interest in merging budgets for primary and secondary care. In theory, unified budgets provide more powerful incentives to ensure that investment in primary care is matched by reductions in expenditure on specialist services. However, the risks are considerable:[14] the creative tension of contestability introduced by the purchaser provider split will be diluted if budgets are vertically integrated. Personal medical services pilot schemes provide a potential test-bed for the arrangements likely to be obtained in primary care trusts, and should be carefully evaluated.

The advent of PCGs may fundamentally change the nature of general practice. New systems of corporate governance and accountability with new intermediate structures carry implications for independent contractor status. The research agenda outlined above is of vital importance to patients and to the future development of the National Health Service.

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