New oral contraception study: pilot trial report

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SUMMARY. As a preliminary to a new large cohort study of steroidal contraception, two pilot studies have been carried out. The first estimated that the prevalence of never-use of oral contraceptives among sexually active women aged 16 to 29 years was only 5.1% which means it will be impractical to recruit never-user controls for the main study. The prevalence of cigarette smoking in ever-users of oral contraceptives was 37% in contrast to never-users of whom only 20% smoked.

The second pilot study tested the acceptability of a new recruitment procedure. Two hundred and seventy doctors recruited 1574 women — 98% of these women understood and accepted the need to record their National Health Service number. The mean age of this patient cohort was 22.5 years, 65% were single and 37% were cigarette smokers. One-tenth of women had had coitus before the age of 16 years, but only 4% had started using oral contraceptives before that age.

Introduction

THE current Royal College of General Practitioners' Oral Contraception Study, which began in 1968, is still in progress.[1] While valuable information is still being collected, most of the subjects of this study are now reaching the climacteric. A new large-scale cohort study of steroidal contraception is in prospect which will be similar in design to the earlier study.

A new survey is required, because oral contraceptives have changed considerably over the past 20 years with material reductions in both oestrogen and progestogen content. Thus, many of the health risks associated with the earlier, high-dose, oral contraceptives may have been reduced. Moreover, women now begin taking the 'pill' at an earlier age, irrespective of marital status, so that they are exposed to its effects during their early reproductive years and for a potentially longer portion of their life. A study which evaluates the effect of current formulations and patterns of use on the health of women is urgently needed.

Before embarking on the large study it is necessary to determine the willingness of general practitioners to participate, and to assess the acceptability of recruitment procedures by both doctors and patients alike. Determining the National Health Service (NHS) number of a patient is a potentially sensitive issue but vitally important in that it allows the patient to be traced if she changes her general practitioner, or should further information be required from her about her health in the future. Approval for this has been obtained from the RCGP Clinical Trials Ethical Committee. It is also necessary to determine whether there are sufficient numbers of sexually-active young women who have never used the 'pill' to make the recruitment of control groups practicable.

Two pilot studies have been performed to answer these questions.

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Method

The Royal College of General Practitioners provided a list of 2400 members who were invited to participate in the two pilot studies.

For the study of the prevalence of never-users of the 'pill', 600 doctors were each asked to interview 14 women aged 16 to 29 years inclusive, who presented consecutively for a normal consultation. As it was suspected that a considerable proportion of young women might be attending for contraceptive services, a further 600 doctors were asked to send a simple questionnaire to 14 women in their own homes to obtain a more representative sample of the general population. These doctors selected the first woman in alphabetical order born in each of the years 1955 to 1968 inclusive, using their age–sex registers. The women posted their completed questionnaires directly to the research unit.

For the study of the acceptability of a new recruitment procedure, 1200 general practitioners were invited to participate. Doctors were asked to interview the first four women in each calendar month of a two-month period who attended for new or repeat steroidal contraceptive prescriptions. Thus, each participating doctor should have recruited eight women in total.

In the prevalence study, patients could not be identified by the research unit but in the recruitment study the patient's NHS number was recorded. Both trials were conducted between 1 July and 31 December 1985. Women were defined as being sexually active if they had ever used any form of contraception.

Results

Prevalence study

Of the 600 doctors 157 (26.2%) returned 2023 valid questionnaires for women attending the surgery. Just over 28% of the consultations were for contraceptive services and of these 90% were for oral contraception. In the second part of the study, 184 doctors sent questionnaires to women in their practice, and 1142 women returned complete replies. As the results from both groups of women were not materially different they have been combined and the contraceptive practice of the women is shown in Table 1.

As expected, there was a progressive decrease with increasing age in the number of women who had never used any form of contraception. When women who were not sexually active were excluded, only 5.1% of the women (95% confidence interval 4.3 to 5.9) had never used the 'pill'. Of 'pill' users 48.8% were single compared with 83.2% of non-users. There was a contrast between the proportion of 'pill' users (36.9%) and non-users (19.9%) who currently smoked cigarettes.

Recruitment assessment study

Of the 1200 doctors invited 410 (34.2%) agreed to take part in this study, but only 67 doctors recruited the full complement of eight subjects. The total number of women recruited was 1574.

Most of the women were aged less than 25 years (72.4%), the mean age being 22.5 years. They were mostly single (64.6%), non-smokers (62.6%), white (97.6%) and had finished full-time education by the age of 17 years (55.7%). Three hundred and sixty women (22.9%) were reported to have a relevant previous medical history, and 403 (25.6%) had a relevant family medical history.

The majority (66.0%) of women had started menstruating before the age of 14 years and 65.8% were nulliparous. One-

Table 1. The contraceptive practice of women recruited for the prevalence study.

Year of birth	No. (%) of women		No. (%) of sexually active women[a]	
	All	Never used 'pill'	All	Never used 'pill'
1955	135	10 (7.4)	131	6 (4.6)
1956	194	19 (9.8)	184	9 (4.9)
1957	215	22 (10.2)	205	12 (5.9)
1958	212	21 (9.9)	206	15 (7.3)
1959	251	30 (12.0)	230	9 (3.9)
1960	234	27 (11.5)	219	12 (5.5)
1961	249	21 (8.4)	237	9 (3.8)
1962	257	38 (14.8)	230	11 (4.8)
1963	246	37 (15.0)	216	7 (3.2)
1964	261	40 (15.3)	228	7 (3.1)
1965	264	34 (12.9)	236	6 (2.5)
1966	239	68 (28.5)	184	13 (7.1)
1967	217	83 (38.2)	144	10 (6.9)
1968	191	92 (48.2)	113	14 (12.4)
Total	3165	542 (17.1)	2763	140 (5.1)

[a]Those who have used at least one form of contraceptive.

tenth of the women interviewed had had their first coitus before the age of 16 years, although only 4.2% of the women had started taking oral contraceptives before that age. Over half of the women (56%) had had sexual intercourse before their eighteenth birthday. Most women had taken the 'pill' prior to the recruitment consultation (92.6%) and 52.9% of these had taken the 'pill' continuously. Combined oral contraceptives containing ethinyloestradiol (30 μg) and levonorgestrel (150 μg) were most frequently prescribed (38.2%), although triphasic preparations were also commonly prescribed (30.9%). The NHS number was recorded on 98% of the patients' forms and in each case the doctor confirmed that he had obtained the patient's informed verbal consent.

Discussion

The investigation of the prevalence of never-use of the 'pill' in two different populations proved worthwhile, in that it showed that the surgery attenders interviewed were not unrepresentative of the female population as a whole. The results obtained from these studies demonstrate the problems of selecting a suitable control population. The mean age of the women in the recruitment study was 22.5 years, and the prevalence study shows that only 3.2% of women of this age had never used the 'pill'. This means that for every 'pill' user doctors would have to interview 29 women, on average, to find one age-matched never-user. That would make the study unacceptable. Furthermore, never-users are not an appropriate comparison group, since they are likely to have special characteristics, especially personality differences, which would be difficult to measure — the difference in smoking habits demonstrated in the prevalence study is important evidence in this respect. Undoubtedly, the absence of never-users will present problems in interpretation of the data, but where relationships to dose, duration of use and other variables can be demonstrated these provide better evidence of associations than comparisons with the experience of never-users, because of the reduced likelihood of biased observations.

Approximately 120 000 women will need to be recruited to the main study if the postulated small changes in risks associated with low-dose steroidal contraceptives are to be assessed. This will require approximately 3000 doctors recruiting 40 patients each. Of the doctors invited to participate in the recruitment pilot trial 34% did so — a higher proportion than expected — but it was disappointing that few doctors managed to recruit the target number of eight subjects. One of the main reasons for this poor recruitment is likely to have been that the pilot trial was conducted during the summer holiday period. The main study will be launched in spring or autumn. There may also be less enthusiasm to participate in a pilot trial than a main study. There was excellent compliance with the request for the patients' NHS numbers.

The proportion of women who smoke (37%) has fallen when compared with the proportion (48%) recruited in 1968 for the current Oral Contraception Study.[1] However, a greater proportion of 'pill' users smoke than never-users. Ten per cent of the women had experienced their first coitus before the age of 16 years, although only 4% had started using the 'pill' before then. As the prevalence study indicated that only a small number of sexually active women used contraceptive methods other than the 'pill', this suggests that there might be an undesirably high proportion of teenage women having unprotected sexual intercourse.

In summary, the present pilot studies have indicated the lack of feasibility of recruiting non-users of the 'pill' as suitable controls for a new steroidal contraception study. An acceptable level of enthusiasm to participate in a new large cohort study is indicated, and the recruitment procedure adopted in the pilot trials can be used in the main study with only minor adjustments.

Reference

1. Royal College of General Practitioners. *Oral contraceptives and health*. London: Pitman Medical, 1974.

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Risk of heart disease in the young

The relationship between risk factors for cardiovascular disease and early atherosclerotic lesions in the aorta and coronary arteries was assessed in 35 young people (mean age at death 18 years). Aortic involvement with fatty streaks was greater in Black people than in White (37 versus 17%, $P<0.01$). However, aortic fatty streaks were strongly related to antemortem levels of both total and low-density lipoprotein cholesterol ($r = 0.67$, $P<0.0001$ for each association), independently of race, sex and age, and were inversely correlated with the ratio of high-density lipoprotein cholesterol to low-density plus very-low-density lipoprotein cholesterol ($r = -0.35$, $P = 0.06$). Coronary-artery fatty streaks were correlated with very-low-density lipoprotein cholesterol ($r = 0.41$, $P = 0.04$). Mean systolic blood pressure levels also tended to be higher in the four subjects with coronary-artery fibrous plaques than in those without them: 112 mmHg as compared with 104 ($P = 0.09$). These results document the importance of risk-factor levels to early anatomical changes in the aorta and coronary arteries. The progression of fatty streaks to fibrous plaques is uncertain, but these data suggest that a rational approach to the prevention of cardiovascular disease should begin early in life.

Source: Newman WP, Freedman DS, Voors AW, *et al.* Relation of serum lipoprotein levels and systolic blood pressure to early atherosclerosis. The Bogalusa heart study. *N Engl J Med* 1986; **314**: 138-144.