Diabetologia (1992) 35: 967–972

Diabetologia

Oral contraceptive use and the risk of Type 2 (non-insulin-dependent) diabetes mellitus in a large prospective study of women

E. B. Rimm,[1] J. E. Manson,[4] M. J. Stampfer,[1,4] G. A. Colditz,[1,4] W. C. Willett,[1,2,4] B. Rosner,[3,4] C. H. Hennekens[4] and F. E. Speizer[4]

Departments of [1] Epidemiology, [2] Nutrition, and [3] Biostatistics, Harvard School of Public Health and the [4] Channing Laboratory, Department of Medicine, Harvard Medical School and the Brigham and Women's Hospital, Boston, Massachusetts, USA

Summary. We examined the association between oral contraceptive use and incidence of Type 2 (non-insulin-dependent) diabetes mellitus among 115117 female nurses free of diabetes, cardiovascular disease and cancer in 1976 and followed-up for 12 years. During 1237440 person years of follow-up, 2276 women who provided information on oral contraceptive use were clinically diagnosed with Type 2 diabetes. Women who used oral contraceptives in the past had only a slight and marginally increased relative risk of 1.10 (95% confidence interval 1.01, 1.21) compared to those women who had never used oral contraceptives after controlling for known risk factors of disease. We found no evidence of increased risk with longer duration of use or with shorter interval since last use. Current users did not have an increased risk of Type 2 diabetes (relative risk = 0.86, 95% confidence interval 0.46, 1.61) when compared to women who had never used the drug. There was no effect modification by obesity, family history of diabetes, or physical activity. These data suggest that past or current oral contraceptive use does not substantially influence subsequent risk of Type 2 diabetes.

Key words: Oral contraceptives, diabetes mellitus, epidemiology, prospective study.

Current use of oral contraceptives increases serum glucose and insulin levels after a standard glucose challenge [1–4] and may also adversely alter lipid profiles [5]. Although current users of oral contraceptives may have a higher risk of cardiovascular disease compared with never-users [6], the long-term effects of oral contraceptives on the development of Type 2 (non-insulin-dependent) diabetes mellitus remain relatively unexplored.

Goldman [7] suggests that long-term oral contraceptive use may contribute to a deterioration of glucose tolerance. This additional stress on the endocrine system may increase the risk of diabetes among a population of women already at high risk of developing diabetes [4, 8]. Previous studies have found no clear association between oral contraceptives and Type 2 diabetes [9, 10]. However, small to moderate effects may not have been detected due to inadequate statistical power or lack of information on potential confounders. To determine whether an association between current or past use of oral contraceptives is associated with an increase in Type 2 diabetes and whether any such association is altered by established risk factors for Type 2 diabetes, we examined the relationship prospectively among 115117 participants in the Nurses' Health Study.

Subjects and methods

Population

The Nurses' Health Study cohort was established in 1976 when 121700 female registered nurses, aged 30–55 years, living in 11 states of the United States returned mailed questionnaires. The baseline questionnaires included sections for past history of disease, height, weight, smoking status, oral contraceptive use, post-menopausal hormone use, and other demographic variables. Every 2 years, participants are mailed follow-up questionnaires to update information on oral contraceptive use and other risk factors and to ascertain newly-diagnosed diseases. This report includes all women with newly-diagnosed Type 2 diabetes between 1976 and 1988. Additional information was collected in 1980 and 1982 to ascertain physical activity levels, alcohol consumption [11] and family history of diabetes.

Oral contraceptives

A complete history of past and present oral contraceptive use was obtained from those who responded to the 1976 baseline questionnaire. Subsequent use of oral contraceptives was ascertained from the next three (1978–1982) biennial follow-up questionnaires. Current use was defined as oral contraceptive use within 1 month of questionnaire return. Past use was defined as use that had ceased at least 1 month before the date of return of the questionnaire. Variables for total months of current and past use were constructed by

Table 1. Baseline characteristics according to oral contraception status among 115,117 women from the United States, 30–55 years of age, free from cardiovascular disease, cancer, and Type 2 (non-insulin-dependent) diabetes mellitus in 1976[a]

Characteristic	Oral contraceptive status				Current
	Never	Past			
		1–11 months	12–59 months	60 + months	
Number[b] (*n*)	60,331	12,201	21,088	11,985	7,062
Mean age (years) (SD)	49.1 (6.6)	43.6 (6.5)	41.9 (6.4)	44.7 (6.3)	41.3 (6.0)
BMI (kg/m^2)	24.1	23.8	23.6	23.7	23.3
Family history[c] of diabetes	16.6	16.5	17.0	17.0	14.3
Alcohol[d] (g/day)	5.1	5.8	6.4	7.2	6.9
Physical activity[e]/ week	1.2	1.2	1.2	1.2	1.2
Physician visits[f]					
0	44.7	37.9	38.9	38.2	38.1
1	20.4	20.8	21.5	22.2	23.7
2 +	34.9	41.3	39.6	39.6	38.2

[a] All characteristics are directly age-standardized to the population of never users.
[b] Information was missing on contraception status of 2450 women in 1976;
[c] A family history of diabetes is defined as a mother, father or sibling with diagnosed diabetes (1982 follow-up questionnaire);
[d] Average alcohol per day measured from a food frequency questionnaire administered in 1980;
[e] Average number of weekly episodes of physical activity which lasted long enough to work up a sweat (1980 follow-up questionnaire);
[f] Number of physician visits during the previous year (1980 follow-up questionnaire)

summing information from baseline and follow-up questionnaires. Duration since last use was updated every 2 years using history of oral contraception from the baseline questionnaire and follow-up questionnaires. Information on specific brands and dosages of oral contraceptives was not available.

Definition of Type 2 diabetes

Among the 121 700 women originally enrolled in the Nurses' Health Study, 115 117 were free from diabetes, coronary heart disease, and cancer in 1976. We mailed a supplementary questionnaire to women who responded positively on any follow-up questionnaire to the question, "have you been physician-diagnosed with diabetes?". We defined confirmed cases of diabetes if at least one of the following conditions was reported on the supplementary questionnaire: 1) one or more classic symptoms (thirst, polyuria, weight loss, hunger, genital pruritus) plus an elevated fasting ($\geq$ 7.8 mmol/l) or random ($\geq$ 11.1 mmol/l) plasma glucose, or 2) at least two elevated plasma glucose levels (fasting at least 7.8 mmol/l or random at least 11.1 mmol/l or 11.1 mmol/l after more than 2 h post glucose tolerance test) in the absence of symptoms, or 3) treatment with a hypoglycaemic medication. We excluded 63 cases of Type 1 (insulin-dependent) diabetes and 7 women with gestational diabetes only. Criteria for the classification of diabetes have been published in detail elsewhere [12].

The validity of the diagnosis was documented using a random sample of participants reporting diabetes. Of 84 women with confirmed diabetes by supplementary questionnaire, 71 provided permission to obtain medical records; 62 (87%) had available medical records. An endocrinologist (J. E. M.), without knowledge of the information provided by the supplementary questionnaire, confirmed the diagnosis from medical records in 98.4% (61 of 62) of the women using the National Diabetes Data Group criteria [13].

Statistical analysis

Person-months of follow-up were accumulated for each category of oral contraceptive use. Exposure categories were updated every 2 years. Women accumulated person-time of exposure until the date they were diagnosed with diabetes, cancer, or heart disease or the time in which they moved to a different exposure category or until the end of follow-up in 1988. Relative risks (RR) were initially calculated adjusting for 10 categories of BMI (kg/m^2) and 5-year age intervals using the Mantel-Haenszel summary statistic. We also calculated 95% confidence intervals (CI) and, where applicable, Mantel-extension tests for trend across increasing past duration and time since last use of oral contraceptives. Cox proportional hazard models were used to control simultaneously for potential confounders. Because alcohol intake and physical exercise were not measured until 1980, proportional hazard models with these potential confounders only include incident diabetes after the return of the 1980 follow-up questionnaire.

Results

In 1976, 52 336 (46.5%) women reported past or current use of oral contraceptives (Table 1). Many characteristics differed among the groups. Compared to women who never used oral contraceptives, past users were younger, slightly less obese, reported more alcohol consumption in 1980, and were more likely to have seen a physician in the year previous to the return of the 1980 questionnaire. Among past users, alcohol consumption increased with longer duration of past oral contraceptive use. Except for being slightly younger and having a lower prevalence of familial diabetes, women who were current oral contraceptive users in 1976 were similar to past users.

Among women who provided information on oral contraceptive use, we confirmed 2276 incident cases of Type 2 diabetes during 1 237 440 person-years of follow-up. Follow-up was more than 98% complete for all women who answered the baseline 1976 questionnaire. Compared to women never using oral contraceptives, current users did not have an increased risk of Type 2 diabetes (Table 2). After adjusting for age and BMI, past users of oral contra-

Table 2. Age- and obesity (kg/m^2)-adjusted relative risks of Type 2 (non-insulin-dependent) diabetes mellitus among never, past and current users of oral contraceptives. Data from 1237440 person-years of follow-up between 1976 and 1988 among women from the Nurses' Health Study

Type 2 diabetes diagnosed ($n = 2276$)	Oral contraceptive use		
	Never	Past	Current
Cases	1,482	783	11
Person-years	686,524	527,319	23,596
Age-adjusted relative risk (95% CI)[a]	1.0 (Referent)	1.04 (0.95, 1.14)	0.56 (0.31, 1.02)
Age- and obesity-adjusted relative risk (95% CI)[b]	1.0	1.11 (1.01, 1.23)	0.77 (0.41, 1.46)
Multivariate relative risk (95% CI)[c]	1.0	1.10 (1.01, 1.21)	0.86 (0.46, 1.61)
Symptomatic cases only ($n = 1616$)			
Cases	1,042	567	7
Age- and obesity-adjusted relative risk (95% CI)[b]	1.0 (Referent)	1.13 (1.01, 1.27)	0.60 (0.27, 1.36)
Multivariate relative risk (95% CI)[c]	1.0	1.09 (0.98, 1.22)	0.71 (0.32, 1.57)

[a] Controlling for 5-year age categories.
[b] Controlling for 5-year age categories and 10 categories of obesity (kg/m^2).
[c] Controlling for 5-year age categories, 10 categories of obesity (kg/m^2), smoking (never, past, current (1–14 cigarettes/day, 15–24 cigarettes/day, 25 + cigarettes/day)), menopause, post-menopausal hormone use, family history of diabetes (yes/no), and 2-year time periods. Women with missing information of past duration of use were included in the past use category

ceptives had a slightly elevated risk of development of Type 2 diabetes (RR = 1.11, 95% CI 1.01, 1.23) compared with women who had never used them. Because only 11 of the 794 women who had ever used oral contraceptives were diagnosed with Type 2 diabetes as a current user, the relative risk of Type 2 diabetes among women who had ever used oral contraceptives (RR = 1.11, 95% CI 1.00, 1.22), as compared to having never used was very similar to the risk among past users. Multivariate adjustment for age, BMI, family history of diabetes, cigarette smoking, menopause, and post-menopausal hormone use did not appreciably alter any of these results (Table 2).

In 1980, current and past users of oral contraceptives were more likely than women never using oral contraceptives to have seen a physician in the previous year, and therefore may be more likely to have been screened for diabetes. To reduce the possible bias due to the incidental diagnosis of diabetes among women seeing a physician for a separate reason, we repeated the analyses including only the symptomatic cases, specifically women who reported one or more classic symptoms (thirst, polyuria, weight loss, hunger, genital pruritus) at presentation. The multivariate risk of Type 2 diabetes, among this subset of women ($n = 1616$ cases), was 1.09 (95% CI 0.98, 1.22) for past users and 0.71 (95% CI 0.32, 1.57) for current users as compared to women never using oral contraceptives. Further, controlling for the number of physician visits in a multivariate model that included only incident cases occurring after 1980 also did not appreciably alter the relative risk of diabetes among women with a history of past and current use of oral contraceptives, as compared to women who had never used them.

We previously reported moderate inverse associations between physical activity [12] and alcohol consumption [14] and the risk of subsequent diabetes. Because data on alcohol intake and physical activity were first collected on the 1980 follow-up questionnaire, only incident cases after the return date of the 1980 questionnaire were included in multivariate models which controlled for physical activity and alcohol intake, as well as the above-mentioned potential confounders. Adding physical activity and alcohol consumption (1980–1988 cases only) to the multivariate model did not substantially change the relative risk of Type 2 diabetes for past users (RR = 1.10, 95% CI 0.98, 1.23), too few women were current users (only 1574 person-years) after 1980 for a meaningful analysis.

To investigate further the association between past oral contraceptive use and future development of Type 2 diabetes, past use was classified into three categories of duration. No clear pattern of risk was found with increased duration of past use (Table 3). There was no evidence of increasing risk with increased duration of past use (p, trend = 0.67). The total person-years of current oral contraceptive use was too small to stratify by duration of use.

If oral contraceptive use were to increase risk of Type 2 diabetes through acute serum glucose elevation we would have expected to see a diminution of effect with increased time since last use. We categorized time since last use of oral contraceptives into four categories of 0–11 months, 1–5 years, 5–10 years and greater than 10 years since last use. We found no significant reduction in risk of Type 2 diabetes among past users with increase in time since last use (p, trend = 0.11). Compared to women who never used oral contraceptives, the relative risk of Type 2 diabetes among women who had stopped using them during the past 1 to 11 months was 1.25 (95% CI 0.84, 1.96); 1–5 years was 0.75 (95% CI 0.57, 1.00); 5–10 years was 1.19 (95% CI 1.01, 1.40); and more than 10 years ago was 1.14 (95% CI 1.01, 1.28). The increase in risk of Type 2 diabetes among past users was marginally significant only among women whose oral contraceptive use had ceased for at least 5 years.

Since obesity and family history of diabetes are associated with oral contraceptive use and are also strong predictors of Type 2 diabetes in this population [15], we analysed differences in risk associated with past oral contraceptive use within categories of obesity or family history. Using categories of BMI derived from this population in a previous report [15], we found that the lack of association between oral contraceptive use and risk of Type 2 diabetes did not vary appreciably by BMI categories (Table 4). Similarly, risk of Type 2 diabetes from oral contraceptive use was not altered by a positive or negative family history of diabetes. Among women with a family history of diabetes, the relative risk of Type 2 diabetes for past users of oral contraceptives was 1.07

Table 3. Relative risks of Type 2 (non-insulin-dependent) diabetes mellitus according to duration of past oral contraceptive use among past users of oral contraceptives. Data from 12 years of follow-up between 1976 and 1988 among women from the Nurses' Health Study

Type 2 diabetes diagnosed	Never	Duration of past oral contraceptive use		
	(Referent)	1–11 Months	12–59 Months	60 + Months
Cases	1,482	346	243	194
Age-adjusted relative risk (95% CI)[a]	1.0	1.09 (0.96, 1.23)	1.00 (0.87, 1.16)	0.96 (0.82, 1.12)
Age- and obesity-adjusted relative risk (95% CI)[b]	1.0	1.10 (0.97, 1.25)	1.12 (0.96, 1.31)	1.09 (0.92, 1.28)
Multivariate relative risk (95% CI)[c]	1.0	1.12 (0.96, 1.30)	1.12 (0.99, 1.28)	1.04 (0.91, 1.20)
Symptomatic cases only (n = 1,616)				
Cases	1,042	250	162	155
Age- and obesity-adjusted relative risk (95% CI)[b]	1.0	1.14 (0.98, 1.32)	1.01 (0.83, 1.23)	1.21 (1.00, 1.46)
Multivariate relative risk (95% CI)[c]	1.0	1.10 (0.93, 1.31)	1.05 (0.90, 1.23)	1.08 (0.92, 1.27)

[a] Controlling for 5-year age categories;
[b] Controlling for 5-year age categories and 10 categories of obesity (kg/m^2);
[c] Controlling for 5-year age categories, 10 categories of obesity (kg/m^2), smoking (never, past, current (1–14 cigarettes/day, 15–24 cigarettes/day, 25 + cigarettes/day)), menopause, post-menopausal hormone use, family history of diabetes (yes/no), and 2-year time periods

(95% CI 0.91, 1.25) as compared to women who never used them.

Discussion

In these prospective cohort data, we found no evidence of a positive association between current oral contraceptive use and risk of Type 2 diabetes. Women who had previously used oral contraceptives had a marginally increased risk of Type 2 diabetes compared with women who had never used them. This risk was not associated with longer duration of past use or shorter time since last use. The relative risk of Type 2 diabetes among past and current users of oral contraceptives was not appreciably modified by obesity or family history of diabetes.

We have not validated self-reports of oral contraceptive use in this population. However, Coulter et al. [16] previously found that women accurately self-report past and present oral contraceptive use. Among a subset of this population, we have reported on the favourable validity of self-reported diet [17], circumference measurements and weight [18], as well as other risk factors for chronic disease [19]. Further, we, as have others [6, 20–22] found that current oral contraceptive use was a significant predictor of cardiovascular disease [23] and that past oral contraceptive use did not increase the risk of cardiovascular disease [23], consistent with a meta-analysis of the published literature [24]. The reliability of other self-reported exposure measurements among this population and the consistency of our data with other studies of the association between oral contraceptives and cardiovascular disease suggest the nurses in this cohort accurately self-report oral contraceptive use.

The prospective nature of the study reduces the risk of bias associated with differential recall of past contraceptive use. Because oral contraceptive users are more likely to visit their physician, surveillance bias among users may inflate the diagnosis rate in this population. If increased surveillance among past or current oral contraceptive users artificially increased the rate of diagnosis, we would expect an inflated relative risk among current oral contraceptive users. However, current users of oral contraceptives had no increased risk and possibly even a reduced risk of Type 2 diabetes as compared to never-users or past users in our population. Furthermore, restricting the analyses to symptomatic cases of diabetes did not appreciably alter the findings.

Alternatively, if oral contraceptives adversely affect a subpopulation of susceptible women, we may expect these women to discontinue oral contraceptives after failing a glucose tolerance test. This could artificially create an association among recent past users. However, we only found a significant positive association between past use of oral contraceptives and risk of Type 2 diabetes among women who had stopped taking oral contraceptives for 5 or more years, a time long after which the transitory effects of oral contraceptives on glucose tolerance would have ended [25]. Therefore, surveillance bias only among distant past users of oral contraceptives is unlikely to explain the reported association.

After controlling for 10 categories of relative weight, residual confounding may still exist among the top categories where the increased relative risk of diabetes was over 20 times that of the leanest women [15]. However, past users of oral contraceptives were less obese than women who had never used them. Therefore, residual confounding by relative weight would, if anything, attenuate the association between oral contraceptives and Type 2 diabetes. Other possible confounders that we have previously shown to be associated with diabetes, including alcohol [14] and exercise [12] were controlled in the analyses.

During the past few decades there has been a general shift from high- to low-dose preparations of oral contra-

Table 4. Age-adjusted relative risks and 95% confidence intervals of Type 2 (non-insulin-dependent) diabetes mellitus by BMI at baseline among never, past and current users of oral contraceptives. Data from 1,237,440 person-years of follow-up between 1976 and 1988 among women from the Nurses' Health Study[a]

BMI (kg/m^2)	n	Oral contraceptive use		
		Never	Past	Current
< 23.9	207	1.00 (Referent)	1.24 (0.91, 1.67)	0.59 (0.03, 3.97)
24.0–26.9	226	1.00	1.17 (0.88, 1.56)	0.88 (0.17, 4.49)
27.0–28.9	233	1.00	1.28 (0.96, 1.69)	0.77 (0.11, 5.26)
29.0–31.9	400	1.00	1.04 (0.83, 1.29)	0.47 (0.07, 3.20)
32 +	818	1.00	1.07 (0.92, 1.25)	1.00 (0.41, 2.42)

[a] Type 2 diabetes was documented among 1,884 women with valid exposure information for oral contraceptive use and BMI in 1976

ceptives [26]. Women in this cohort reporting contraceptive use before 1976 may have been prescribed higher doses. Because information was not available on specific brands and dosages, we cannot account for dosage in our analyses. Therefore, our relative risk estimates among past users are a summary risk estimate over all dosage preparations, potentially attenuating a moderate association among women taking high dosages.

In summarizing experimental studies of high-dose oral contraceptives, Gaspard and Lefebvre [26] concluded that combined oral contraceptives (oestrogen plus progestins) may chronically increase blood glucose and insulin levels as well as the incidence of impaired glucose tolerance, suggesting a possible link with development of overt diabetes. The trend in the 1960s and 1970s to move from high- to low-dose oral contraceptives (or from higher to lower risk of glucose intolerance) may explain the null association we found among women in the current use category, where all current use was after 1976.

Current oral contraceptive use clearly alters carbohydrate metabolism [2, 26]. Depending on type and dose, the transient diabetogenic stress has been shown to cause an increase in impaired glucose tolerance among high-dose users as compared to women not using oral contraceptives [25, 27]. However, the increase in post-load glucose levels among current high-dose oral contraceptive users is generally reversible [26, 28], supporting the hypothesis that past oral contraceptive users should not have a large increase in risk of Type 2 diabetes. Indeed, proposed mechanisms for risk of diabetes suggest that the acute metabolic changes from oral contraceptives impair glucose tolerance. If women who currently use oral contraceptives are at higher risk of diabetes (although our data were unable to show this perhaps due to increasing trends toward lower dose preparations or small numbers in this category), we would still expect to see a positive trend in risk with increased duration and shorter time since last use. Because risk does not increase with longer duration of use or shorter time since last use, our data support the hypothesis that oral contraceptives do not substantially increase a woman's risk of clinical Type 2 diabetes.

Others have examined the association between oral contraceptives and overt Type 2 diabetes, although no consistent relationship has been reported. Duffy and Ray [10] prospectively followed 593 women who had failed a 1-h glucose screening test (75 g glucose load followed by serum glucose > 11.1 mmol/l). After an average of 8.55 years of follow-up 54 women were diagnosed with incident impaired glucose tolerance or diabetes. They found a significantly increased risk of impaired glucose tolerance or diabetes among women currently using oral contraceptives (compared to past users or women who had never used them) only among the subset of women at lowest risk from other causes (no family history and not obese). Among all women with prevalent or incident impaired glucose tolerance or diabetes during the study period ($n = 118$ or 19.9%), no increased risk was associated with past or current use of oral contraceptives.

Hannaford and Kay [9] found no increased risk of clinical diabetes among current (RR = 0.80, 95% CI 0.49, 1.32) or past users (RR = 0.82, 95% CI 0.59, 1.13) of oral contraceptives as compared to women who never used them after following 46000 women for up to 21 years as part of the Royal College of General Practitioners' oral contraception study. Although risk factors for diabetes such as BMI and family history were not adjusted for in their analysis, it is unlikely that confounding would substantially alter these reported rates. Age-adjusted relative risks in our population were only slightly different from risk estimates adjusted for obesity, family history, and other potential confounders.

Although oral contraceptive use may cause transitory elevation of glucose, triglyceride, and lipid levels, some of which may potentially be atherogenic, most effects are reversible after discontinuation [26]. Our findings from this large prospective cohort of women provide strong evidence that, after controlling for known risk factors of Type 2 diabetes, current use of oral contraceptives (presumably low-dose preparations) do not increase a woman's risk of Type 2 diabetes. Although we do report a marginal increase in risk of Type 2 diabetes among past users of oral contraceptives, the risk reached statistical significance only among women who had used oral contraceptives in the distant past, supporting the hypothesis that recent trends toward lower dose preparations may eliminate the marginal risk of Type 2 diabetes attributable to past oral contraceptive use.

Acknowledgements. Supported by Research Grants DK 36798 and CA 40356 from the National Institutes of Health. Dr. E. Rimm was supported by a National Institute of National Research Service Award 5T32 CA09001. The authors thank the participants of the Nurses' Health Study for their continued cooperation and participation. The authors are also indebted to Ms. M. Ireland, Ms. K. Corsano, Mr. M. Shneyder, Mr. G. Chase, Ms. M. Johnson, and Mr. S. Stuart for their expert and unfailing assistance.

References

1. Eschwège E, Fontbonne A, Simon D et al. (1990) Oral contraceptives, insulin resistance and ischemic vascular disease. Int J Gynecol Obstet 31: 263–269

2. Godsland IF, Crook D, Simpson R et al. (1990) The effects of different formulations of oral contraceptive agents on lipid and carbohydrate metabolism. N Engl J Med 323: 1375–1381
3. Spellacy WN (1976) Carbohydrate metabolism in male infertility and female fertility-control patients. Fertil Steril 27: 1132–1141
4. Russell-Briefel R, Ezzati TM, Perlman JA, Murphy RS (1987) Impaired glucose tolerance in women using oral contraceptives: United States, 1976–1980. J Chronic Dis 40: 3–11
5. Gespard UJ (1987) Metabolic effects of oral contraceptives. Am J Obstet Gynecol 157: 1029–1041
6. Mann JI, Vessey MP, Thorogood M, Doll R (1975) Myocardial infarction in young women with special reference to oral contraceptive practice. Br Med J 2: 241–245
7. Goldman JA (1978) Intravenous glucose tolerance after 18 months on progestogen or combination-type oral contraceptive. Israel J Med Sci 14: 324–327
8. Wynn V, Doar JWH (1966) Some effects of oral contraceptives on carbohydrate metabolism. Lancet II: 715–719
9. Hannaford PC, Kay CR (1989) Oral contraceptives and diabetes mellitus. Br Med J 299: 1315–1316
10. Duffy TJ, Ray R (1984) Oral contraceptive use: prospective follow-up of women with suspected glucose intolerance. Contraception 30: 197–208
11. Giovannucci E, Colditz GA, Stampfer MJ et al. (1991) The assessment of alcohol consumption by a simple self-administered questionnaire. Am J Epidemiol 133: 810–817
12. Manson JE, Rimm EB, Stampfer MJ et al. (1991) Physical activity and incidence of noninsulin-dependent diabetes mellitus in women. Lancet 338: 774–778
13. National Diabetes Data Group (1979) Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 28: 1039–1057
14. Stampfer MJ, Colditz GA, Willett WC et al. (1988) A prospective study of moderate alcohol drinking and risk of diabetes in women. Am J Epidemiol 128: 549–558
15. Colditz GA, Willett WC, Stampfer MJ et al. (1990) Weight as a risk factor for clinical diabetes in women. Am J Epidemiol 132: 510–513
16. Coulter A, Vessey M, McPherson K, Crossley B (1986) The ability of women to recall their oral contraceptive histories. Contraception 33: 127–137
17. Willett WC, Sampson LS, Stampfer MJ et al. (1985) Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol 122: 51–65
18. Rimm EB, Stampfer MJ, Colditz GA, Chute EG, Litin LB, Willett WC (1990) Validity of self-reported waist and hip circumferences in men and women. Epidemiology 1: 466–473
19. Colditz GA, Martin P, Stampfer MJ et al. (1986) Validation of questionnaire information on risk factors and disease outcomes in a prospective cohort study of women. Am J Epidemiol 123: 894–900
20. Shapiro S, Slone D, Rosenberg L, Kaufman DW, Stolley PD, Miettinen OS (1979) Oral-contraceptive use in relation to myocardial infarction. Lancet I: 743–747
21. Hennekens CH, Evans D, Peto R (1979) Oral contraceptive use, cigarette smoking and myocardial infarction. Br J Fam Plann 5: 66–67
22. Ory H (1977) Association between oral contraceptives and myocardial infarction: a review. JAMA 237: 2619–2622
23. Stampfer MJ, Willett WC, Colditz GA, Speizer FE, Hennekens CH (1988) A prospective study of past use of oral contraceptive agents and risk of cardiovascular disease. N Engl J Med 319: 1313–1317
24. Stampfer MJ, Willett WC, Colditz GA, Speizer FE, Hennekens CH (1990) Past use of oral contraceptives and cardiovascular disease: a meta-analysis in the context of the Nurses' Health Study. Am J Obstet Gynecol 163: 285–291
25. Russell-Briefel R, Ezzati T, Perlman J (1984) Impaired glucose tolerance and diabetes in women using oral contraceptives. Fed Proc Fed Am Soc Exp Biol 43: 666 (Abstract)
26. Gaspard UJ, Lefebvre PJ (1990) Clinical aspects of the relationship between oral contraceptives, abnormalities in carbohydrate metabolism, and the development of cardiovascular disease. Am J Obstet Gynecol 163: 334–343
27. Perlman JA, Russell-Briefel R, Ezzati T, Lieberknecht G (1985) Oral contraceptive tolerance and the potency of contraceptive progestins. J Chronic Dis 38: 857–864
28. Philips N, Duffy T (1973) One-hour glucose tolerance in relation to the use of contraceptive drugs. Am J Obstet Gynecol 116: 91–100

Received: 9 April 1992
and in revised form: 10 June 1992

Dr. E. B. Rimm
Channing Laboratory
180 Longwood Avenue
Boston, MA 02115
USA