



A Prospective Study of Oral Contraceptive Use and Risk of Myocardial Infarction among Swedish Women

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Background

- Oral contraceptives (OC) have been used by more than 80% of US women born after 1945
- OC increasingly used by women > age 35
- Risk of MI with modern pills controversial
- Few prospective cohort studies comparing MI risk in OC users vs. non-users, all conducted when many pills contained high-dose estrogen

Purpose

To determine the risk for incident MI in women exposed to modern formulations of oral contraceptives

Women's Lifestyle and Health Study

- Prospective population-based cohort study of 49,259 Swedish women aged 30-49
- Sampled from Uppsala Health Care Region in 1990-1991
- Completed questionnaire regarding health history and risk factors
- Detailed history of oral contraceptive use by self-report

Ascertainment of MI outcomes

- Linkages with existing nationwide health registers
 - Emigration (Statistics Sweden)
 - National Cause of Death Register
 - National Hospital Discharge Register (ICD-9 and ICD-10 codes for acute MI)
- These methods have been shown to be sensitive and specific for ascertaining fatal and non-fatal MI

Statistical Analysis

- Excluded previous MI, missing data on OC or smoking, use of only IM/implanted progesterone (N=48,321)
- Cox proportion hazard models adjusted for age, education, BMI, smoking, alcohol, physical activity, hypertension, diabetes, MD advice not to use OC and menopause

Characteristics of WLH women

	Never used	Former user	Current user
Subjects, N (%)	8013 (16.6)	33507 (69.3)	6801 (14.1)
Age at enrolment, mean (years)	41.5	39.9	36.7
Body Mass Index, mean (kg/m²)	23.9	23.5	23.0
Education, mean (years)	11.9	12.3	12.3
Ever smoking, %	44.0	63.4	57.5
Current smoking, %	21.4	30.4	26.3
Physical activity, % High or Very High	23.4	25.4	27.1
Hypertension, %	9.4	9.4	8.4
Diabetes, %	1.9	1.2	0.9

Patterns of OC use

	Former user %	Current user %
Age at first use (years)		
<20	61.8	54.9
20-24	23.8	31.7
25-29	7.9	9.1
30+	6.9	3.3
Duration of use (years)		
<5	48.6	14.5
5-9	28.3	22.7
10-14	15.3	30.4
15+	6.2	31.8
Has a doctor ever recommended to stop use	15.5	7.3
Used combined OC only	65.2	52.2
Used only 2 nd or 3 rd generation of progestin in combined OC	30.2	30.0
Used only low dose estrogen in combined OC	13.3	21.9
Current use of progestin-only (including injected or implanted)		27.9
Current use of 2 nd or 3 rd generation of progestin in combined OC		81.9
Current use of low dose estrogen in combined OC		81.7

See portrait slide

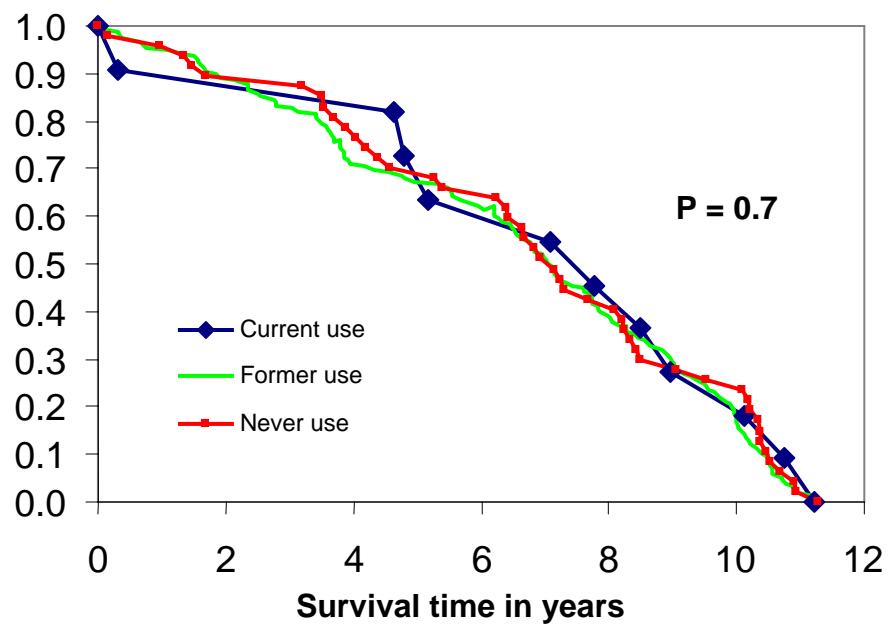
Risk of MI According to Participant Characteristics

- Table 3, slide 9 – see portrait slides

Risk of MI by Pattern of OC Use

- Table 3, slide 10, see portrait slides

Time to developing MI



Strengths and Limitations

- Large prospective cohort study with complete follow-up
- Nurses' Health Study 1976-1986 showed 2.5-fold elevated risk of MI, but high-dose estrogen was common
- Self-reported OC use
- OC exposure only at and prior to enrollment, MI risk may wane rapidly on discontinuation of OC

Conclusions

Current and past use of oral contraceptives was not associated with a statistically significant increased risk of MI in this study, in which most current users of OCs were taking low-dose estrogen and 2nd or 3rd generation progestins

Implications for Practice

Women aged 30-49 who use current formulations of oral contraceptives may not have an increased risk of MI. It would still be prudent to use caution in prescribing OC to women who smoke or have heart disease risk factors

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Risk of MI According to Participant Characteristics

Variable	MI cases	Age-adjusted RR (95%CI)	Multivariate RR (95% CI)*
Never used OC	47	Reference	Reference
Ever user OC	167	1.0 (0.7-1.4)	1.0 (0.7-1.4)
Former user	156	1.0 (0.7-1.4)	1.0 (0.7-1.4)
Current user	11	0.6 (0.3-1.2)	0.7 (0.4-1.4)
Age at first use (years)			
<20	53	0.9 (0.6-1.4)	0.8 (0.6-1.4)
20-24	66	0.9 (0.6-1.3)	0.9 (0.6-1.3)
25-29	30	1.2 (0.7-1.8)	1.2 (0.7-1.9)
30+	10	0.9 (0.5-1.9)	1.0 (0.5-1.9)
P for trend		0.9	0.7
Duration of use (years)			
<5	76	0.9 (0.7-1.3)	0.9 (0.6-1.4)
5-9	38	0.9 (0.6-1.4)	1.0 (0.6-1.5)
10-14	29	1.2 (0.7-1.9)	1.1 (0.7-1.9)
15+	14	0.7 (0.4-1.2)	0.7 (0.4-1.4)
P for trend		0.6	0.7
Ever recommended to stop use			
No	111	0.8 (0.6-1.1)	0.8 (0.6-1.2)
Yes	54	1.9 (1.3-2.8)	1.4 (1.0-2.1)

Note: No significant associations except MD recommendation to stop use.

Risk of MI by Pattern of OC Use

Type of OC	MI cases	Age-adjusted RR (95% CI)	Multivariate RR (95% CI) *
Never used	47	Reference	Reference
Type of OC in ever users			
Progestin-only	3	0.9 (0.3-2.8)	0.9 (0.3-2.7)
Combined OC only	103	1.0 (0.7-1.4)	1.0 (0.7-1.4)
Mixed	61	1.0 (0.7-1.5)	1.0 (0.7-1.5)
Progestin generation in ever combined OC users			
Second or third	28	0.8 (0.5-1.4)	0.8 (0.5-1.4)
All others	139	1.0 (0.7-1.4)	1.0 (0.7-1.4)
Estrogen dose in ever combined OC users			
Only low dose	7	0.7 (0.3-1.7)	0.8 (0.3-1.9)
All others	160	1.0 (0.7-1.4)	1.0 (0.7-1.4)
Type of contraceptive in current users			
Progestin-only	6	0.9 (0.4-2.1)	0.9 (0.4-2.1)
Combined OC	5	0.4 (0.2-1.1)	0.6 (0.2-1.5)
Progestin generation in current combined OC users			
Second or third	4	0.5 (0.2-1.3)	0.6 (0.2-1.5)
First	1	0.4 (0.1-2.7)	0.5 (0.1-3.5)
Estrogen dose in current combined OC users			
Low dose	2	0.2 (0.1-1.0)	0.3 (0.1-1.4)
High dose	3	1.0 (0.3-3.2)	1.2 (0.4-3.9)

Note: No significant Associations