

***Contraception and Ectopic Pregnancy Risk:
A Prospective Observational Analysis***

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Objective: To estimate the rates of ectopic pregnancy in women stratified by contraceptive method used and compare these rates to participants using no contraceptive method or condoms. We hypothesized that women using highly to moderately effective contraceptive methods (intrauterine device (IUD), implant, injectable contraception, and oral contraceptives (OCs), patch, or ring) would have a lower rate of ectopic pregnancy than women using no method or condoms.

Study Design: This is a secondary analysis of the Contraceptive CHOICE Project (CHOICE), a prospective cohort study of 9,256 participants, who were provided the contraceptive method of their choice at no cost and followed for 2-3 years duration.¹ Reported incident ectopic pregnancy during actual use of the contraceptive method was collected during follow-up telephone surveys. We estimated the incidence of ectopic pregnancy by each contraceptive method category: copper IUD, levonorgestrel IUD, implant, depot medroxyprogesterone acetate (DMPA), and one combined category consisting of OCs, contraceptive patch, and vaginal ring. Our control or referent group included women using no method or condoms. Inclusion and exclusion criteria followed that of the CHOICE Project.¹ Percentage of ectopic pregnancies was calculated using number of ectopic pregnancies divided by number of pregnancies (intrauterine and ectopic, method specific) and multiplied by 100. Ectopic pregnancy rates per 1,000 women-years were calculated using number of ectopic pregnancies divided by the total length of method use and multiplied by 1,000.² Cox proportional hazard models calculated the hazard ratio (HR) for ectopic pregnancy in each contraceptive method compared to no method or condoms.

Results: Participants provided 20,381 women-years of follow-up with 13 ectopic pregnancies identified. Follow-up rates were 93.5%, 84.1%, and 78.9% at 1, 2, and 3 years, respectively. Crude results are shown in Table 1. Seven participants in the no contraception/barrier group had

an incident ectopic pregnancy. There were 6 contraceptive users who reported an incident ectopic pregnancy; 4 levonorgestrel IUD users, one copper IUD user, and one OC user. Rates of ectopic pregnancy per 1,000 women-years were: no method/condoms 6.90; levonorgestrel IUD 0.50; copper IUD 0.46; OCs/patch/ring 0.22; implant 0; and DMPA 0. Use of the levonorgestrel IUD (HR 0.06, 95% confidence interval (CI) 0.02 to 0.23), copper IUD (HR 0.08, CI 0.01 to 0.62), OCs/patch/ring (HR 0.04, CI 0.01 to 0.37) reduced the risk of ectopic pregnancy compared to no method/condoms. Participants choosing implant and DMPA contraception had no reported ectopic pregnancies. Given the small number of ectopic events, we report only the unadjusted HR.

Conclusion: Women using the levonorgestrel IUD, copper IUD, DMPA, implant, and OCs/patch/ring had a significantly lower risk of ectopic pregnancy compared to women using no contraception or barrier methods of contraception. The CHOICE Project is one of the largest prospective cohort studies to investigate contraceptive use and ectopic pregnancy rates across multiple forms of contraception. Our study covers a wider range of contraceptive methods than previous studies, and the forms of contraception included in our study are more contemporary than currently included in the prior literature.³⁻⁵ One limitation of our work is that the incidence of ectopic pregnancy was low across all methods. This is not unexpected with over 75% of our cohort using a highly effective method and having a low risk of contraceptive failure. Additionally, recall bias is a possible limitation in defining ectopic pregnancy by using telephone call follow-up surveys and patient self-report.

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Table 1. Ectopic pregnancies by contraceptive method and Cox proportional hazard ratios

Method	Number of pregnancies*	Number of Ectopics	% Ectopic	Women-years	Rate per 1,000 Women-years**	95% Confidence Interval (Rate)		Hazard Ratio (HR)	95% Confidence Interval (HR)	
No method / condom use	510	7	1.37%	1014	6.90	2.78	14.22	Reference		
LNG-IUD	51	4	7.84%	8060	0.50	0.14	1.27	0.06	0.02	0.23
Copper-IUD	24	1	4.17%	2198	0.46	0.01	2.53	0.08	0.01	0.62
Implant	15	0	0.00%	2886	0.00	-	-	-	-	-
DMPA	32	0	0.00%	1571	0.00	-	-	-	-	-
OCs/patch/ring	363	1	0.28%	4652	0.22	0.01	1.20	0.04	0.01	0.37

* Both intrauterine and ectopic pregnancies are included in the reported number

** Denominator includes all pregnancies (intrauterine and ectopic)

LNG = levonorgestrel
IUD = intrauterine device
DMPA = depot medroxyprogesterone acetate
OC = oral contraceptive