Time to fertility return after discontinuation of Intra-uterine contraceptive device: A systematic review and meta-analysis

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Abstract

Background: Time to fertility return and rate of pregnancy after discontinuation of contraceptive is important to provide effective family planning counseling on the method-specific choice and designing a strategy to avert such concerns and problems. The aim of this study was to determine the time to fertility return and rate of pregnancy after discontinuation of Intra-uterine contraceptive.

Methods: The review was conducted through a systematic search of published articles in English language between 1967- 2017. Information was extracted using a standardized form of Joana Brigg's Institute guidelines. After cleaning and sorting, analysis was performed using STATA version 11. Heterogeneity was assessed by the I^2 and publication bias through funnel plot.

Results: A total of 27 studies with 8,037 women who discontinued contraceptive methods for pregnancy desire were included for analysis. The pooled time interval from contraceptive discontinuation to conception was 3.1 months for Intra-uterine contraceptive device. On the other hand, the pooled pregnancy rate was 84.5% at one year and 90% at two years after Intra-uterine contraceptive device removal.

Conclusion: Intra-uterine contraceptive users experienced a slight delay in fertility return compared with those who did not use contraception but not sustained in the long term. This study recommends a family planning counseling approach that includes time for fertility return after discontinuation to avoid confusion of contraceptive users. [*Ethiop. J. Health Dev.* 2021;35(SI-5):45-54]

Keywords: time to fertility return, pregnancy rate, IUCD, contraceptive, meta-analysis

Background

Family planning allows individuals and couples to decide when to have children and the use of a birth control method to attain their desired number of children, spacing and timing of their births (1). Family planning contributed to reduces maternal mortality (2). The ability to space and limit the pregnancies has a direct impact on the health and well-being as well as on the outcome of each pregnancy (1). Globally, 14.3% of women in reproductive age (15-49) used intrauterine contraceptive device (IUCD), however the use of IUCD varies by country with some being less than 2% and others above 40% (3).

Nonetheless, IUCD has been steadily gaining preference and importance as a contraceptive method over the last 20 years (4,5). The rate of pregnancy in women following contraceptive cessation shows that 1-year pregnancy rates after copper IUDs and injectable contraceptives were high, ranging between up to 91% and 83%, respectively (6). Oral contraceptives showed a fertility pattern less favorable than seen in those discontinuing short term IUCD (< 42 months), with increasing duration of intrauterine device use being associated with decreasing fertility (7). Moreover, the rate of pregnancy was 83.1% within the first 12 months of IUCD discontinuation (8). Any fertility delay following the cessation of a given contraceptive method may be associated with reduced use and poor user satisfaction especially in young women (9).

Family planning clients will benefit from knowing the approximate delay in fertility return after discontinuing a contraceptive method. Delay of fertility after discontinuing contraception remains a big concern for women who are using contraception. Particularly, women who ever experienced post-pill amenorrhea or failed to become pregnant within the expected date of fertility after termination of contraception have speculated that the contraceptive method was responsible for the delayed return of fertility (10). Family planning users not clearly understand which FP affect their pregnancy dalliance, and when to expect their fertility return after discontinuing. Evidence not properly documented about each FP use and fertility return after discontinuation.

Despite the absence of definitive evidence, some women have expressed concern regarding the return of fertility following discontinuation of IUCD. There is limited data on the time to fertility return after discontinuing IUCD. However, to make a valid comparison regarding return to fertility after IUCD use, one must understand normal fertility and fecundity. In the general population, the average time for a couple to conceive is approximately 6 months (7). This review article describes the prospective studies, and meta-analyses that evaluated the return to fertility after discontinuation of IUCD and estimates the global pooled time for fertility return. The synthesis of the reviewed articles is important to provide effective and evidence-based FP counseling on method-specific choice and designing a strategy to avert unwanted pregnancy.

Methods

Search strategy:

This systematic review and meta-analysis were conducted accordingly to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (11). Systematic literature search of articles was done. Published research articles were

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systematically examined (collected) from September 28 to October 10, 2019, using electronic database, including PubMed, Google Scholar, HINARI, SCOPUS, Cochrane library and Research Gate. Search terms were identified as Condition, Context, Population themes and used Boolean operators in a variety of combinations for fertility return and contraceptive delay after time to fertility "Intrauterine contraceptive device, contraceptives use, Fertility after stopping reversible long-acting contraceptive, Cessation of a continuous long-acting contraceptive". To minimize time-lag bias, the search process was updated on April 18, 2020, by EA and AE were involved in searching the articles.

The standard review protocol, Preferred Reporting Items for Systematic and Meta-Analysis (PRISMA) checklist, was followed to establish minimum information that should be included when reviewing and reporting (12). Moreover, the protocol was registered at the International prospective register of systematic reviews (PROSPERO) with registration number CRD42019122825.

Inclusion and exclusion criteria:

Observational studies, including cohort and RCT designs reporting fertility return after intrauterine contraceptive (IUCD) cessation was included. Published articles in English language between 1967 and 2017 were included in the review. Articles without abstracts and/or full text or did not report the outcome of interest, commentaries, anonymous reports, letters, editorial, and duplicate studies were excluded.

Study selection procedure:

The search returned 644 studies recorded from Google Scholar, PubMed, HINARI and SCOPUS, and using reference list searching. The review authors independently screened the titles and abstracts yielded by the search against the inclusion criteria. Accordingly, 32 full articles were screened reading titles and abstracts, five articles were excluded because of quality of the articles which evaluated using JBI critical appraisal checklist, and 27 articles were included for the final synthesis (Fig 1).

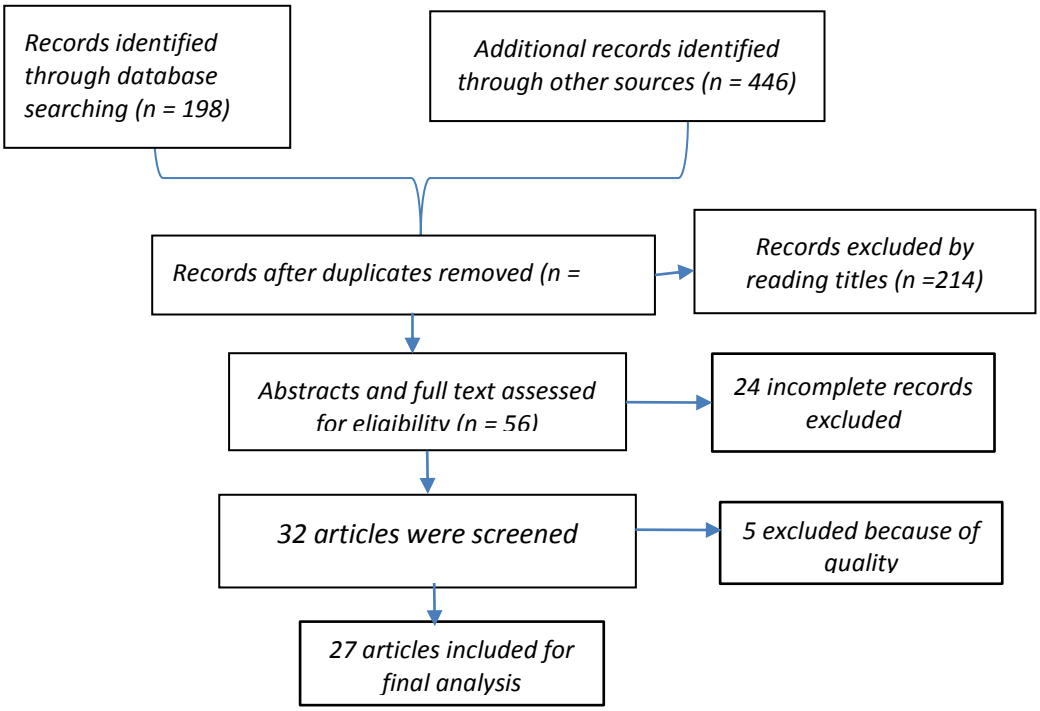


Figure 1: **Study flow diagram**

Critical appraisal

Authors independently reviewed each included study's methodological quality using the Joanna Briggs Institute (JBI) critical appraisal checklists for different study designs as appropriate (13-15). Retrieved studies were exported to the EndNote X8 citation manager and duplicated articles were excluded. The two investigators (EA & AE) screened and evaluated studies independently. The selections of identified studies were done in two stages. In the first stage, a selection of relevant studies was done based on titles and abstracts. In the second stage, studies that met the inclusion criteria and assessed the detail of the full articles against the inclusion criteria. Two reviewers (BB and LA) performed the study eligibility assessment independently by using JBI checklists. The quality of articles was assessed using JBI critical appraisal checklist (12). To obtain an overall quality score, publications scored "1" point for each item fully met and "0" for none or very little information reported. Studies that scored 75% or more were categorized as high quality, scores in the range of 50-74% were ranked as a medium, and scores less than 50% were rated as poor and excluded from the analysis. According to the JBI quality appraisal tool, ten of the selected (6 cohort and 4 RCT) studies were high quality (85%) and 17 cohort studies scored medium quality (70%) which lacked strategies to deal with confounding. Five cohort studies were scored low

quality (45%) and excluded from the analysis. There were no conflicts in final selection decisions.

Data extraction process

A standardized data extraction form of JBI used to extract the necessary data. The data extraction tool was piloted by considering the inclusion criteria to check consistency and to ensure that all the relevant information was captured. After selection of articles, data were extracted by two investigators independently (EA and LA) and presented through Microsoft excel 2016 (containing author, year of publication, setting, design, sample size, time to fertility delay, pregnancy rate within one and two years of IUCD discontinuation) (Table 1). During the extraction process, data discrepancy among data extractors was resolved by referring to the original study.

Types of outcome measures

The time to fertility return was measured the average months that pregnancy delayed and/or the rate of pregnancy in 12-or24-months following discontinuation of IUCD among women discontinued contraception because of pregnancy intention.

Data synthesis

A narrative synthesis was used to analyze and interpret the findings. A random-effects meta-analysis model was used to pool fertility rate and determine time to fertility for the variability among studies using Stata v11. The results were presented as the pooled estimates (odds ratio (OR) and proportion) with 95% confidence intervals (CI), at less than 0.05 significant levels. The P-value of the Chi-squared test of heterogeneity and the I^2 and Tau^2 statistics were examined for heterogeneity between the studies and estimates Cochrane's Q statistic and I-square estimate greater than 75% was considered as indicative of moderate to high levels of heterogeneity (16). Sub-group analysis two different subgroup analyses were conducted to investigate whether the observed fertility return is consistent across time to removal of IUCD and examine the pooled time to fertility varied by time to removal. Moreover, sensitivity analysis was conducted to examine the effect of studies that are exclusively reported of the fertility return after IUCD removal. We also investigated the presence of publication and other bias in the extracted data using a funnel plot and Egger's test (17).

Results

Characteristics of included studies:

The sample size of included studies ranged from a minimum of 15 women conducted in Canada (18) to a maximum of 1,770 women conducted in 14 countries (19). A total of 8,037 women who discontinued IUCD contraception for pregnancy were included in the review. A summary of all relevant features and main findings of the 27 articles were included and presented in the table1. Among those, the highest time interval (29.8 months) was recorded in France (20), while the shortest time interval was 1 month from removal to conception (21). The lowest proportion of pregnancy within one year was recorded, 39.3% (8), and the highest 96.4% (22) following the removal of IUCD. Similarly, fertility after 2 years of IUCD removal ranged from 73.9% in Multi-center study (21) to in Brussels, Belgium 99% (23) (Table 1).

Table 1. **Characteristics of studies included in the review which was published in English from 1967 to 2017**

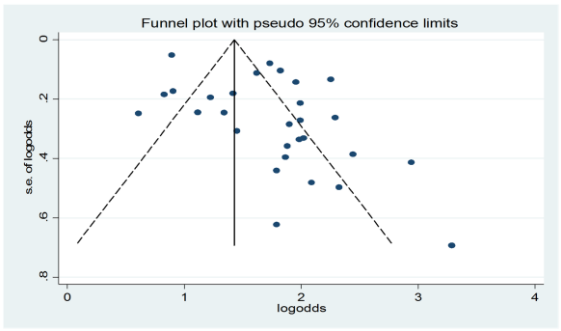
Author's name	Publication Year	Study Setting	Design	Sample size	Pregnancy rate Year -1	Year-2	TFR Months
(21) Andersson K, et al	1992	5 countries but not specified	RCT	138	69.6	73.9	1
(24) Andolsek L, et al	1986	Ljubljana, Yugoslavia	Cohort	540		86.7	
(4) Anwar, M., et al	1993	Yogyakarta, Indonesia	Cohort	90	75.3		
(25) Batar, I. et.al	1980	Hungary	Cohort	649	90.5		
(22) Belhadj, H., et al.	1986	New York,USA	Cohort	110	96.4		3
(23) Delbarge W., et al.	2002	Brussels, Belgium	Cohort	128	88	99	
(26) Díaz, S., et al.	1987	Chile	Cohort	44	89		
(8) Doll, H., et al	2001	England and Scotland.	Cohort	162	39.3	76.5	
(27) Eisenberg D, et al.	2015	United State	Cohort	68	86.8		
(28) Gupta, B. K., et al.	1989	India	Cohort	91	92	97	4.4
(29) Kaplan, B., et al.	2005	Tel Aviv in Israel.	Cohort	48	75	85.5	
(30) Nilssonet.al	1982	Helsinki, Finland	Cohort	21	85.7		
(31) Pyörälä T., et al.	1982	Denmark, Finland, Sweden	Cohort	150	77.3	88.9	
(20) Randic L., et al.	1978	France	Cohort	208	88		29.8
(32) Randic L., et al.	1985	Rijeke, Yugoslavia	Cohort	576	83.5	89.8	5.4
(18) Rioux J.-E., et al	1986	Quebec, Canada	Cohort	42			9
(47) Rioux J.-E., et al	1986	Quebec, Canada	Cohort	15			5.5
(33) Sivin I., et al	1992	Pori, Finland	RCT	194	80.5	88	
(34) Skjeldesta et al	1988	Trondheim, Norway	RCT	101	79.3	90.1	
(35) GarmoHov G., et al	2007	Trondheim, Norway	RCT	109	87	96	
(36) Soeprono, R	1988	Indonesia	Cohort	55	86.6	94.5	5.9
(37) Stoddard A. M, et al	2015	St. Louis, Missouri	Cohort	69	81		
(38) Tadesse, E.	1996	Ethiopia	Cohort	780	86.1		
(39) Wilson, J. C.	1989	New Zealand	Cohort	1254	85	92	
(19) Zhu, H., et al.	2013	14 counties	Cohort	1770	70.96		
(40) WAJNTRAUB	1970	Jerusalem, Israel	Cohort	174	90.8		

(41) Linn, S., et al.	1982	Boston, USA	Cohort	451	87.6

Publication bias

The funnel plot appeared symmetrical, which suggests no evidence indicates the presence of publication bias. More studies are found on the right sides of the funnel plot margin. The estimated bias coefficient (intercept) of Egger's test was 0.22 with a standard error of 1.26 at (95% CI: − 2.36-2.81), p > 0.05, no statistical evidence about the issues of publication bias. The Egger's test also indicated the low possibility of publication bias. The visual examination of the funnel plot showed an asymmetric distribution of studies indicates for the presence of publication bias (Fig 2).

One year after discontinuation



two years after discontinuation

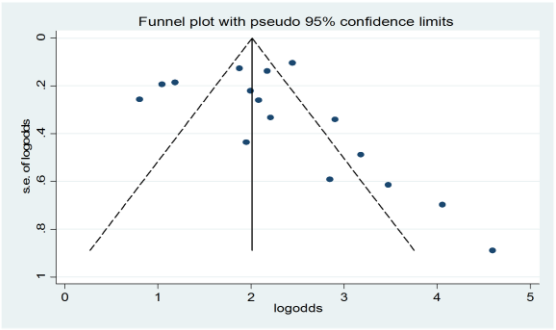


Fig 2. **Meta funnel presentation of the pregnancy rate**

Table 2: **Eggers test for pregnancy rate within one year after discontinuation of IUCD**

Egger's test

Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	84.16284	2.721816	30.92	0.000	78.57813	89.74754
bias	.2243495	1.261378	0.18	0.860	−2.363785	2.812484

Sensitivity analysis

We conducted three different analyses by excluding studies on after one year discontinuation of IUCD which is also a large sample (19,38), after two years discontinuation (24), and both one- and two-years discontinuation (32,39). Following the removal of a study on the one-year discontinuation, the overall pooled estimate was not changed. On the other hand, excluding studies on two years discontinuation, the pooled estimate was decreased to 13% (95% CI: 0.10-0.21) without lowering heterogeneity between studies, and excluding both studies on one- and two-years discontinuation, the fertility return decreased to 11% (95% CI: 0.09-0.19) with reduced heterogeneity. As a result, we conducted a sub-group analysis after one year and two-year removal of IUCD to compare the rate of fertility returns with their counterparts.

Time to fertility return

The overall pooled fertility delay after discontinuation of IUCD to using the random effect model was 3.1 months (1.88 to 4.32 months). The meta-analysis weights of the IUCD studies were ranging from 1.05 to a maximum of 14.96. The presence of heterogeneity among the studies was tested using I-squared statistics. The I^2 test result showed moderate heterogeneity I^2=43.7%, p-value 0.046 for IUCD studies (Fig 3).

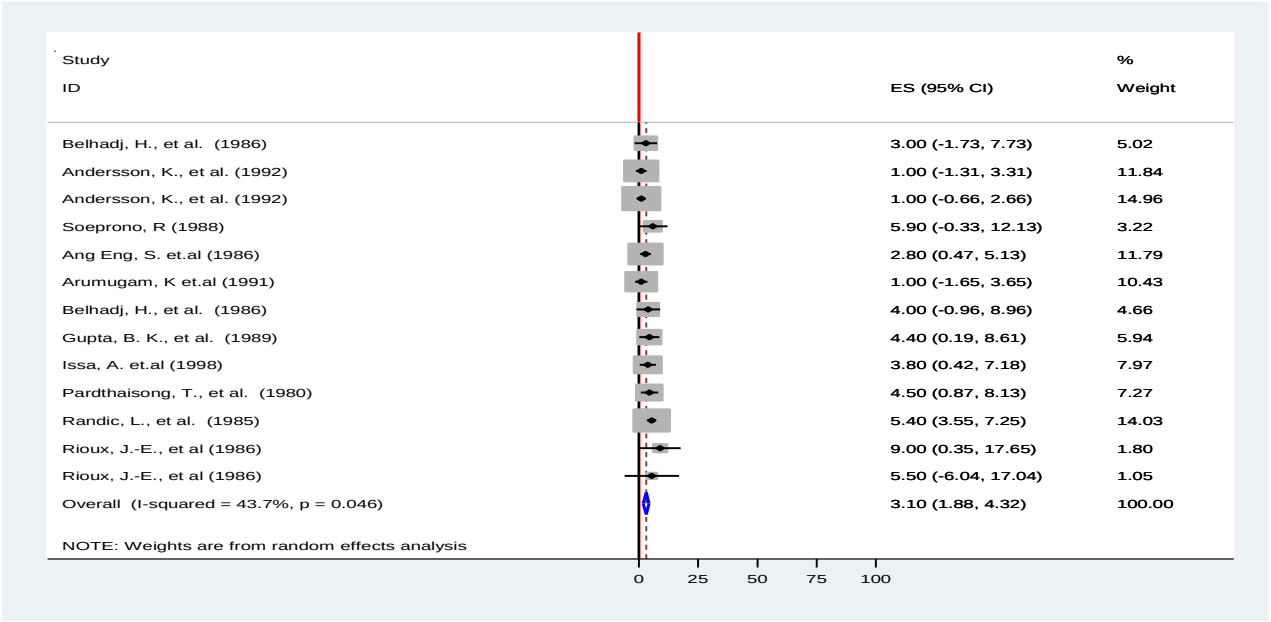


Figure 3. **Time to fertility after discontinuation/removal of IUCD**

Pregnancy rate

The estimated overall pooled pregnancy rate using the random effect model was 84.48% (95% CI: 81.58-87.38%) at one year and 89.99% (95% CI, 87.05-92.92%) within two years after the removal of the IUCD. The weights of the studies were ranging from 1.98 to a maximum of 4.11. The I^2 statistics test for heterogeneity showed high variability of studies (I2 =91.3%, p-value <0.001). After two years of removal, the weights of the studies were ranging from 3.76 to a maximum of 7.45. The I^2 statistics test for heterogeneity showed sustainable heterogeneity (I^2=91.7%, p-value <0.001) (Fig 4).

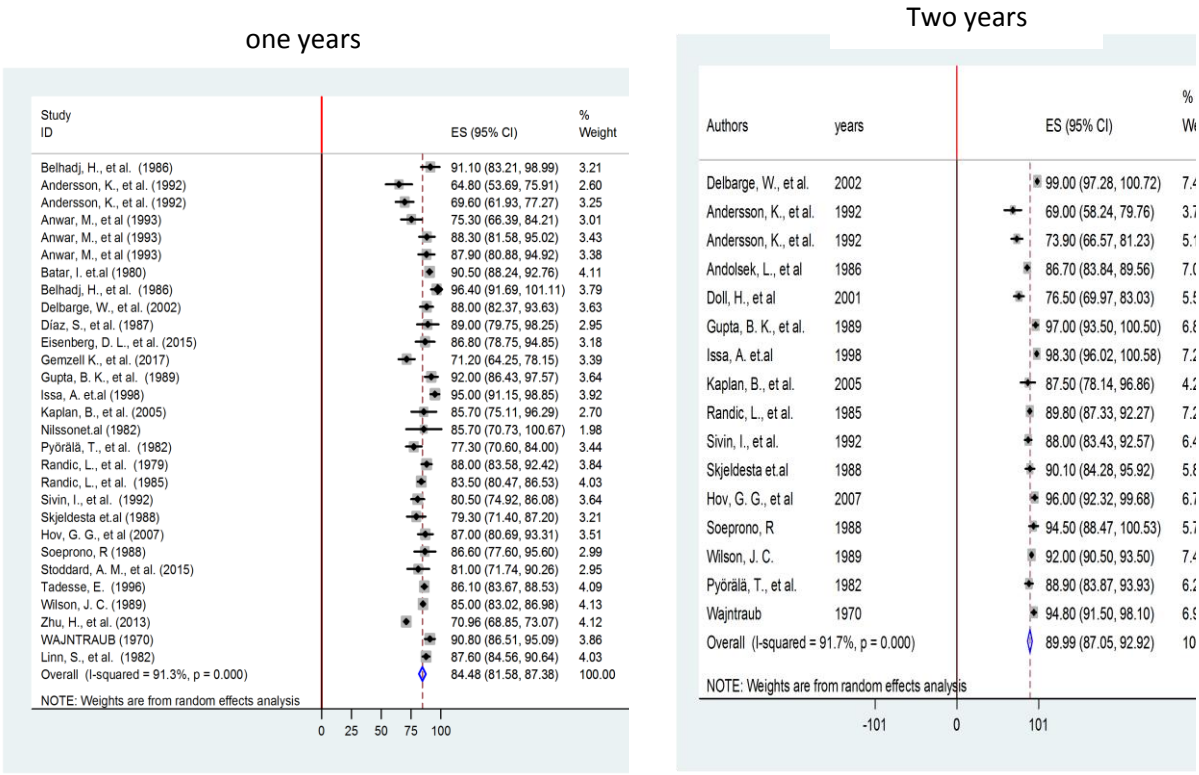


Fig 4. **Pregnancy rate after discontinuation of IUCD**

Sub-analysis after one year and two-year removal of IUCD

In sub-group analysis after one-year removal by study design, the highest pooled rate of pregnancy was occurred among prospective follow up studies 87.47% (95% CI;85.31-89.62) and retrospective studies 83.89% (95% CI;71.47-96.3%). The sub-group analysis indicated the presence of heterogeneity across retrospective study designs (I^2=98.1%, p-value <0.001).

On other hand, subgroup analysis after two years removal based on study design showed that the pooled pregnancy rate was found from 72.35% (95% CI: 66.29%-78.40%) and 93.40% (95% CI: 84.42, 102.93) among studies conducted in randomize comparative and retrospective studies, respectively. Heterogeneity test among the study design were not significant for randomized comparative studies (I^2=0.0%, p-value=0.461) and randomize prospective studies (I^2=74.5%, p-value=0.020) **(Fig 5).**

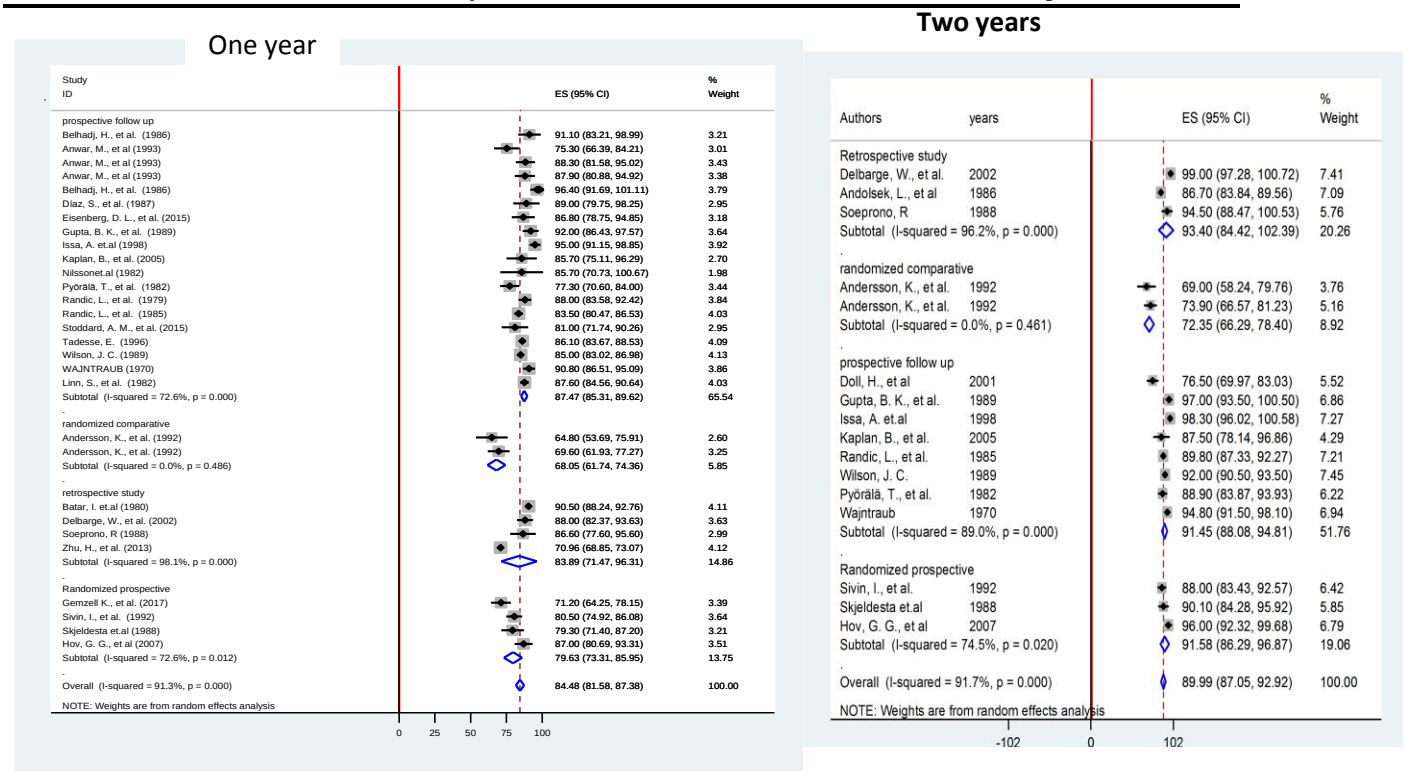


Fig 5. **Sub-group analysis for pregnancy rate within one & two year of IUCS removal**

Discussion

The overall pooled time interval of fertility returns after IUCD discontinuation was 3.1 months (95% CI: 1.88-4.32). The pooled time to pregnancy return after discontinuation of IUCD was comparable to a comprehensive review, 3.4 months (6). Moreover, the IUCD delay of pregnancy is higher as compared with Healthwise reports, immediate or within one month (42). The pregnancy delay of this review is lower than the WebMD scientific report delay for 6 months to a year (43). The possible reason for the variation might be due to the variation of participants age, as the age of women increases the ability to get pregnancy decrease, mainly after 25 years and also varies from person to person due to the health condition and menstrual irregularity affects the fertility (42).

The pooled time to fertility return after IUCD discontinuation was lower than a report from different contraceptive methods Norethisterone Enanthate and Cyclofem (4.8 months), Implants (5.3 months) and Mini-pills (6 months) (44), however higher than oral contraceptives (2.8 months) (6), Combination pills 2 months (1 to 3 months) (43), and barrier methods such as condoms or diaphragms, not affect a woman's fertility (44). The possible difference may be due to the qualitative and quantitative composition of hormones estrogen or progestin of contraceptive method which affects the H-P-O axis or process resulting in temporarily suppress ovulation which affects the fertility of women (27). Besides, barrier methods such as a diaphragm, cervical cap, male condom, female condom, and spermicidal foam, sponge, gel, suppository, and film used as a mechanical barrier of pregnancy and can get pregnant on the next time stop using the method (27, 29).

Fertility declines with increasing maternal age. However, it is reassuring that the overall birth rates seen in previous IUCD users are comparable to those seen in the general population after 6 months of attempting to conceive (7). This review of the currently available literature indicates that, although IUCD users may experience a slight delay (3.1 month) in the return to fertility compared with those who did not use contraception or those discontinuing other contraceptive methods, fertility impairment is not sustained in the long term. Furthermore, a comprehensive review of available data evaluating the time to conception in women discontinuing contraception suggests that the return to fertility associated with IUCD is comparable to that observed with a broad range of contraceptive methods.

Moreover, in this review, the pooled pregnancy rate after IUCD removal was 84.5% at one year and 90% for two years. The pregnancy rate within a year was comparable to other reports on contraception, 84.5% of IUCD (6), and 87.5% (79–96%) for Levonorgestrel IUCD (45). But lower pregnancy rate as compare to 81% (95% CI:71-91%) for copper IUDs (45), 80% (33), 79.4% (46) at 1 year. In this review, the rate of pregnancy after 1 year of IUCD interruption was in lined with oral contraceptives 87% (95% CI:78-95%), but higher pregnancy rate as compared with 80% of implants and 77.5% (95%CI:75-80%) of injectable (45). Globally, new version or updated contraceptive methods are distributed but there was/is no latest study on fertility return after contraceptive discontinuation is the limitation of this study.

Conclusion

This review of the available literature indicates that, although IUCD users experience a slight delay (3.1 month) in the return to fertility compared with those who did not use contraception or those discontinuing other contraceptive methods, fertility impairment is not sustained in the long term. Even though many scientific reports explained an immediate return of fertility after IUCD removal, this review showed that there was a significant difference in the fertility return within different contraceptive users. Therefore, it needs to focus on counseling approach on the time of fertility return and to avoid contraceptive use at a time of women infertile period that avoid unwanted and unplanned pregnancy due to the limitation of family planning counseling.

Declaration

Competing interests

The authors declare they have no competing interests.

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