Intrauterine Devices in Adolescents: A Systematic Review

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ABSTRACT

Background: Adolescent pregnancy is a major public health problem in the United States associated with negative sequelae for women, families, and children. Most of the recent decline in adolescent pregnancy in the United States is due to contraception; however the rate of adolescent pregnancy in the United States is still higher than in other developed nations. Long-acting reversible contraception is underutilized in this respect.

Purpose: To review the literature on the outcomes of pregnancy rate, expulsion rate, and continuation rate in adolescent women using an IUD for contraception

Data sources: MEDLINE, ISI Web of Science, and POPLINE searches; relevant reference lists

Data extraction: 2670 titles and abstracts were reviewed, of which 213 were given full text reviews. 13 studies were included in the final review.

Study selection: Studies were given relative weight based on the type of study and their strength of internal and external validity

Data synthesis: The data are mixed for all three primary outcomes of the review with a large amount of heterogeneity in types of devices used. More and higher quality studies are needed to determine the effective rates as compared to other contraceptive interventions.

Conclusion: The evidence currently available in the literature is currently insufficient to ascertain the appropriateness of IUDs as a first-line contraceptive for adolescents.

Teenage pregnancy has many negative consequences to health and society in the United States. Recent declines in teenage pregnancy and birth have most likely been due to an increase in the use of contraception by teenagers. Long-acting reversible contraception, such as that provided by the copper and progesterone-secreting intrauterine devices (IUDs), is likely the most effective solution for contraception, but these methods have not been adequately studied in the teenage population.

INTRODUCTION

1. Teenage Pregnancy in the United States

Teenage pregnancy has serious personal and societal consequences. With more than half of teenagers in the United States who become pregnant giving birth, this represents a substantial number of births: 435,436 in 2006.[1] A population-based cohort study found that teenage mothers compared to those who become mothers later in life have an increased risk of premature death in later life independent of socio-economic status (rate ratio 1.6), meaning that reduction of teenage pregnancy and thus birthrate could have a significant positive influence on women's health well beyond the teenage years.[2]

The children of teenage mothers are also at risk of negative health outcomes compared to children born to older mothers. Teenage pregnancy is independently associated with worse fetal outcomes, including preterm delivery, low birth weight, and neonatal mortality.[3] Teenage mothers are more likely to have a diet deficient in micronutrients (such as iron), which may explain the increased incidence of small for gestational age infants in children born to teenage mothers.[4] There are also longer term sequelae for children born to teenage mothers; being

born as result of a teenage pregnancy leads to worse outcomes in adults in various facets of health, education, inactivity, and earnings.[5]

Despite recent decreases, teenage pregnancy and birth remains a serious problem in the United States. The teenage pregnancy rate (women ages 15-19) reached a peak of 116.9 per 1,000 women in 1990 and steadily declined through 2005 to 69.5 per 1,000, which represents the lowest rate in over 30 years. However, in 2006 (the last year for which finalized data are available), this increased to 71.5 per 1,000.[1] Preliminary data for the rate of birth to teenage mothers are available through the year 2009, and they show a similar trend to pregnancy, with a peak of 61.8 births per 1,000 in 1991 and a decrease through 2005. There was a slight increase through 2006-2007, but this was reversed in 2008 and 2009, with 2009 having a rate of 39.1 per 1,000 women.[6] These encouraging trends belie the fact that the United States still has a higher pregnancy and birth rate than those of all European nations, including former Soviet bloc nations.[7]

The National Survey of Family Growth (administered by the National Center for Health Statistics) periodically conducts a nationally representative survey of women ages 15-44. As part of this survey, respondents are asked questions to determine whether each of their pregnancies had been intended or unintended. Pregnancies are classified as unintended if they are either mistimed (the woman would have liked to become pregnant in the future, but did not desire pregnancy at that point) or unwanted (the woman did not desire pregnancy at that time or in the future). Pregnancies about which women were indifferent are classified as intended. Based on data from the 2002 survey and using census data as a denominator, Finer

and Henshaw estimated that one fifth of all unintended pregnancies in the United States are to teenagers, and 82% of all teenage pregnancies are unintended.[8]

It must be noted that relative statistics such as the proportion of pregnancies which are unintended can be misleading. For example if the intended pregnancy rate suddenly rose without a change in the unintended pregnancy rate, the proportion of unintended pregnancies would suddenly drop, without a change in the absolute number. The data used by Finer and Henshaw shows that the 82% statistic may belie the fact that teenage pregnancy rates are decreasing for both unintended (from 82 per 1000 to 67 per 1000 from 1994 to 2001) and intended pregnancies (from 25 per 1000 to 15 per 1000 during the same time period).[8] The data also comes from a retrospective survey, which means that recall bias is likely to affect the results, and in this case it may underestimate the intendedness of the pregnancy at the time of the conception. An analysis of the 2002 National Survey for Family Growth shows that dichotomous classification of pregnancy intendedness is not sufficient to predict pregnancy outcomes, and a multidimensional model incorporating aspects such as timing and desire is a much stronger predictor.[9] Wantedness rather than intendedness may better correlate with outcomes; however, dichotomous intendedness outcomes continue to be the main reported statistic in this area of consideration.[10,11]

Although it is unclear how large this majority is, and unclear further how important of a measure intendedness actually is, the fact that the majority of adolescent pregnancies are unintended leads to the conclusion that proximal factors such as adolescent sexual behavior are an appropriate point for intervention to decrease teenage pregnancy and birth. One

intervention that has been popular in recent years is abstinence-only or abstinence-based sex education in schools; however, this has proven marginally effective at best, with most studies showing no effectiveness in decreasing adolescent pregnancy, while comprehensive sex education has been more effective.[12] This has been corroborated by an analysis of data from the 2002 National Survey of Family Growth, which found that those reporting receiving comprehensive sex education had a statistically significantly decreased risk of reporting adolescent pregnancy compared to those who reported receiving abstinence-only or no sex education, between which there was no significant difference. This was despite no significant difference in reported vaginal intercourse.[13] It must be taken into consideration that these data are from a retrospective study and thus recall bias for all of these statistics is an important possibility. If the association is true, however, the proximal factor likely to have had the largest effect on decreasing pregnancy rates is contraception, as reporting of vaginal intercourse was not significantly affected by a report of either intervention.

2. Contraceptives

According to analyses of data from the 1995 and 2002 National Survey of Family Growth by Santelli, et al., the recent decline in teenage pregnancy and births is 86% attributable to increased use of contraceptive use, with the rest of the decline attributable to a decrease in sexual activity, mostly among women ages 15-17.[14,15] The slight increase in teen pregnancy and birth rates in 2006 and 2007 was accompanied by a slight decrease in use of contraception as measured by the Youth Risk Behavior Survey in those years, with no significant change in sexual activity, meaning that decreased contraceptive use is the likely proximal cause for the increased

teen pregnancy and birth rates.[15] The disparity between teenage pregnancy rates in the United States and Europe is also explained by a difference in the rate of contraceptive use.[15] Like the decreases in teen pregnancy and birth rate in the United States, the decreases in Europe cannot be explained by a decrease in sexual activity; in fact, the age at sexual initiation has decreased in both the United States and Europe during the same time period.[16] Thus, contraception is likely the best choice for a proximal intervention to prevent teenage pregnancy and birth, given its crucial role in recent decreases in the teen pregnancy and birth rate.

The 1960s saw the development of two radical and effective methods of birth control. In 1960, the FDA allowed the makers of Enovid (an oral combination of an estrogen and a progesterone) to market on its contraceptive claims after three years of indication only for gynecological disorders.[17] In the early 1960s, Gynekoil was introduced as the first mass-produced intrauterine device (IUD) in the United States, and since that time 8 other IUDs have entered the market.[18] Since the 1960s, many hormonal and non-hormonal birth control methods have been added to the market; a summary of these methods as well as their typical and actual use effectiveness rates as determined by systematic review are shown in table 1.

Table 1. Methods of contraception currently available in the United States.[19]

Method	**Mechanism of action**	**% of Women with Unintended Pregnancy within One Year**	
		Typical Use	**Perfect Use**
No method	n/a	85%	85%
Spermicides	Spermicidal action of foam/gel/film inserted into vagina prior to each intercourse	29%	18%
Withdrawal	Partner ejaculates outside of the vagina	27%	4%
Fertility awareness-based methods	Timing of intercourse based on charting of menstrual cycle	25%	3-5%
Sponge	Combined barrier and spermicidal method inserted over the cervix prior to intercourse	32% (parous) 16% (nulliparous)	20% (parous) 9% (nulliparous)
Diaphragm	Barrier method placed over the cervix used at each intercourse	16%	6%
Condom	Barrier method placed in the vagina (female) or on the penis (male) used at each intercourse	21% (female) 15% (male)	5% (female) 2% (male)
Combined pill and progestin-only pill	Daily pill with either estrogen and progestin (combined pill) or progestin only	8%	0.3%
Evra patch	Hormonal patch containing estrogen and progestins; changed weekly	8%	0.3%
NuvaRing	Ring containing estrogen and progestins inserted into vagina for three weeks of each month	8%	0.3%
Depo-Provera	Injection containing a depot of progestin administered every 12 weeks	3%	0.3%
IUD	Intrauterine device with either copper (copper T) or progestin (LNG-IUS) left for either 10 years (copper T) or 5 years (LNG-IUS)	0.8% (copper T) 0.2% (LNG-IUS)	0.6% (copper T) 0.2% (LNG-IUS)
Implanon	Plastic rod with progestin inserted into subcutaneous tissue and left for 3 years	0.05%	0.05%
Female Sterilization	Bilateral tubal ligation performed as a permanent surgical procedure	0.5%	0.5%
Male Sterilization	Both vas deferentia are severed as a permanent surgical procedure	0.15%	0.10%

Of the many methods of contraception available, there are currently only two IUDs on the market in the United States: a copper-containing IUD, or copper T380A and a progesterone-secreting IUD, or LNG-IUS.

3. IUDs Currently on the Market in the United States

Based on a systematic review of the literature on contraceptive failure, these methods are highly effective, with a failure rate of 0.8% for the copper T and 0.2% for LNG-IUS in the first year under typical use; with perfect use, the failure rate for the copper T is 0.6%.[20] The fact that there is little difference in failure rates between perfect and typical use underlines the fact that IUDs have the advantage of not requiring patient action each day, and not surprisingly, thus prove more effective than typical use of combined oral contraceptive pills (OCPs), which have a failure rate of 8% with typical use, and 0.3% with perfect use.[20,21] As well as the advantage of being "forgettable" (i.e. requiring no patient action in normal use) LNG-IUS may also hold an advantage over OCPs in terms of continuation. A trial that randomized nulliparous women ages 18-25 to either OCPs or LNG-IUS found that the continuation rate at one year was higher for LNG-IUS than OCPs, with 20% of women discontinuing that IUD and 27% of women discontinuing the OCPs.[22] A larger prospective cohort study (Contraceptive CHOICE) has found that among women given a choice of free contraceptive methods, those who chose the IUDs had the highest continuation rates (88% for LNG-IUS, 84% for copper T), as well as higher satisfaction compared to OCPs (54% of OCP users were satisfied).[23]

Although it is beyond the immediate scope of this review, IUDs also confer non-contraceptive benefits to women. For example, the LNG-IUS can be used to treat chronic pelvic

pain, and heavy menstrual bleeding, and it has been shown to decrease the risk of endometrial cancer.[24] The copper-T shows promise as an emergency contraception technique that uniquely continues to provide contraceptive benefit, with a failure rate of 0.09% found by a systematic review of non-randomized studies.[25]

In Europe as in the United States, the dominant method of long-acting reversible contraception is the IUD. All Western European nations, however, have much higher overall rates of use, with a full 27% of women using contraception in Norway utilizing an IUD, the highest proportion of any nation.[26] This difference in IUD use between the United States and Western Europe may be partly because provider and public attitudes in the United States towards the IUD as birth control were negatively affected by the Dalkon Shield, an aberrant device in the 1970s that caused septic miscarriages and was subsequently removed from the market.[26] After the Dalkon Shield entered and quickly exited the market, the rate of IUD use among women in the United States dropped precipitously from a high of nearly 10% of all contraceptive users in the early 1970s to a low of 1% of all contraceptive users in 1995, which represented the lowest rate of use in any developed nation at that time.[27,28] Since that time, there has been an increase in long-acting reversible contraception (LARC) to 5.5% of all contraceptive users in 2006-2008, most of which is due to increased use of IUDs, and particularly LNG-IUS.[27] This increase was most pronounced in women younger than 24 and older than 35. Additionally, those who had first intercourse at age 17 or younger experienced an increase in IUD use among users of contraception of 2.5% to 7.8% from 2002 to 2006-2008[28]

4. Summary

In the Contraceptive CHOICE trial, more than 60% of adolescents (69% of participants 14-17 and 61% of participants 18-20) chose long acting reversible contraception (including both IUDs and implantable hormonal birth control) when given a full range of contraceptive options.[29] A study that compared patient satisfaction with IUDs to patient satisfaction with implantable hormonal birth control found that at six months, more women were satisfied with the IUD than with the implantable hormonal birth control.[30] Despite the popularity of the IUD when presented as an option, a survey of adolescents and young women found that only 45.4% had heard of the IUD, and a survey of primary care obstetrician-gynecologists found that only 18% "always" presented the IUD when discussing options for contraception.[31,32] While the American Congress of Obstetricians and Gynecologists has issued a Committee Opinion that agrees with the World Health Organization's assessment that IUDs are an appropriate choice of contraceptive for adolescents, the most recent systematic review of available data (including studies through 2008) shows that the existing literature was promising but insufficient to confirm this stance.[33,34] Thus, we need a current systematic review of the important clinical question: are IUDs an appropriate option for first-line contraception for adolescents in the United States?

METHODS

1. Clinical Question

The focused clinical question that this paper will address is: "Are IUDs an appropriate option for first-line contraception for adolescents in the United States?" For the purposes of this systematic review, IUDs will exclude the Dalkon shield as an aberrant device. The comparison was initially to be made to condoms and OCPs, as these are, respectively, the most used and second most used contraceptives by adolescents in the United States.[35] However, this stipulation was abandoned based on the initial lack of appropriate studies in the literature search. Appropriateness will be based on continuation rate, pregnancy rate, and expulsion rate. Adolescents will be defined as females who are 18 years of age or younger.

Table 2. PICOTS Table of the Clinical Question for this Systematic Review.

Patient/Problem	Adolescent women ≤22 seeking contraception
Intervention	IUD (except Dalkon Shield or other aberrant device)
Comparison	Any or none
Outcome	Continuation rate, pregnancy rate, and expulsion rate
Timing of outcome	Greater than or equal to 6 months
Timing of Study	No limit
Studies	Randomized (RCT) and nonrandomized controlled trials, cohort studies, case-control studies, case-series
Setting	Primary care setting in any country with a "Very High" Human Development ranking

This review originally considered adolescence to be between the ages of 10-21, which is the definition typically accepted in pediatrics.[36] However, one study found during the literature review would have been acceptable other than the inclusion of women up to age 22, and the decision was made to raise the limit. This review will not consider the outcome of satisfaction

with the method of contraception, as satisfaction mirrors continuation rate, and continuation rate is a more objective measure and thus more likely to be reported and quantified.[37] This review will not consider the outcome of pelvic inflammatory disease (PID) since PID is rare in the United States even in high risk populations receiving IUDs as found by a meta-analysis that examined the use of antibiotics in preventing PID as well as an earlier systematic review exploring the association between IUD insertion and PID.[38,39] Additionally, a previous systematic review has shown that while women with a sexually transmitted infection (STI) at the time of IUD insertion have an increased risk of PID in comparison to women without a STI at the time of IUD insertion, it is unclear whether this represents a risk in IUD insertion itself or an increased background risk for women with STIs. [39,40] This review will not consider the effect of parity on IUDs in adolescents, instead focusing on the problem of IUDs in adolescents *in toto*.

2. Eligibility Criteria

This review included English language studies with the goal of examining pregnancy rate and/or birth control continuation rate and/or IUD expulsion rate in women 21 or younger as compared to OCPs or condoms (for pregnancy rate and continuation rate). Also included were studies with a subgroup analysis of a subgroup that is within the definition of an adolescent as being from ages 10-22. The followup period needed to be at least 6 months. Studies conducted at any time were included. To maximize the number of results, no stipulation was made concerning the type of IUD, save that it was not the Dalkon Shield or other aberrant device, as a previous review found no studies of the devices currently in use in the United States.[34] As the review is focusing on the appropriateness of IUDs in adolescents in the United

States, at least one of the study settings must be a similarly developed nation. Developed nations for this review will be defined as those on the list of the United Nations' list of countries with a "Very High" rating of Human Development as of 2010, based on the Human Development Index which takes into account health, education, and living standards.[41] Box 1 outlines the 43 nations that are included in this definition.

Box 1. Nations with a Very High Human Development Rating.[41]

- Norway
- Australia
- New Zealand
- United States
- Ireland
- Liechtenstein
- Netherlands
- Canada
- Sweden
- Germany
- Japan
- Korea, Republic of
- Switzerland
- France
- Israel
- Finland
- Iceland
- Belgium
- Denmark
- Spain
- Hong Kong, China (SAR)
- Greece
- Italy
- Luxembourg
- Austria
- United Kingdom
- Singapore
- Czech Republic
- Slovenia
- Andorra
- Slovakia
- United Arab Emirates
- Malta
- Estonia
- Cyprus
- Hungary
- Brunei Darussalam
- Qatar
- Bahrain
- Portugal
- Poland
- Barbados

3. Search Strategy

The author searched PubMed, ISI Web of Science, and Popline to find relevant studies. All searches were designed to broadly capture any article with relevance to IUDs and adolescents. The PubMed search involved the use of Medical Subject Heading (MeSH) terms to include any documents that had been indexed under "Intrauterine Devices," which includes both medicated and copper devices, as well as "Adolescent" or "Young Adult", which includes the age ranges 13-18 and 19-24, respectively. The PubMed search also used a broad spectrum of

terms which could be construed as fitting either IUD or adolescent in order to include articles that had not been indexed to the appropriate MeSH term. The ISI Web of Science and Popline searches both used a similar spectrum of terms. The PubMed, ISI Web of Science, and Popline searches yielded 1852, 278, and 497 records, respectively. In addition to this search strategy, the bibliography of the only previous systematic review of this topic in the literature was examined. This article included 43 citations. The actual strategies and results are shown in table 3.

Table 3. Search Strategies and Results.

Source	**Search Strategy**	**Records***	**Full Text Reviewed***	**Met Criteria***
PubMed MEDLINE (Limits activated: English)	("Intrauterine Devices"[Mesh] OR IUD OR IUCD OR IUS OR intrauterine contracepti* OR intrauterine system* OR intrauterine device*) AND ("Adolescent"[Mesh] OR "Students"[Mesh] OR "Young Adult"[Mesh] OR adolescen* OR student* OR teen* OR youth)	1852	162	14
ISI Web of Science	(IUD* OR IUS OR IUCD* OR intrauterine device* OR intrauterine system* OR intrauterine contracepti*) AND (adolescen* OR youth OR student* OR teen*)	278	24	8
Popline	(IUD*/IUS/IUCD*/intrauterine device*/intrauterine contracepti*/intrauterine system*) & (adolescen*/teen*/youth/student*)	497	14	4
Deans and Grimes. "Intrauterine devices for adolescents: a systematic review"	Bibliography review	43	13	7

*Note: there was overlap between the sources in all of these categories.

4. Quality Criteria

The original intent of the review was to exclude case studies, case series, and, case-control studies in favor of controlled trials and cohort studies, since cohort studies provide a greater level of evidence (Level 3; Level 2 if the study is well-conducted and demonstrates a dramatic effect) than do case-control studies (Level 4) according to Oxford's Centre for Evidence Based Medicine (OCEBM).[42] The levels of evidence for treatment benefits and harms according to OCEBM are illustrated in table 3. However, due to the relative dearth of the literature on this subject, descriptive studies were included in the review.

Table 3: Levels of Evidence for Treatment Benefits and Treatment Harms.[42]

	Treatment Benefits	**Treatment Harms**	
		Common	**Rare**
Level 1	Systematic review of randomized trials or *n*-of-1 trials	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Systematic review of randomized trials or *n*-of-1 trial
Level 2	Randomized trial or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Randomized trial or (exceptionally observational study with dramatic effect
Level 3	Non-randomized controlled cohort/follow-up study	Non-randomized controlled cohort/follow-up study (post-marketing) surveillance) provided there are sufficient numbers to rule out a common harm (for long-term harms the duration of follow-up must be sufficient)	
Level 4	Case-series, case-control studies, or historically controlled studies	Case-series, case-control, or historically controlled studies	
Level 5	Mechanism-based reasoning	Mechanism-based reasoning	

This review used the United States Preventive Services Task Force's (USPSTF) guidelines for assessing the internal validity of all comparative studies. The criteria used for the guidelines are specific to each study type, with randomized controlled trials and cohort studies having nearly identical criteria except for those which account for their mechanistic differences. A study received a rating of "good" if it met all criteria and maintained appropriate follow-up, "fair" if it had any of the problems listed in Table 4 but no flaw fatal enough to invalidate the results, or "poor" if there were flaws in the study that were fatal enough to invalidate the results.[43] The criteria and the rating system are outlined in box 2 and table 5. The internal validity of the case-series was also assessed along a good/fair/poor gradient based on author's judgment, as there are no specific USPSTF criteria for case-series since no comparison is being made.

Box 2: USPSTF Minimal Criteria for Randomized Controlled Trials and Cohort Studies.[43]

- Initial assembly of comparable groups:
    - For RCTs: adequate randomization, including first concealment and whether potential confounders were distributed equally among groups.
    - For cohort studies: consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination).
- Important differential loss to follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment).
- Clear definition of interventions.
- All important outcomes considered.
- Analysis: adjustment for potential confounders for cohort studies, or intention to treat analysis for RCTs

Table 5: USPSTF Internal Validity Ratings for RCTs and Cohort Studies.[43]

Good rating	Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (follow-up at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention to confounders in analysis. In addition, for RCTs, intention to treat analysis is used.
Fair rating	Studies will be graded "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred with follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention to treat analysis is done for RCTs.
Poor rating	Studies will be graded "poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. For RCTs, intention to treat analysis is lacking.

In addition to considering internal validity, the review also assessed the external validity of the studies using the USPSTF's criteria for generalizability and criteria for assessing external validity.[44] The external validity of all included studies was assessed as compared to the source population in the United States. A study received a rating of "good" if it minimally differed from the generalizability requirements with regards to the study's population, situation, and providers. A study received a rating of "fair" if it moderately differed from the generalizability requirements with regards to the study's population, situation, and providers. A study received a rating of "poor" if it majorly differed from the generalizability requirements with regards to the study's population, situation, and providers. Table 6 illustrates the USPSTF ratings system for external validity.

Table 6: USPSTF External Validity Ratings.[44]

Good	The study differs minimally from the US primary care population/situation/providers and only in ways that are unlikely to affect the outcome; it is highly probable (>90%) that the clinical experience with the intervention observed in the study will be attained in the US primary care setting.
Fair	The study differs from the US primary care population/situation/providers in a few ways that have the potential to affect the outcome in a clinically important way; it is only moderately probable (50-89%) that the clinical experience with the intervention in the study will be attained in the US primary care setting
Poor	The study differs from the US primary care population/situation/providers in many ways that have a high likelihood of affecting the clinical outcomes; the probability is low (<50%) that the clinical experience with the intervention observed in the study will be attained in the US primary care setting.

5. Study Selection

The titles and abstracts of the articles identified through the search strategy were reviewed by the author. If it was absolutely clear from the title and/or abstract that the given article met exclusion criteria, the article was discarded; every effort was made for a sensitive rather than a specific approach to abstract and title review. The articles that remained after this exclusion process were given a full text review. Articles in which full text review did not reveal any exclusion criteria were included in the abstraction process for systematic review.

6. Abstraction Process

The author performed the data abstraction solely for the articles that were selected for the systematic review after full text review using a standard form for each study. The following information was extracted for each study: general information (including citation and country of origin), study question, source of funding, source population, study population, design,

intervention, comparison, potential for selection bias, population characteristics (including randomization and group similarity), outcome assessment, measurement, potential for measurement bias, potential for confounding, type of analysis, results, attrition (number of dropouts), overall judgment of internal validity, and external validity. Table 7 illustrates the standard data extraction form used.

Table 7. Example Data Extraction Form.

Study	JAMA Citation: Country:
Study Question:	
Source of Funding:	
Source Population:	
Study Population:	 Exclusion criteria:
Design:	Study design: Sample size:
Intervention:	Type of IUD?
Comparison:	
Potential for Selection Bias:	
Population Characteristics:	Parity: Randomization? Groups similar at baseline?
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? --Timing? Cumulative expulsion rate? --Timing? Continuation rate? --Timing?
Measurement	Study groups: Exposure measures: Outcomes: Outcome measures:
Potential for Measurement Bias:	
Potential for Confounding:	
Analysis:	
Results:	Unintended pregnancy rate: Cumulative expulsion rate: Continuation rate:
Attrition:	Number of dropouts?
Overall Judgment of Internal Validity (Quality Rating):	
External Validity:	

7. Synthesis of Evidence

As this review assesses a topic on which the vast majority of the literature is non-randomized and focused on a very heterogeneous group of devices which are not currently in use in the United States, a meta-analysis based on pooled data is not appropriate at this time. The evidence extracted from each study will be entered into template with a narrative interpretation of the results for each study. An example of the template is shown in table 8. The templates will then be combined into a single table, and the overall evidence profile of all studies will be performed for each of the primary outcomes for this review: pregnancy rate, expulsion rate, and continuation rate. In synthesizing the final results for the review, attention will be paid to the results of the studies, as well as their respective size, type, and quality.

Table 8. Template for Synthesis of Studies.

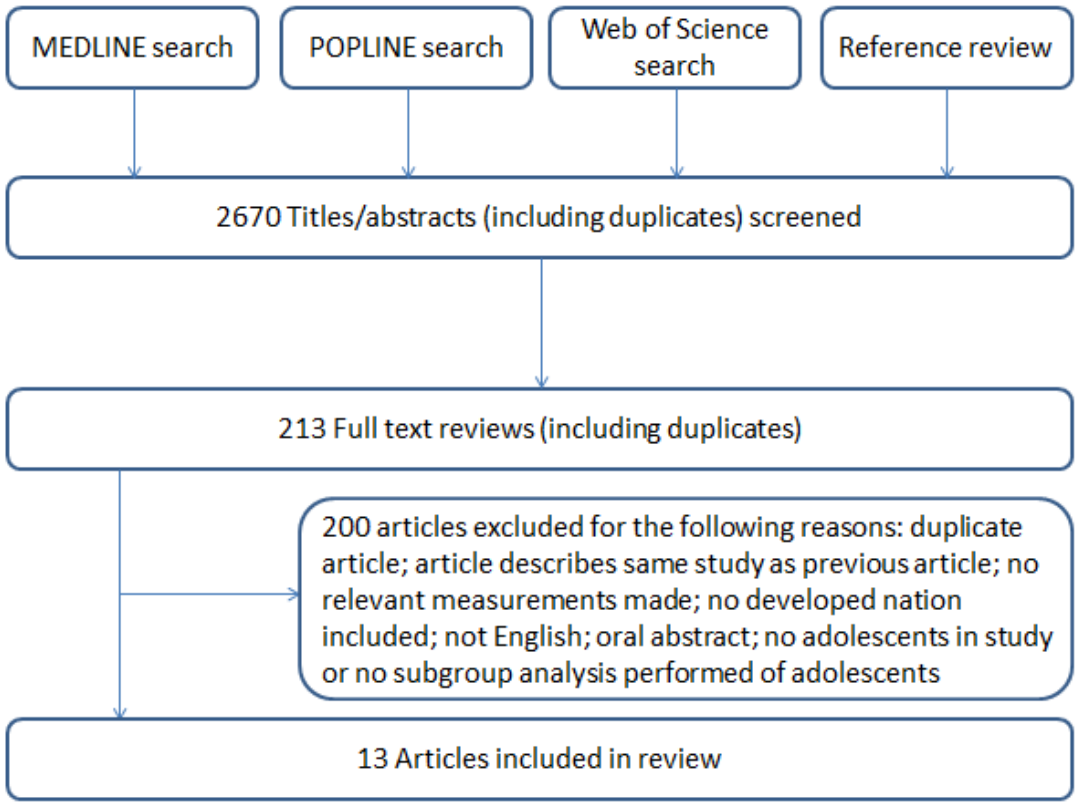
Citation	Number of participants	Ages	Parity	Internal Validity	External Validity	IUDs used	Results	Timing

RESULTS

1. Study Selection

A total of 2670 title/abstract combinations were reviewed based on the results of the literature search. Of these 2670 articles, 213 underwent full text review. Of the 213 which underwent full text review, 13 met the final inclusion criteria for the systematic review. Of these 13, there were 5 cohort studies, 6 case-series, 1 randomized controlled trial, and 1 synthesis of pooled data from multiple trials, Figure 1 illustrates the flow of information through the phases of the review, and summarizes the reasons for exclusion based on full text review.

Figure 1. PRISMA Diagram.



Studies were reviewed in alphabetical order by first author last name. Full data extraction tables are included in Appendix A.

Study 1

Citation	Behringer T, Reeves MF, Rossiter B, Chen BA, Schwarz EB. Duration of use of a levonorgestrel IUS amongst nulliparous and adolescent women. *Contraception*. 2011;84(5):e5-e10.
Study Design	Retrospective cohort
Study population (number, ages, parity)	131 adolescents, ages 14-20, 18.3% nulliparous 697 adult women ages 21-50, 11.5% nulliparous
Length of follow-up	36 months
IUDs used	LNG-IUS
Internal validity	Fair
External validity	Fair
Results: Pregnancy rate: Expulsion rate: Continuation rate	 Not measured 9.9% at 36 months 80.9% at 36 months

The Behringer et al. study, "Duration of use of a levonorgestrel IUS amongst nulliparous and adolescent women" is a retrospective cohort published in *Contraception* in 2011. Participants were selected by retrospective chart review of women aged 14-50 years old seen in an academic clinic in Pittsburgh, PA and receiving an LNG-IUS for contraception, dysmenorrhea, or menorrhagia between June 2005 and April 2008. In this study, women from 14-20 were considered to be adolescents. There were 131 adolescents, of which 18.3% were nulliparous. The clinical outcomes of adolescents and adults were compared, as were the clinical outcomes of nulliparous patients and parous patients.[45]

The internal validity of the study was deemed to be "fair" based on the moderate potential for selection bias and confounding, and low to moderate potential for measurement bias. The external validity of the study was deemed to be "fair" as it was not clear that the source population is highly comparable to the primary care population of the United States. Although adolescents had a non-statistically significant higher expulsion rate (9.9% vs. 5.4%), the adolescent group was found to have no statistically significant difference in expulsion rate or continuation rate at 36 months as compared to adult women (aged 21-50) based on hazard ratios which controlled for confounders.

Study 2

Citation	Godfrey EM, Memmel LM, Neustadt A, et al. Intrauterine contraception for adolescents aged 14-18 years: A multicenter randomized pilot study of levonorgestrel-releasing intrauterine system compared to the copper T 380A. *Contraception*. 2010;81(2):123-127.
Study Design	Randomized controlled trial
Study population (number, ages, parity)	23 women, ages 14-18, 12 nulliparous
Length of follow-up	6 months
IUDs used	Copper-T380A (11 participants), LNG-IUS (12 participants)
Internal validity	Fair
External validity	Fair
Results: Pregnancy rate: Expulsion rate: Continuation rate	 N = 0 in LNG-IUS, N = 1 in copper-T380A at 6 months N = 0 in LNG-IUS, N = 2 in copper-T380A at 6 months 75% (N = 9 of 12) in LNG-IUS, 45% (N = 5 of 11) in copper-T380A

The Godfrey et al. study "Intrauterine contraception for adolescents aged 14-18 years: A multicenter randomized pilot study of levonorgestrel-releasing intrauterine system compared to the copper T 380A is a single-blind randomized controlled trial published in *Contraception* in

2010. Participants were selected from patients seen in an academic family planning and family medicine clinic in Chicago. Of the 37 approached, 23 were eligible and randomized to either LNG-IUS (12 patients) or copper-T 380A (11 patients). The patients were blinded to the intervention, but the investigators and study coordinators were not. The clinical outcomes of the two groups were compared.[46]

The internal validity of this study was deemed to be "fair" based on the moderate to low potential for selection bias, measurement bias, and confounding. The external validity of this study was deemed to be "fair" based on the fact that although the study population likely was characteristic of the United States primary care population, the study size was too small to be able to draw definitive conclusions. The study found no statistically significant difference in pregnancy rate, cumulative expulsion rate, or continuation rate at 6 months between users of the LNG-IUS and users of the copper T 380A.

Study 3

Citation	Goldman JA, Dekel A, Reichman J. Immediate postabortion intrauterine contraception in nulliparous adolescents. *Isr J Med Sci*. 1979;15(6):522.
Study Design	Prospective cohort
Study population (number, ages, parity)	162 women, ages 13-18, all nulliparous (126 primigravid, 36 multigravid)
Length of follow-up	12 months
IUDs used	Lippes loop A, copper-7, copper-T
Internal validity	Poor
External validity	Poor
Results: Pregnancy rate: Expulsion rate: Continuation rate	 3.7% for all methods 11.1% for all methods 69.1% for all methods

The Goldman et al. study "Immediate postabortion intrauterine contraception in nulliparous adolescents" was published in the *Israeli Journal of Medical Science* in 1979. In this prospective cohort study, 300 pregnant teenagers (ages 13-18) referred for abortion were offered immediate postabortion intrauterine contraception. 162 adolescents consented to the study. 56 were allocated to the Lippes loop A, 45 to the copper-7, and 61 to the copper-T. Clinical outcomes of pregnancy rate, expulsion rate, and continuation rate were obtained for both the individual devices and the overall study population.[47]

The internal validity of this study was deemed to be "poor" due to the high potentials for selection bias, measurement bias, and confounding. The external validity of this study was deemed to be "poor" due to the lack of information regarding characteristics of those who did and did not participate in the study. The study found an unintended pregnancy rate of 3.7% at 12 months for all methods, a cumulative expulsion rate of 11.1% at 12 months for all methods, and a continuation rate of 69.1% at 12 months for all methods.

Study 4

Citation	Goldman JA, Reichman J. Contraception in the teenager. A comparison of four methods of contraception in adolescent girls. *Isr J Med Sci*. 1980;16(7):510.
Study Design	Prospective cohort
Study population (number, ages, parity)	160 women, ages 14-18, all nulliparous N = 72 receiving OCPs N = 30 receiving IUD N = 38 advised to use condoms N = 20 receiving contraceptive foam
Length of follow-up	24 months
IUDs used	Copper-7, copper-T
Internal validity	Poor
External validity	Poor
Results: Pregnancy rate: Expulsion rate: Continuation rate	 N = 1 of 30 at 24 months N = 2 of 30 at 24 months 73.3% at 24 months

The Goldman and Reichman study "Contraception in the teenager. A comparison of four methods of contraception in adolescent girls" is a prospective cohort study published in the *Israeli Journal of Medical Science* in 1980. Participants were selected from women aged 14-18 "of high socioeconomic standing" who were referred to a clinic or private practitioner by their parents or school nurse following request for contraception. 160 adolescents were enrolled, and given access to and counseling on four contraceptive methods: OCPs., IUD, condoms, and contraceptive foam. 72 chose OCPs, 30 chose IUDs, 38 chose condoms, and 20 chose contraceptive foam. Clinical outcomes at 24 months were then compared amongst the groups.[48]

The internal validity of this study was deemed "poor" due to high potential for selection bias, measurement bias, and confounding. External validity was deemed "poor" as it was

unclear exactly what characteristics were of the source population, and how participants were selected from the source population. The study found 1 unintended pregnancy (of 30 participants receiving IUD) at 24 months, compared to 0 (of 72) for OCPs, 2 (of 38) for condoms, and 1 (of 20) for foam. There were 2 expulsions (of 30 receiving the IUD) of the IUD at 24 months. There was a continuation rate of 73.3% at 24 months for IUDs, compared to 72% for OCPs, 78.9% for condoms, and 15.8% for contraceptive foam.

Study 5

Citation	Hirvonen E, Kaivola S. A new copper IUD (Fincoid) in adolescent and young nulliparous women. *Contracept Deliv Syst*. 1983;4:149.
Study Design	Case-series
Study population (number, ages, parity)	241 women, ages 15-21, all nulliparous
Length of follow-up	12 months
IUDs used	Fincoid
Internal validity	Poor
External validity	Poor
Results: Pregnancy rate: Expulsion rate: Continuation rate	 4.2 per 100 women at 12 months 1.9 per 100 women at 12 months 73.1% at 12 months

.The Hirvonen and Kaivola study "A new copper IUD (Fincoid) in adolescent and young nulliparous women" is a case-series published in *Contraceptive Delivery Systems* in 1983. 241 adolescents aged 15-21 were recruited from adolescents seeking contraception at an outpatient clinic in Helsinki in whom OCPs had caused side-effects or were contraindicated. The study participants received the Fincoid IUD, and clinical outcomes were assessed after 12 months.[49]

The internal validity of this study was deemed "poor" due to the high potential for selection bias, and measurement bias. The external validity of this study was deemed "poor" due to the lack of information about the source population. The unintended pregnancy rate was 4.2 per 100 women at 12 months, the cumulative expulsion rate was 1.9 per 100 women at 12 months, and the continuation rate was 73.1% at 12 months.

Study 6

Citation	Jorgensen V. One-year contraceptive follow-up of adolescent patients. *Am J Obstet Gynecol*. 1973;115(4):484.
Study Design	Prospective cohort
Study population (number, ages, parity)	184 women, ages 11-17, all parous N = 90 selecting OCPs N = 82 selecting IUD N = 2 selecting diaphragm
Length of follow-up	12 months
IUDs used	Lippes loop, copper-T
Internal validity	Poor
External validity	Poor
Results: Pregnancy rate: Expulsion rate: Continuation rate	 5 of 184 at 12 months (all methods) 5 of 82 IUDs at 12 months 88% for IUD

The Jorgensen study "One-year contraceptive follow-up of adolescent patients" is a prospective cohort study published in the *American Journal of Obstetrics and Gynecology* in 1973. 221 "high risk" postpartum women seen in an adolescent obstetrics and gynecology clinic were assessed for eligibility, and 213 were given 5 weeks of OCPs for the interim between discharge and 5 week follow-up. At the 5 week follow-up, 184 returned to clinic and selected either OCPs, IUD, or diaphragm. Clinical outcomes were then assessed.[50]

The internal validity of this study was deemed "poor" due to moderate to high potential for selection bias and measurement bias and high potential for confounding. The external validity of this study was deemed "poor" due to the lack of information concerning the source population. There were 5 overall pregnancies in the study group at 12 months (of 184 participants using all methods). The cumulative expulsion was 5 (of 82 IUD users) at 12 months, and the continuation rate was 88% for IUDs vs. 70% for OCPs at 12 months.

Study 7

Citation	Kulig JW, Rauh JL, Burket RL, Cabot HM, Brookman RR. Experience with the copper 7 intrauterine device in an adolescent population. *J Pediatr*. 1980;96(4):746.
Study Design	Case-series
Study population (number, ages, parity)	120 participants, ages 13-22, 81% nulliparous
Length of follow-up	36 months
IUDs used	Copper-7
Internal validity	Poor
External validity	Fair
Results: Pregnancy rate: Expulsion rate: Continuation rate	 3 of 120 at 36 months (2.0 per 100 woman-years of IUD insertion) 18% expulsion rate at 36 months 39% continuation rate at 36 months

The Kulig et al. study "Experience with the copper 7 intrauterine device in an adolescent population" is a case-series published in the *Journal of Pediatrics* in 1980. Participants were selected from adolescent patients seen in the Cincinnati Adolescent Clinic choosing an IUD for contraception from 7/1974 to 6/1978. There were 120 participants, all of whom received the copper-7 IUD. Clinical outcomes were assessed at 36 months.[51]

The internal validity of this study was deemed "poor" due to moderate to high potential for selection bias and measurement bias. The external validity of this study was deemed "fair" since the sample was likely broadly representative of the U.S. primary care population. The study found that n = 3 of 120 had an unintended pregnancy at 36 months, that the cumulative expulsion rate was 18% at 36 months, and that the continuation rate was 39% at 36 months.

Study 8

Citation	Lane ME, Sobrero AJ. Experience with intrauterine contraception by adolescent women. *Mt Sinai J Med*. 1975;42(4):337.
Study Design	Case-series
Study population (number, ages, parity)	101 patients, ages 13-19, 96% nullilparous
Length of follow-up	9 months
IUDs used	Loop C, Loop D, LEM, W
Internal validity	Fair
External validity	Poor
Results: Pregnancy rate: Expulsion rate: Continuation rate	 N = 4 at 9 months N = 21 at 9 months 73.2% at 9 months

The Lane and Sobrero study "Experience with intrauterine contraception by adolescent women" is a case-series published in the *Mount Sinai Journal of Medicine* in 1975. Of 399 adolescent patients aged 13-19 seen at the Margaret Sanger Teen Center from 3/1971-12/1972, 101 selected the IUD as their contraceptive method. The patients were fitted with one of four devices: either Loop C (N = 44), Loop D (N = 1), LEM (N = 54), or W (N = 2). The patients were followed for 9 months.[52]

The internal validity of the study was deemed "fair" due to a low number of dropouts, as well as a moderate potential for measurement bias and moderate potential for selection bias. The external validity of the study was deemed "poor" because of a lack of information about the source population and how it relates to the U.S. primary care population. The study found N = 4 (of 101) unintended pregnancies at 9 months, an N = 21 (of 101) expulsions at 9 months, and a continuation rate of 73.2% at 9 months.

Study 9

Citation	Larsson B, Hagström B, Viberg L, Hamberger L. Long-term clinical experience with the Cu-7-IUD. Evaluation of a prospective study. *Contraception*. 1981;23(4).
Study Design	Prospective cohort
Study population (number, ages, parity)	179 women, ages 15-19 1267 women, ages 20-49 Overall parity: 59 nulliparous (unclear how this was stratified by age)
Length of follow-up	24 months
IUDs used	Copper-7
Internal validity	Poor
External validity	Poor
Results: Pregnancy rate: Expulsion rate: Continuation rate	 6.1% at 24 months for 15-19 12.9% at 24 months for 15-19 77.2% at 24 months for 15-19

The Larsson et al. study "Long-term clinical experience with the Cu-7-IUD. Evaluation of a prospective study" is a prospective cohort published in *Contraception* in 1981. 1446 women aged 15-49 receiving contraception at a private clinic in Stockholm or one of two family planning centers in Huddinge from 1971-1979 were selected for the study, of which 179 were adolescents aged 14-19. The participants who elected for IUDs received the copper-7 IUDs, and comparisons of clinical outcomes were made between the different age groups.[53]

The internal validity of the study was deemed "poor" based on the high potential for selection bias, measurement bias, and confounding. The external validity of the study was deemed "poor" based on the lack of information on the characteristics of the source population. The study found a pregnancy rate of 6.1% at 24 months in those ages 15-19; this was higher, but not statistically significantly higher than that found in those ages 20-49 (1.4-5.4%). There was a cumulative expulsion rate of 12.9% at 24 months in those ages 15-19, which was statistically significantly higher than the expulsion rate of those ages 20-49 ($p < 0.05$ vs. 20-24 and $p < 0.01$ vs. 25-49). The continuation rate for those aged 15-19 was 77.2% at 24 months, but was not analyzed with respect to significant differences with the other age groups.

Study 10

Citation	Patchen L, Berggren EK. Use of the copper T380A intrauterine device by adolescent mothers: Continuation and method failure *J Pediatr Adolesc Gynecol*. 2011;24(2):71-73.
Study Design	Retrospective case-series
Study population (number, ages, parity)	39 women, ages 15-21, all parous
Length of follow-up	24 months
IUDs used	Copper-T 380A
Internal validity	Fair
External validity	Poor
Results: Pregnancy rate: Expulsion rate: Continuation rate	 10% at 24 months 15% at 24 months 39% at 24 months

The Patchen and Berggren study "Use of the copper T380A intrauterine device by adolescent mothers: Continuation and method failure" is a retrospective case-series published in the *Journal of Pediatric and Adolescent Gynecology* in 2011. The charts of 318 adolescent

mothers aged 15-21 participating in a teen secondary pregnancy prevention program who had delivered prior to age 18 were reviewed. Of these 318, 39 had a copper-T 380A IUD inserted as a contraceptive and were included in the study; 93% were Hispanic. Outcomes at 24 months post-insertion were determined by chart review.[54]

The overall judgment of internal validity was deemed "fair" because of a moderate potential for measurement bias and a moderate potential for selection bias. The overall judgment of external validity was deemed "poor" as the study population was small and likely not representative of the U.S. primary care population. The study found an unintended pregnancy rate of 10% at 24 months, a cumulative expulsion rate of 15% at 24 months, and a continuation rate of 39% at 24 months.

Study 11

Citation	Paterson H, Ashton J, Harrison-Woolrych M. A nationwide cohort study of the use of the levonorgestrel intrauterine device in New Zealand adolescents *Contraception*. 2009;79(6):433-438
Study Design	Retrospective case-series
Study population (number, ages, parity)	133 responders to questionnaire, ages 10-19, n = 114 nulligravid
Length of follow-up	12 months
IUDs used	LNG-IUS
Internal validity	Fair
External validity	Fair
Results: Pregnancy rate: Expulsion rate: Continuation rate	 N = 0; time unspecified N = 11; time unspecified 85% at 12 months

The Paterson et al. study "A nationwide cohort study of the use of the levonorgestrel intrauterine device in New Zealand adolescents" is a retrospective case-series published in *Contraception* in 2009. Despite being named a cohort study, the design was that of a case-series as there was no comparison group. 177 adolescents 10-19 were identified as having received the LNG-IUS through New Zealand's Intensive Medicine Monitoring Program, and of those, 133 were included in the study based on response to a questionnaire sent to their provider.[55]

The internal validity was deemed "fair" due to a moderate potential for selection bias and a moderate potential for measurement bias. The external validity was deemed "good" as this study represented a broad sample of adolescents throughout a developed nation. The study found no pregnancies in the study population, although time period for this was not specified, and the study was not powered to assess pregnancy rate. The study found a "cumulative incidence" of 11 expulsions in the 133 patients; however, this was not given a time period and thus is not a true measure of incidence. The study found a continuation rate of 85% at 12 months.

Study 12

Citation	Sivin I, Stern J. Long-acting, more effective copper T IUDs: A summary of U.S. experience, 1970-75. *Stud Fam Plann*. 1979;10(10).
Study Design	Pooled data from random assignment and cohort studies
Study population (number, ages, parity)	N = 706 women <20 receiving TCu 380A N = 2830 women >20 receiving TCu 380A N = 465 women <20 receiving TCu 220C N = 1385 women >20 receiving TCu 220C N = 2280 women <20 receiving TCu 200 N = 7558 women >20 receiving TCu 200 Parity for TCu 200 acceptors was 42.8%, parity for TCu 380A acceptors was 63.7%, and parity for TCu 220C acceptors was 70.3%; no information regarding parity by age group
Length of follow-up	24 months
IUDs used	Copper-T 200, copper-T 380A, copper-T 220C
Internal validity	Poor
External validity	Fair
Results: Pregnancy rate: Expulsion rate: Continuation rate	For women <20: 1.0 per 100 acceptors for TCu 380A at 24 months 2.2 per 100 acceptors for TCu 220C at 24 months 6.6 per 100 acceptors for TCu 200 at 24 months 14.6 per 100 acceptors for TCu 380A at 24 months 12.6 per 100 acceptors for TCu 220C at 24 months 17.5 per 100 acceptors for TCu 200 at 24 months Not stratified by age

The Sivin and Stern study, "Long-acting, more effective copper T IUDs: A summary of U.S. experience, 1970-75" is an analysis of pooled data from 42 random assignment and cohort studies that was published in *Studies in Family Planning* in 1979. This study selected studies carried out in the U.S. (with one in Canada) on three models of copper IUDs, with the exclusion criteria that none of the included studies have a dropout rate over 30%. These data were stratified by multiple characteristics, including age (with a stratum of <20), and the results were reported.[56]

The internal validity of the study was deemed "poor" due to high potential for selection bias, moderate to high potential for measurement bias, and high potential for confounding. The external validity of the study was deemed "fair" due to the large amount of aggregate data on thousands of women, which in sum are more likely to represent the U.S. population than any individual study. For women <20, the 24 month rate of unintended pregnancy was 1.0 per 100 acceptors for TCu 380A, 2.2 per 100 acceptors for TCu 220C, and 6.6 per 100 acceptors for TCu 200. Also for women <20, the 24 month rate of expulsion was 14.6 per 100 acceptors for TCu 380A, 12.6 per 100 acceptors for TCu 220C, and 17.5 per 100 acceptors for TCu 200.

Study 13

Citation	Weiner E, Berg AA, Johansson I. Copper intrauterine contraceptive devices in adolescent nulliparae. *Br J Obstet Gynaecol*. 1978;85(3):204.
Study Design	Prospective case-series
Study population (number, ages, parity)	243 women, ages 13-20, all nulligravidae
Length of follow-up	6 months
IUDs used	Copper-T 200 and copper-7
Internal validity	Poor
External validity	Poor
Results: Pregnancy rate: Expulsion rate: Continuation rate	 2% at 6 months 11.5% at 6 months 78.8% at 6 months

The Weiner et al. study "Copper intrauterine devices in adolescent nulliparae" is a prospective case-series published in the *British Journal of Obstetrics and Gynaecology* in 1978. The patients were drawn from a group of 772 women in Sweden aged 13-20 seeking contraception at the Department of School Health in Uppsala Sweden from 3/1973-6/1975.

The study population was the 243 patients from that group that elected to receive an IUD. Clinical outcomes were then assessed at 6 months.[57]

The internal validity of this study was deemed to be "poor" due to high potential for selection bias and moderate to high potential for measurement bias. The external validity of this study was deemed to be "poor" due to lack of characteristic information about the source population. At 6 months, the unintended pregnancy rate was 2%, the cumulative expulsion rate was 11.5%, and the continuation rate was 78.8%.

Synthesis of the Evidence

Of the 13 studies, none had "good" internal or external validity. Three studies had "fair" internal and external validity. Two studies had "poor" internal validity and "fair" external validity. Two studies had "fair" internal validity and "poor" external validity. Two studies had "poor" internal validity and "fair" external validity. Six studies had "poor" internal and external validity.

The IUDs used in the studies included the LNG-IUS, copper-T 380A, Lippes loop A, copper 7, Fincoid, Lippes loop C, Lippes loop D, LEM, W, copper-T 220C, and copper-T 200. Of these devices, only two (LNG-IUS and copper-T 380A) are currently approved for use in the United States. Eight studies included at least one of those two methods. Only three contained only methods currently available in the United States. There was substantial heterogeneity in the results of the studies as well. Tables 9-11 provide a summary of each of the three primary outcomes being assessed in this systematic review.

Table 9. Pregnancy Rates.

Citation	N = ?	Ages	Parity	Internal Validity	External Validity	IUDs used	Pregnancy rate	Timing
Behringer, et al.[45]	131	14-20	18.3% nulliparous	Fair	Fair	LNG-IUS	Not measured	36 months
Godfrey, et al.[46]	12 11	14-18	12 nulliparous	Fair	Fair	LNG-IUS TCu 380A	N = 0 N = 1	6 months
Goldman, et al.[47]	162	13-18	100% nulliparous	Poor	Poor	Lippes loop A, Cu-7, TCu	3.7%	12 months
Goldman and Reichman[48]	30	14-18	100% nulliparous	Poor	Poor	Cu-7, TCu	N = 1	24 months
Hirvonen and Kaivola[49]	241	15-21	100% nulliparous	Poor	Poor	Fincoid	4.2 per 100	12 months
Jorgensen[50]	82	11-17	100% parous	Poor	Poor	Lippes loop, TCu	Not measured for subgroup	12 months
Kulig, et al.[51]	120	13-22	81% nulliparous	Poor	Fair	Copper-7	N = 3 2.0 per 100 woman-years	36 months
Lane and Sobrero[52]	101	13-19	96% nulliparous	Fair	Poor	Loop C, Loop D, LEM, W	N = 4	9 months
Larsson, et al.[53]	179	15-19	Unclear	Poor	Poor	Copper-7	6.1%	24 months
Patchen and Berggren[54]	39	15-21	100% parous	Fair	Poor	TCu 380A	10%	24 months
Paterson, et al.[55]	133	10-19	N = 114 nulligravid	Fair	Fair	LNG-IUS	N = 0	Not specified
Sivin and Stern	706 465 2280	<20	Unclear	Poor	Fair	TCu 380A TCu 220C TCu 200	1.0/100 2.2/100 6.6/100	24 months
Weiner, et al.[57]	243	13-20	100% nulligravidae	Poor	Poor	TCu 200, Copper-7	2%	6 months

Table 10. Expulsion Rates.

Citation	N = ?	Ages	Parity	Internal Validity	External Validity	IUDs used	Expulsion Rate	Timing
Behringer, et al.[45]	131	14-20	18.3% nulliparous	Fair	Fair	LNG-IUS	9.9%	36 months
Godfrey, et al.[46]	12 11	14-18	12 nulliparous	Fair	Fair	LNG-IUS TCu 380A	N = 0 N = 2	6 months
Goldman, et al.[47]	162	13-18	100% nulliparous	Poor	Poor	Lippes loop A, Cu-7, TCu	11.1%	12 months
Goldman and Reichman[48]	30	14-18	100% nulliparous	Poor	Poor	Cu-7, TCu	N = 2 of 30	24 months
Hirvonen and Kaivola[49]	241	15-21	100% nulliparous	Poor	Poor	Fincoid	1.9 per 100 women	12 months
Jorgensen[50]	82	11-17	100% parous	Poor	Poor	Lippes loop, TCu	N = 5 of 82	12 months
Kulig, et al.[51]	120	13-22	81% nulliparous	Poor	Fair	Copper-7	18%	36 months
Lane and Sobrero[52]	101	13-19	96% nulliparous	Fair	Poor	Loop C, Loop D, LEM, W	N = 21	9 months
Larsson, et al.[53]	179	15-19	Unclear	Poor	Poor	Copper-7	12.9%	24 months
Patchen and Berggren[54]	39	15-21	100% parous	Fair	Poor	TCu 380A	15%	24 months
Paterson, et al.[55]	133	10-19	N = 114 nulligravid	Fair	Fair	LNG-IUS	N = 11	Not specified
Sivin and Stern	706 465 2280	<20	Unclear	Poor	Fair	TCu 380A TCu 220C TCu 200	14.6/100 12.6/100 17.5/100	24 months
Weiner, et al.[57]	243	13-20	100% nulligravidae	Poor	Poor	TCu 200, Copper-7	11.5%	6 months

Table 11. Continuation Rates.

Citation	N = ?	Ages	Parity	Internal Validity	External Validity	IUDs used	Continuation rate	Timing
Behringer, et al.[45]	131	14-20	18.3% nulliparous	Fair	Fair	LNG-IUS	80.9%	36 months
Godfrey, et al.[46]	12 11	14-18	12 nulliparous	Fair	Fair	LNG-IUS TCu 380A	75% 45%	6 months
Goldman, et al.[47]	162	13-18	100% nulliparous	Poor	Poor	Lippes loop A, Cu-7, TCu	69.1%	12 months
Goldman and Reichman[48]	30	14-18	100% nulliparous	Poor	Poor	Cu-7, TCu	73.3%	24 months
Hirvonen and Kaivola[49]	241	15-21	100% nulliparous	Poor	Poor	Fincoid	73.1%	12 months
Jorgensen[50]	82	11-17	100% parous	Poor	Poor	Lippes loop, TCu	88%	12 months
Kulig, et al.[51]	120	13-22	81% nulliparous	Poor	Fair	Copper-7	39%	36 months
Lane and Sobrero[52]	101	13-19	96% nulliparous	Fair	Poor	Loop C, Loop D, LEM, W	73.2%	9 months
Larsson, et al.[53]	179	15-19	Unclear	Poor	Poor	Copper-7	77.2%	24 months
Patchen and Berggren[54]	39	15-21	100% parous	Fair	Poor	TCu 380A	39%	24 months
Paterson, et al.[55]	133	10-19	N = 114 nulligravid	Fair	Fair	LNG-IUS	85%	12 months
Sivin and Stern	706 465 2280	<20	Unclear	Poor	Fair	TCu 380A TCu 220C TCu 200	Not stratified by age	24 months
Weiner, et al.[57]	243	13-20	100% nulligravidae	Poor	Poor	TCu 200, Copper-7	78.8%	6 months

DISCUSSION

1. Interpretation of the Evidence

The purpose of this systematic review was to determine the appropriateness of the IUD as a first-line contraceptive for adolescents in the United States. Appropriateness was to be determined by the pregnancy rate, expulsion rate, and continuation rate. The evidence obtained on data extraction presents a mixed picture, with a wide range for each of those three measures. There was also discordance in the type of IUD used in the studies, with ten of the thirteen studies containing at least some IUDs not currently on the market in the U.S., and five of those containing no IUDs currently on the market in the U.S.

2. Pregnancy Rate

Eleven of the thirteen studies provided pregnancy rate within a specified time period. One retrospective cohort reported N = 0 for pregnancies in the study population, but did not provide a time period for this measure. [55] Another study did not assess pregnancy rate.[45] Only one study with both "fair" internal and external validity reported pregnancy rate, with N = 1 out of 11 at 6 months for copper-T 380A IUD, and N = 0 out of 12 at 6 months for LNG-IUS. The highest rate reported was 10% at 24 months.[54] The studies in this review tended to have a small number of participants; only 4 had more than 150 participants, and thus the data for a relatively rare event (failure rate 0.8% per year and 0.2% per year for copper-T 380A and LNG-IUS, respectively, found for all women) are more likely to be inaccurate.[19,20] Fertility naturally declines with age after peaking in the early- to mid-twenties, and thus it may not be appropriate to use the pregnancy rates of older women on the same method of birth control as

a comparison for the pregnancy rates of adolescents and young women.[58] It is deemed not possible to estimate the pregnancy rate for adolescents receiving the IUD based on the results of this systematic review.

3. Expulsion Rate

Twelve of the thirteen studies provided expulsion rate with a specified time period. One retrospective cohort provided a number of expulsions but did not provide a denominator of a time period.[55] The two studies with "fair" internal and external validity which measured expulsion rates reported rates of 9.9% at 36 months for the LNG-IUS and N = 0 of 12 at 6 months and N = 2 of 11 at 6 months for the LNG-IUS and copper-T 380A, respectively.[45,46] The expulsion rate overall ranged from 1.9 per 100 women to 18% in time periods from 6 months to 36 months. Given the heterogeneity of the devices used in terms of size as well as material and medication, and the small sizes of the studies, it is deemed that it is not possible to estimate the expulsion rate in adolescents at this time based on the results of this systematic review.

4. Continuation rate

Twelve of the thirteen studies reported continuation rate within a specified time period. The analysis of pooled data reported a continuation rate but did not stratify the rate by age.[56] The three studies with an internal and external validity of "fair" reported continuation rates of 80.9% at 36 months, 75% (LNG-IUS) and 45% (copper-T) at 6 months, and 85% at 12 months.[45,46,55] The lowest reported continuation rates were 39% at 36 months and 39% at 24 months, while the highest reported continuation rate was 88% at 12 months.[51,54] As with the

data for pregnancy rate and expulsion rate, it is deemed that it is not possible to estimate the continuation rate of the IUD based on the results of this systematic review.

5. Limitations of This Review and Overall Grade of Evidence

As with any review of the literature, this review is subject to publication bias. The main limitation of this review, however, was the quantity and quality of the available literature on the subject. The inclusion criteria were extremely sensitive as opposed to specific, and even then only 13 studies were found to be suitable for review. The study designs were a limiting factor, with only one randomized controlled trial found. This study was extremely limited by sample size (N = 23), as were many of the other studies (albeit to a lesser extent), limiting their ability to accurately describe or compare pregnancy rates, given that pregnancy while using an IUD for contraception is a relatively rare event.

Six of the studies included were descriptive rather than comparative studies, providing a lower level of evidence than comparative studies such as cohort studies or randomized controlled trials. Additionally, the internal and external validity of the included studies were a strong limiting factor. No studies had either a "good" internal validity or external validity, and only three studies had "fair" internal and external validity. Thus, the overall grade of the evidence is deemed to be poor; the evidence found in this systematic review is not sufficient to make a definitive statement regarding acceptability of the IUD as a first-line contraceptive in adolescents at this time.

6. Future Directions

Due to the nature of the intervention, it is likely not feasible to conduct large-scale randomized controlled trials comparing the IUD to other methods of contraception. Blinding (unless it is blinding as to type of IUD) is relatively impossible and most likely unethical. Thus, future studies could address this question through the use of prospective or retrospective cohort designs. Retrospective cohort studies would have the advantage of being able to capture a much larger study population as compared to prospective cohort studies due to their lower cost. Ideally, the cohort study would compare the IUD to current first-line contraception for adolescents, and the groups would be matched for a wide array of potential confounders, such as age, parity, gravidity, socioeconomic status, race, etc. Cohort studies have an inherent advantage over case-series as they directly compare the measures of interest within the same setting and using the same analyses.

Current opinions from the World Health Organization and the American Congress of Obstetricians and Gynecologists state that IUDs are appropriate first-line contraception for adolescents. However, these practice guidelines are based on expert opinion, as the level of evidence is simply lacking on this important clinical subject. As in a previous review of this topic, perhaps the most important finding of this systematic review is the overall lack of a meaningful quantity of high quality evidence. A related and promising finding, however, was the emergence of a few new studies on this topic since the last systematic review. Their improvement in quality compared to previous studies is also encouraging.

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Appendix A. Data Abstraction Forms.

Study 1	JAMA Citation: Behringer T, Reeves MF, Rossiter B, Chen BA, Schwarz EB. Duration of use of a levonorgestrel IUS amongst nulliparous and adolescent women *Contraception*. 2011;84(5):e5-e10. Country: United States
Study Question:	What are the rates and reasons for discontinuing LNG-IUS in adolescents compared to older women and nulliparous compared to parous women?
Source of Funding:	Doris Duke; NIH grants
Source Population:	Women aged 14-50 years seen in an academic clinic in Pittsburgh, PA and receiving an LNG-IUS for contraception, dysmenorrhea, or menorrhagia between June 2005 and April 2008
Study Population:	All women fitting criteria in retrospective medical chart review Age considered adolescent: 14-20 Exclusion criteria: No information on parity; >50
Design:	Study design: Retrospective cohort Sample size: 131 adolescents (14-20), 697 adult women
Intervention:	Type of IUD? LNG-IUS
Comparison:	Adolescent vs. non-adolescent
Potential for Selection Bias:	Moderate Potential for sampling bias: Are there differences in adolescent vs. adult populations who utilize the academic medical center? Were the 36 subjects excluded due to lack of information on parity significantly different from study population?
Population Characteristics:	Parity: 18.3% nulliparous in adolescent group; 11.5% nulliparous in adult group Randomization? No Groups similar at baseline? No. Statistically significant difference in race ($p = 0.03$), marital status ($p < 0.001$), and parity (0.03); controlled for in analysis by interaction term for parity and age
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 36 months Cumulative expulsion rate? Yes --Timing? 36 months Continuation rate? Yes --Timing? 36 months
Measurement	Study groups: N = 131 adolescents $\underline{<}$20 N = 697 adult women 21-50 Exposure meaures: Insertion recorded in medical record; age recorded in medical record Outcomes: IUS expulsion, IUS removal, method failure Outcome measures: Medical record review
Potential for Measurement Bias:	Low to moderate Trained research assistants abstracted relevant data from medical records Discontinuation may be underreported as patients could have had device removed at another clinic or self-removed
Potential for Confounding:	Moderate. No randomization was performed as this was a cohort study No data was provided about comparability in terms of socio-economic status The statistically significant differences in parity, race, and marital status were controlled for in the data analysis, with an interaction term included for parity and age
Analysis:	Primary: Women not seen following placement assumed to have continued use Secondary: Examined only those making 1+ follow-up visits Cox proportional hazard models in both scenarios controlled for age, race, and marital status; interaction term included to ensure that parity was not affecting outcome coefficients Kaplan-Meier curves created and log-rank tests performed to test for equality of time to IUS removal Chi-square and Fisher's Exact Tests used to test associations
Results:	Unintended pregnancy rate: Not measured Cumulative expulsion rate: 9.9% in adolescents, 5.2% in adults ($p = 0.03$) at 36 months Continuation rate: 80.9% in adolescents, 82.6% in adults at 36 months
Attrition:	Number of dropouts? 36 adolescents and 219 adults did not return to the study clinic after insertion (27.5% and 31.4%)
Overall Judgment of Internal Validity (Quality Rating):	Fair.
External Validity:	Fair.

Study 2	JAMA Citation: Godfrey EM, Memmel LM, Neustadt A, et al. Intrauterine contraception for adolescents aged 14-18 years: A multicenter randomized pilot study of levonorgestrel-releasing intrauterine system compared to the copper T 380A. *Contraception*. 2010;81(2):123-127. Country: United States
Study Question:	What are the rates of pregnancy, expulsion, continuation, infection, side effects, bleeding, and satisfaction for two FDA-approved IUC methods among 14-18 year old adolescents?
Source of Funding:	Anonymous foundation
Source Population:	37 women 14-18 seen in Section of Family Planning in the Department of Obstetrics and Gynecology at the University of Chicago and the Department of Family Medicine at the University of Illinois-Chicago seeking intrauterine contraception who reported regular menstrual cycles and desired long-acting, reversible IUC approached regarding study
Study Population:	23 of initial 37 eligible and randomized Age considered adolescent: 14-18 Exclusion criteria: Known uterine or cervical anomaly, untreated cervical infection, pelvic infection within the past 3 months, previous IUC use, chronic disease (e.g., malignancy, liver or kidney disease), genital bleeding of unknown etiology or allergy to device ingredients
Design:	Study design: Randomized, single-blind (participant) controlled trial Sample size: 23 adolescents (11 copper T 380A, 12 LNG-IUS)
Intervention:	Type of IUD? LNG-IUS and copper T 380A
Comparison:	LNG-IUS vs. copper T 380A
Potential for Selection Bias:	Moderate to low 11 refused screening visit (wanted to choose type of device, desired other birth control, did not meet inclusion criteria, not interested in study, parent/guardian refused consent); 3 excluded due to refusal to participate Unknown characteristics of those not selected vs. those selected
Population Characteristics:	Parity: 8 nulliparous in LNG-IUS, 4 nulliparous in CuT380A Randomization? Yes – 4 blocks with sets of 6; numbers in sealed, opaque envelopes, generated sequentially by statistician uninvolved in study Groups similar at baseline? Yes; however small size of study groups precluded use of statistical tests for significant differences
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 6 months Cumulative expulsion rate? Yes --Timing? 6 months Continuation rate? Yes --Timing? 6 months
Measurement	Study groups: N = 11 receiving copper T 380A N = 12 receiving LNG-IUS Exposure measures: Insertion as performed by study providers Outcomes: uterine perforations, removal, STI diagnosis, continuation rates, pregnancy rate, expulsion rate, removal rate, side effects, satisfaction Outcome measures: Clinical evaluation at study visits; side effects assessed via journal; satisfaction assessed via Likert scale at last visit
Potential for Measurement Bias:	Moderate to low Investigators and coordinators were not blinded to type of device inserted (participants were blinded to the device inserted) Outcome measures were not readily subjective
Potential for Confounding:	Moderate to low Randomization was performed However, due to the small size of the study groups, there was still some potential for confounding
Analysis:	Intention to treat (participants were included in originally assigned groups for assessment of outcomes)
Results:	Unintended pregnancy rate: 0 in LNG-IUS, 1 in copper T 380A at 6 months Cumulative expulsion rate: 0 in LNG-IUS, 2 in copper T 380A at 6 months Continuation rate: 75% (n = 9 of 12) in LNG-IUS, 45% (n = 5 of 11) in copper T 380 A
Attrition:	Number of dropouts? 2 in LNG-IUS, 2 in CuT380A
Overall Judgment of Internal Validity (Quality Rating):	Fair.
External Validity:	Fair.

Study 3	JAMA Citation: Goldman JA, Dekel A, Reichman J. Immediate postabortion intrauterine contraception in nulliparous adolescents. *Isr J Med Sci*. 1979;15(6):522. Country: Israel
Study Question:	What are the rates of expulsion, uterine bleeding, uterine contraction/pain, mild pelvic inflammation, discontinuation/removal, and pregnancy for adolescents receiving three different IUDs
Source of Funding:	Unknown
Source Population:	300 pregnant teenagers referred for abortion and deemed to be of low intelligence and/or low motivation and with a primarily low socioeconomic background offered IUD contraception from two different clinics
Study Population:	162 of those referred consented Age considered adolescent: 13-18 Exclusion criteria: not stated
Design:	Study design: prospective cohort Sample size: 162 adolescents (56 Lippes loop A, 45 copper-7, 61 copper-T)
Intervention:	Type of IUD? Lippes loop A, copper-7, copper-T
Comparison:	Lippes loop A vs. copper-7 vs. copper-T
Potential for Selection Bias:	High Only about half of those deemed eligible by nebulous criteria consented to the study. None of the characteristics of those who refused to participate are available.
Population Characteristics:	Parity: 126 primigravid, 36 multigravid; all nulliparous Randomization? No No information regarding comparability of groups or method of selection of type of IUD
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 12 months Cumulative expulsion rate? Yes --Timing? 12 months Continuation rate? Yes --Timing? 12 months
Measurement	Study groups: N = 56 receiving Lippes loop A N = 45 receiving copper-7 N = 61 receiving copper-T Exposure measures: Insertion as performed by study providers Outcomes: Expulsion of IUD, uterine bleeding, uterine contractions (or pain), mild pelvic inflammation, removal of IUD, dropout, pregnancy Outcome measures: Unclear for some measures of outcome (uterine bleeding, uterine contractions or pain, mild pelvic inflammation); likely clinical assessment otherwise
Potential for Measurement Bias:	High No blinding was performed The method of determining the clinical outcomes was not stated by the authors
Potential for Confounding:	High There is no information on the comparability of the groups, and the groups were not randomized. There is also no information on how the exposures (types of IUDs) were allocated
Analysis:	Chi-square test for significance
Results:	Unintended pregnancy rate: 4 for Lippes loop A, 1 for copper-7, 1 for copper-T at 12 months; 3.7% for all methods Cumulative expulsion rate: 11 for Lippes loop A, 3 for copper-7, 4 for copper-T at 12 months; 11.1% for all methods Continuation rate: 48.2% for Lippes loop A, 86.6% for copper-7, 75.4% for copper-T at 12 months; 69.1% for all methods Statistically significant difference found for copper-7 and copper-T vs. Lippes loop A
Attrition:	Number of dropouts? Not reported
Overall Judgment of Internal Validity (Quality Rating):	Poor.
External Validity:	Poor.

Study 4	JAMA Citation: Goldman JA, Reichman J. Contraception in the teenager. A comparison of four methods of contraception in adolescent girls. *Isr J Med Sci*. 1980;16(7):510. Country: Israel
Study Question:	What are the continuation rates, complications, and side effects of four types of contraception (OCP, IUD, condom, foam) in adolescent women?
Source of Funding:	Unknown
Source Population:	High-school students referred to a clinic or to private practitioners by their parents or school nurse following request for contraception
Study Population:	160 "highly selected adolescents of high socioeconomic standing" Age considered adolescent: 14-18 Exclusion criteria: not stated
Design:	Study design: prospective cohort Sample size: 160 adolescents (72 OCPs, 30 IUD, 38 condoms, 20 contraceptive foam)
Intervention:	Counseling on and access to contraceptive method (OCPs, IUD, condoms, contraceptive foam) Type of IUD? copper-7 or copper-T
Comparison:	OCPs vs. IUD vs. condoms vs. contraceptive foam
Potential for Selection Bias:	High Nothing stated as to how the adolescents stated to be "highly selected" were actually selected No demographic information given to compare the study population to the source population
Population Characteristics:	Parity: nulliparous Randomization? No No information regarding comparability of groups or method of selection of type of contraception
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 24 months Cumulative expulsion rate? Yes --Timing? 24 months Continuation rate? Yes --Timing? 24 months
Measurement	Study groups: N = 72 receiving OCPs N = 30 receiving IUD N = 38 advised to use condoms N = 20 receiving contraceptive foam Exposure measures: initiation of contraception and counseling as provided by study providers Outcomes: Expulsion of IUD, uterine bleeding, pain, pelvic inflammatory disease, side effects, reported cessation of contraception, pregnancy Outcome measures: Mild signs suggestive of salpingitis for pelvic inflammatory disease; nausea, fluid retention, breast tenderness, depression for side effects; these were most likely measured clinically, however it is not clear from the paper
Potential for Measurement Bias:	High No blinding was performed No information is available as to standardization of the counseling provided by the study providers The method of determining the clinical outcomes was not stated by the authors, and it is highly likely that these measures were subjectively obtained by the authors
Potential for Confounding:	High There is no information on the comparability of the groups, and the groups were not randomized. There is also no information on how the exposures (types of contraception) were allocated
Analysis:	Unspecified; likely chi-square test for significance
Results:	Unintended pregnancy rate: 0 for OCPs, 1 for IUD, 2 for condoms, 1 for foam at 24 months Cumulative expulsion rate: 2 for IUD at 24 months Continuation rate: 72% for OCPs, 73.3% for IUDs, 78.9% for condoms, and 15.8% for foam at 24 months ?statistical significance of difference in continuation rates at 24 months?
Attrition:	Number of dropouts? Not reported
Overall Judgment of Internal Validity (Quality Rating):	Poor.
External Validity:	Poor.

Study 5	JAMA Citation: Hirvonen E, Kaivola S. A new copper IUD (fincoid) in adolescent and young nulliparous women. *Contracept Deliv Syst*. 1983;4:149. Country: Finland
Study Question:	What is the overall performance of a new copper IUD (Fincoid)?
Source of Funding:	Unknown
Source Population:	Nulliparous adolescents seen at an outpatient clinic in Helsinki in whom oral contraceptives had caused side-effects or were contraindicated
Study Population:	241 women in whom the Fincoid was inserted Age considered adolescent: 15-21 Exclusion criteria: not stated
Design:	Study design: case-series Sample size: 241 adolescents
Intervention:	Type of IUD? Fincoid
Comparison:	None
Potential for Selection Bias:	High No information given on how the patient population was selected No demographic information given to compare the study population to the source population
Population Characteristics:	Parity: nulliparous Randomization? No No information regarding comparability of groups or method of selection of participants from source population "Some" of the participants "occasionally forgot or were reluctant to take oral contraceptives"
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 12 months Cumulative expulsion rate? Yes --Timing? 12 months Continuation rate? Yes --Timing? 12 months
Measurement	Study groups: N = 241 receiving Fincoid Exposure measures: Insertion of IUD by study providers Outcomes: Accidental pregnancies, expulsions (total and partial), removals (with indications), continuation rate Outcome measures: Unclear.
Potential for Measurement Bias:	High The method of determining the clinical outcomes was not stated by the authors, and it is highly likely that these measures were subjectively obtained by the authors Also, the providers were aware of the intervention, and may have therefore been able to change the results based on desire to have the method succeed or fail
Potential for Confounding:	N/A Not a comparative study
Analysis:	Life table; rates calculated as per 100 women
Results:	Unintended pregnancy rate: 4.2 (± 1.5) per 100 women at 12 months Cumulative expulsion rate: 1.9 (± 0.9) total expulsions per 100 women at 12 months; 8.5 (± 1.9) partial expulsions per 100 women at 12 months Continuation rate: 73.1% at 12 months
Attrition:	Number of dropouts? 6.8 per 100 women at 12 months lost to follow-up
Overall Judgment of Internal Validity (Quality Rating):	Poor.
External Validity:	Poor.

Study 6	JAMA Citation: Jorgensen V. One-year contraceptive follow-up of adolescent patients. *Am J Obstet Gynecol*. 1973;115(4):484. Country: United States
Study Question:	What are the outcomes of different types of contraception in adolescent women seen at a family planning clinic?
Source of Funding:	Grant from The Population Council, NY, NY
Source Population:	221 "High risk" postpartum women seen in adolescent obstetrics and gynecology clinic (213 receiving OCPs in the interim from 5 days postpartum to 5 weeks postpartum)
Study Population:	184 women returning to 5 week postpartum visit selecting either oral contraceptive, IUD, or diaphragm for contraception Age considered adolescent: 11-17 Exclusion criteria: not stated
Design:	Study design: prospective cohort Sample size: 184 adolescents (90 OCPs, 80 IUD, 2 diaphragm)
Intervention:	Type of IUD? Lippes loop, copper T
Comparison:	OCPs vs. IUD vs. diaphragm
Potential for Selection Bias:	Moderate to high Patients self-selected method of contraception No information regarding comparability of groups in terms of socioeconomic status, race, etc.
Population Characteristics:	Parity: parous Randomization? No No information given regarding characteristics (race, socioeconomic status) of study population as compared to source population
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Not stratified by intervention --Timing? 12 months Cumulative expulsion rate? Yes --Timing? 12 months Continuation rate? Yes --Timing? 12 months
Measurement	Study groups: N = 90 selecting OCPs N = 82 selecting IUDs N = 2 selecting diaphragm Exposure measures: Insertion of IUD by study providers, prescription of OCPs, or prescription of diaphragm Outcomes: Continuation of contraception, expulsion Outcome measures: Office visits at 1, 3, 6, and 12 months
Potential for Measurement Bias:	Moderate to high The method of determining the clinical outcomes was not stated by the authors Also, the providers were aware of the intervention, and may have therefore been able to change the results based on desire to have the method succeed or fail
Potential for Confounding:	High No information available on comparability of groups Are those who choose IUD vs. condoms fundamentally different in a way that affects continuation rate, pregnancy rate, etc? (this is not as likely to affect expulsion rate)
Analysis:	None
Results:	Unintended pregnancy rate: 5 at 12 months (all methods) Cumulative expulsion rate: 5 at 12 months Continuation rate: 88% IUD vs. 70% OCPs
Attrition:	Number of dropouts? 86 (38%) Not much information given regarding characteristics of those who dropped out versus those who completed the study (72 with IUD vs. 63 on OCPs completed the 12 months)
Overall Judgment of Internal Validity (Quality Rating):	Poor. No attention was given to confounders
External Validity:	Poor.

Study 7	JAMA Citation: Kulig JW, Rauh JL, Burket RL, Cabot HM, Brookman RR. Experience with the copper 7 intrauterine device in an adolescent population. *J Pediatr*. 1980;96(4):746. Country: United States
Study Question:	What are the rates of continuation, expulsion, satisfaction, and pregnancy with copper-7 IUDs in an adolescent population?
Source of Funding:	Not specified
Source Population:	Adolescent patients seen from 1974-1978 in the Cincinnati Adolescent Clinic choosing an IUD for contraception
Study Population:	120 consecutive patients from July 1974 to June 1978 Age considered adolescent: 13-22 Exclusion criteria: "medical contraindications to Cu-7" (not specified); patients unwillingness to retain the device and/or return for follow-up
Design:	Study design: case-series Sample size: 120 adolescent patients with 137 total insertions
Intervention:	Type of IUD? Copper-7
Comparison:	N/A
Potential for Selection Bias:	Moderate to high Patients self-selected method of contraception Not clear how study population compares to source population (i.e., are there important differences between women who choose an IUD vs. those who choose OCPs and other methods?)
Population Characteristics:	Parity: 81% nulliparous, 16% primiparous, 3% multiparous Randomization? N/A 58% black/42% white "generally urban" Predominantly from "lower socioeconomic areas"
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 36 months Cumulative expulsion rate? Yes --Timing? 36 months Continuation rate? Yes --Timing? 36 months
Measurement	Study groups: N = 120 selecting IUD for contraception Exposure measures: Insertion of IUD by study providers Outcomes: Continuation of contraception, side effects, removal, expulsions, pregnancy rate Outcome measures: Office visits at 3 weeks post-insertion, and every three months after initial post-insertion visit
Potential for Measurement Bias:	Moderate to high The methods of determining the clinical outcomes were not stated by the authors Also, the providers were aware of the intervention, and may have therefore been able to change the results based on desire to have the method succeed or fail It is not clear that the measurements were performed in an equal, valid, and reliable fashion
Potential for Confounding:	N/A No comparison was made
Analysis:	N/A
Results:	Unintended pregnancy rate: 3 of 120 at 36 months (2.0 per 100 woman-years of IUD insertion) Cumulative expulsion rate: 18% overall (n = 21 of 116) at 36 months; 22% for parous (n = 5 of 22) at 36 months; 17% for nulliparous (n = 16 of 94) Continuation rate: 39% at 36 months
Attrition:	Number of dropouts? 4 (3%) No information regarding characteristics of dropouts
Overall Judgment of Internal Validity (Quality Rating):	Poor.
External Validity:	Fair.

Study 8	JAMA Citation: Lane ME, Sobrero AJ. Experience with intrauterine contraception by adolescent women. *Mt Sinai J Med*. 1975;42(4):337. Country: United States
Study Question:	Purpose: to "describe the experience of the Margaret Sanger Research Bureau with the provision of IUD to clients of its Teen Center"
Source of Funding:	Funded in part by grants from The Population Council, NY, NY
Source Population:	399 adolescent patients seen at the Margaret Sanger Teen Center from 3/1/1971-12/31/1972
Study Population:	101 patients who selected the IUD as their contraceptive method Age considered adolescent: 13-19 Exclusion criteria: "medical contraindication" (not specified); "high level of anxiety" regarding insertion
Design:	Study design: case-series Sample size: 101 adolescents with 130 total IUD insertions
Intervention:	Type of IUD? Loop C, Loop D, LEM, W
Comparison:	N/A- intent of report was not to analyze performance of devices by type
Potential for Selection Bias:	Moderate Patients self-selected method of contraception Not clear how study population compares to source population (i.e., are there important differences between women who choose an IUD vs. those who choose OCPs and other methods?)
Population Characteristics:	Parity: 96% nulliparous; 83% nulligravid Randomization? N/A Median age 16 years
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 9 months Cumulative expulsion rate? Yes --Timing? 9 months Continuation rate? Yes --Timing? 9 months
Measurement	Study groups: N = 101 patients selecting IUD for contraception with 130 total IUD insertions (2 W, 54 LEM, 44 Loop C, and 1 Loop D on first insertion; 2 W, 1 LEM, 13 Loop C, and 13 Loop D on reinsertion) Exposure measures: Insertion of IUD by study providers (85% by two attending physicians, with the other 15% by medical fellows and one family planning nurse practitioner) Outcomes: Accidental pregnancy, expulsion, removal (as well as reason), discomfort of insertion Outcome measures: Office visits at 4 weeks post-insertion, and at least every three months after initial post-insertion visit
Potential for Measurement Bias:	Moderate Exposure measurement was likely equal, valid, and reliable, with two physicians performing the majority (85%) of insertions The methods of determining the clinical outcomes were not stated by the authors Also, the providers were aware of the intervention, and may have therefore been able to change the results based on desire to have the method succeed or fail
Potential for Confounding:	N/A No comparison was made
Analysis:	N/A
Results:	Unintended pregnancy rate: n = 4 of 101 at 9 months Cumulative expulsion rate: n = 21 of 101 at 9 months Continuation rate: n = 73.2% at 9 months
Attrition:	Number of dropouts? 8 (7 lost to follow-up, 1 released to another source of care) No information regarding characteristics of dropouts
Overall Judgment of Internal Validity (Quality Rating):	Fair
External Validity:	Poor

Study 9	JAMA Citation: Larsson B, Hagström B, Viberg L, Hamberger L. Long-term clinical experience with the Cu-7-IUD. Evaluation of a prospective study. *Contraception*. 1981;23(4). Country: Sweden
Study Question:	Objective: Evaluate compiled data of prospective study of copper-7 IUD
Source of Funding:	No information given
Source Population:	Women receiving contraception at a private clinic in Stockholm or two family planning centers in Huddinge from 1971-1979
Study Population:	1446 women Age considered adolescent: subgroup analysis of age group 15-19 Exclusion criteria: Not available
Design:	Study design: prospective cohort Sample size: 179 women 15-19; 444 women 20-24; 518 women 25-29; 128 women 30-34; 134 women 35-39; 43 women 40-49
Intervention:	Type of IUD? Copper-7
Comparison:	Based on age groups
Potential for Selection Bias:	High Unclear how method of contraception was selected, or how study population was selected Not clear how study population compares to source population
Population Characteristics:	Parity: unknown for age strata; overall n = 699 nulligravidae, 59 nulliparae, 337 parous x 1, 351 parous x 2+ Randomization? N/A
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 24 months Cumulative expulsion rate? Yes --Timing? 24 months Continuation rate? Yes --Timing? 24 months
Measurement	Study groups: N = 179 women 15-19 N = 444 women 20-24 N = 518 women 25-29 N = 128 women 30-34 N = 134 women 35-39 N = 43 women 40-49 Exposure measures: Insertion of IUD by study providers (two physicians at private clinic = 665 women; "several doctors and midwives" at family planning clinics) Outcomes: Accidental pregnancy, expulsion, removal (as well as reason), salpingitis, bleeding/pain, planned pregnancy Outcome measures: Unclear
Potential for Measurement Bias:	High The methods of determining the clinical outcomes were not stated by the authors Also, the providers were aware of the intervention, and may have therefore been able to change the results based on desire to have the method succeed or fail for a given outcome for a particular subgroup
Potential for Confounding:	High No information given regarding comparability of different age groups (e.g., marital status, education level, socioeconomic status, etc.)
Analysis:	Chi-square test, Fisher's exact test
Results:	Unintended pregnancy rate: n = 11 (6.1%) at 24 months for 15-19; higher, but not statistically significantly different than other age groups Cumulative expulsion rate: n = 23 (12.9%) at 24 months for 15-19; statistically significantly higher than expulsions for other groups Continuation rate: 77.2% at 24 months
Attrition:	Number of dropouts? 135 women lost to follow-up; unclear how many from each group No information regarding characteristics of dropouts
Overall Judgment of Internal Validity (Quality Rating):	Poor. No adjustment for confounding or attempt to describe characteristics of study groups beyond age
External Validity:	Poor.

Study 10	JAMA Citation: Patchen L, Berggren EK. Use of the copper T380A intrauterine device by adolescent mothers: Continuation and method failure *J Pediatr Adolesc Gynecol*. 2011;24(2):71-73. Country: United States
Study Question:	Objective: To contribute to limited empirical data regarding the use of copper-T 380A IUD among parous adolescents
Source of Funding:	NICHD grants, Center on Health and Education and Department of Human Science in the School of Nursing and Health Studies at Georgetown University
Source Population:	318 adolescent mothers aged 15-21 (who had delivered prior to age 18) while participating in a teen secondary pregnancy prevention program
Study Population:	39 women 93% Hispanic Age considered adolescent: 15-21 Exclusion criteria: older than 21 at IUD insertion, nulliparous
Design:	Study design: retrospective case-series Sample size: 39 women
Intervention:	Type of IUD? Copper-T 380A
Comparison:	N/A
Potential for Selection Bias:	Moderate Unclear how method of contraception was selected Not clear how study population compares to source population However, all charts within the source population were reviewed
Population Characteristics:	Parity: parous Randomization? N/A
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 24 months Cumulative expulsion rate? Yes --Timing? 24 months Continuation rate? Yes --Timing? 24 months
Measurement	Study groups: N = 39 women receiving copper-T 380A IUD Exposure measures: Chart review Outcomes: Accidental pregnancy, expulsion, removal (as well as reason), salpingitis, bleeding/pain, planned pregnancy Outcome measures: Chart review
Potential for Measurement Bias:	Moderate The methods of determining clinical outcomes were explicitly stated Providers were aware of the intervention, and may have therefore been able to change the results based on desire to have the method succeed or fail for a given outcome Chart review was not blinded
Potential for Confounding:	N/A No comparison made
Analysis:	N/A
Results:	Unintended pregnancy rate: n = 4 (10%) at 24 months Cumulative expulsion rate: n = 6 (15%) at 24 months Continuation rate: 39% at 24 months
Attrition:	Number of dropouts? 72% with complete follow-up data to termination of IUD use or 24 months
Overall Judgment of Internal Validity (Quality Rating):	Fair.
External Validity:	Poor. Sample size is very small and likely not indicative of overall U.S. primary care population.

Study 11	JAMA Citation: Paterson H, Ashton J, Harrison-Woolrych M. A nationwide cohort study of the use of the levonorgestrel intrauterine device in new zealand adolescents *Contraception*. 2009;79(6):433-438. Country: New Zealand
Study Question:	Objective: To "determine the indications for insertion of the LNG-IUD in New Zealand adolescents … and to establish patterns of use, including duration of use of the LNG-IUD in the adolescent population and reasons for removal."
Source of Funding:	No external funding source
Source Population:	Adolescent women in New Zealand ages 10-19 receiving the LNG-IUS
Study Population:	177 adolescent women identified through Intensive Medicine Monitoring Program (IMMP) as having received the IUD → 175 (insertion population) → 133 questionnaires completed (responder population) Age considered adolescent: 10-19 Exclusion criteria: deceased, records not available through New Zealand Health Information Service (NZHIS); device not actually inserted
Design:	Study design: retrospective case-series Sample size: 133 women
Intervention:	Type of IUD? LNG-IUS
Comparison:	N/A
Potential for Selection Bias:	Moderate Large-scale database which should identify most cases Not clear how responder population compares to insertion population or source population
Population Characteristics:	Parity: n = 114 nulligravid Randomization? N/A
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? No reported pregnancies, but study not powered to assess unplanned pregnancy rate --Timing? N/A Cumulative expulsion rate? "cumulative incidence" --Timing? Unclear Continuation rate? Yes --Timing? 12 months
Measurement	Study groups: N = 133 women receiving LNG-IUS deemed to be part of the "responder population" Exposure measures: Chart review, questionnaire to provider; characteristics for provider inserting the IUS were available Outcomes: Comorbidities reported with insertion, removal, indications for removal (including expulsion) Outcome measures: Chart review (NZHIS), questionnaire to provider
Potential for Measurement Bias:	Moderate Chart review and questionnaire completion were not blinded
Potential for Confounding:	N/A No comparison made
Analysis:	Product-limit survival estimates; gross discontinuation rates estimated at 1 year following insertion of LNG-IUS
Results:	Unintended pregnancy rate: n = 0; no time period specified Cumulative expulsion rate: n =11 Continuation rate: 85% at 12 months
Attrition:	Number of dropouts? N/A, retrospective chart review
Overall Judgment of Internal Validity (Quality Rating):	Fair.
External Validity:	Good. Broad assessment of LNG-IUS in adolescents in a developed nation.

Study 12	JAMA Citation: Sivin I, Stern J. Long-acting, more effective copper T IUDs: A summary of U.S. experience, 1970-75. *Stud Fam Plann*. 1979;10(10). Country: United States
Study Question:	Objective: To assess the characteristics of 3 different types of copper-T IUDs, including pregnancy rates, expulsion rates, and continuation rates.
Source of Funding:	Not specified
Source Population:	Women in the United States receiving a copper IUD
Study Population:	Women receiving either the copper-T 200, copper-T 380A, and copper-T220C in one of 42 studies Age considered adolescent: <20 Exclusion criteria: women in studies with >30% loss to follow-up were excluded
Design:	Study design: pooled data from random assignment and cohort studies Sample size: 3,536 accepting copper-T 380A; 1850 accepting copper-T 220C; 9,838 accepting copper-T 200
Intervention:	Type of IUD? Copper-T 380A; copper-T 220C; copper-T 200
Comparison:	Copper-T 380A vs. copper-T 220C vs. copper-T 200
Potential for Selection Bias:	High No information regarding how participants were initially selected for the study, or information on how they relate to the source population
Population Characteristics:	Parity: no information regarding parity of <20 subgroup; 42.8% of TCu 200 acceptors; 63.7% of TCu 380A acceptors, and 70.3% of TCu 220C acceptors were nulliparous Randomization? Double-blind randomization in some constituent studies
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 24 months Cumulative expulsion rate? Yes --Timing? 24 months Continuation rate? Not stratified by age --Timing? N/A
Measurement	Study groups: N = 706 women <20 receiving TCu 380A N = 2830 women >20 receiving TCu 380A N = 465 women <20 receiving TCu 220C N = 1385 women >20 receiving TCu 220C N = 2280 women <20 receiving TCu 200 N = 7558 women >20 receiving TCu 200 Exposure measures: based on report from 42 studies; exposure measured with regard to timing of insertion Outcomes: Pregnancy, expulsion, removal for medical reasons, removal for personal reasons, continuation Outcome measures: based on report from 42 studies; visits typically 1, 3, 6, 12 months post-insertion and every 12 months thereafter
Potential for Measurement Bias:	Moderate to high Possibility of interpretation of results meant to skew towards a particular outcome as this is secondary analysis of other studies Not clear that there is homogeneity in assessing outcomes
Potential for Confounding:	High No assessment of or correction for confounding variables
Analysis:	Tietze method of analysis
Results:	Unintended pregnancy rate: in women <20 at 24 months: 1.0 per 100 acceptors for TCu 380A; 2.2 per 100 acceptors for TCu 220C; 6.6 per 100 acceptors for TCu 200 Cumulative expulsion rate: in women <20 at 24 months: 14.6 per 100 acceptors for TCu 380A, 12.6 per 100 acceptors for TCu 220C, 17.5 per 100 acceptors for TCu 200 Continuation rate: not stratified by age
Attrition:	Number of dropouts? <30% for all studies
Overall Judgment of Internal Validity (Quality Rating):	Poor
External Validity:	Fair

Study 13	JAMA Citation: Weiner E, Berg AA, Johansson I. Copper intrauterine contraceptive devices in adolescent nulliparae. *Br J Obstet Gynaecol*. 1978;85(3):204. Country: Sweden
Study Question:	Objective: Report on the clinical outcomes of 243 nulligravidae receiving copper IUCDs
Source of Funding:	Not specified
Source Population:	772 women in Sweden aged 13-20 seeking contraception at the Department of School Health in Uppsala, Sweden from 3/1973-6/1975
Study Population:	243 patients who elected to get IUCD Age considered adolescent: 13-20 Exclusion criteria: Not specified
Design:	Study design: Prospective case-series Sample size: 243 patients
Intervention:	Type of IUD? Copper-T 200 and copper-7
Comparison:	N/A
Potential for Selection Bias:	High No information regarding comparability of study population to source population Unclear whether the source population was composed of solely nulligravidae or only study population
Population Characteristics:	Parity: All were nulligravidae Randomization? N/A
Outcome Assessment:	Primary outcome measures: Unintended pregnancy rate? Yes --Timing? 6 months Cumulative expulsion rate? Yes --Timing? 6 months Continuation rate? Yes --Timing? 6 months
Measurement	Study groups: N = 243 women who had copper IUDs inserted Exposure measures: Insertion as performed by clinic gynecologist Outcomes: Pregnancy, expulsion, removal for medical reasons, removal for personal reasons, continuation, Pearl index Outcome measures: Based on return visit to clinic; unclear how outcomes were specifically measured
Potential for Measurement Bias:	Moderate to high No blinding of participants or investigators to the intervention No standardized method of assessment of outcomes is mentioned; it is not clear exactly how the outcomes were measured
Potential for Confounding:	N/A
Analysis:	None
Results:	Unintended pregnancy rate: N = 5 of 243 (2%) at 6 months Cumulative expulsion rate: N = 28 of 243 (11.5%) at 6 months Continuation rate: 78.8% at 6 months
Attrition:	Number of dropouts? 17 of 243 (7%) at 6 months
Overall Judgment of Internal Validity (Quality Rating):	Poor.
External Validity:	Poor.