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The safety of intrauterine devices among young women: a systematic review☆,☆☆

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Abstract

Objective: The objective was to determine the association between use of intrauterine devices (IUDs) by young women and risk of adverse outcomes.

Methods: We searched Pubmed, CINAHL, Embase, Popline and the Cochrane Library for articles from inception of database through December 2015. For outcomes specific to IUD use (IUD expulsion and perforation), we examined effect measures for IUD users generally aged 25 years or younger compared with older IUD users. For outcomes of pregnancy, infection, pelvic inflammatory disease (PID), and heavy bleeding or anemia, we examined young IUD users compared with young users of other contraceptive methods or no method.

Results: We identified 3169 articles of which 16 articles from 14 studies met our inclusion criteria. Six studies (Level II-2, good to poor) reported increased risk of expulsion among younger age groups compared with older age groups using copper-bearing (Cu-) IUDs. Two studies (Level II-2, fair) examined risks of expulsion among younger compared with older women using levonorgestrel-releasing (LNG-) IUDs; one reported no difference in expulsion, while the other reported increased odds for younger women. Four studies (Level II-2, good to poor) examined risk of expulsion among Cu- and LNG-IUD users combined and reported no significant differences between younger and older women. For perforation, four studies (Level II-2, fair to poor) found very low perforation rates (range, 0%−0.1%), with no significant differences between younger and older women. Pregnancies were generally rare among young IUD users in nine studies (Level I to II-2, fair to poor), and no differences were reported for young IUD users compared with young combined oral contraceptive (COC) or etonogestrel (ENG) implant users. PID was rare among young IUD users; one study reported no cases among COC or IUD users, and one reported no difference in PID among LNG-IUD users compared with ENG implant users from nationwide insurance claims data (Level I to II-2, fair). One study reported decreased odds of bleeding with LNG-IUD compared with COC use among young women, while one study of young women reported decreased odds of removal for bleeding with LNG-IUD compared with ENG implant (Level I to II-2, fair).

Conclusion: Overall evidence suggests that the risk of adverse outcomes related to pregnancy, perforation, infection, heavy bleeding or removals for bleeding among young IUD users is low and may not be clinically meaningful. However, the risk of expulsion, especially for Cu-IUDs, is

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higher for younger women compared with older women. If IUD expulsion occurs, a young woman is exposed to an increased risk of unintended pregnancy if replacement contraception is not initiated. IUDs are safe for young women and provide highly effective reversible contraception.

Keywords

Intrauterine device; Young women; LARC; IUD; Teens; Adolescents

1. Introduction

While the intrauterine device (IUD) is one of the most effective contraceptive methods, some health care providers have concerns about its use among young women [1]. Younger women are at higher risk of sexually transmitted infections (STIs) [2]. There remains concern about whether IUD insertion or use affects the risk of a lower genital tract infection ascending to the upper genital tract, leading to pelvic inflammatory disease (PID) and subsequent infertility. However, despite concerns, evidence shows that the risk of PID is low among IUD users and has not shown that IUDs cause infertility [3–5]. Additionally, women of any age who choose to use an IUD for contraception are potentially at risk for adverse events such as expulsion and perforation, changes in bleeding patterns related to IUD use and IUD failure [6]. There is concern that these risks may be greater in younger compared with older IUD users.

We originally conducted this systematic review to prepare for an Expert Working Group meeting to update the World Health Organization (WHO) Medical Eligibility Criteria for Contraceptive Use (MEC) in March 2014. The resulting fifth edition of the WHO MEC assigns a category 2 for use of copper-bearing (Cu-) and levonorgestrel-releasing (LNG-) IUDs among females from menarche until age less than 20 years [7]. A category 2 is defined as “a condition where the advantages of using the method generally outweigh the theoretical or proven risks.” For women 20 years and older, IUD use is a category 1, with no restriction on use. The objective of this review is to examine two key questions: (a) “Are young women with a Cu- or LNG-IUD at increased risk of expulsion or perforation compared with older women with a Cu- or LNG-IUD?” (b) “Are young women with a Cu- or LNG-IUD at increased risk of serious adverse events (specifically pregnancy, infection, infertility or delayed return to fertility, bleeding, and removals or discontinuations due to any of these outcomes) compared with either young women using other methods of contraception or older women using Cu- or LNG-IUDs?”

2. Materials and methods

We conducted this review according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [8]. We searched the PubMed, Embase, Popline and CINAHL databases for all peer-reviewed articles in any language published from database inception through December 2015 using the search terms found in Appendix A. We also searched the Cochrane Library for relevant systematic reviews using the terms *IUD* and *intrauterine*. To identify additional relevant articles, we hand-searched reference lists of

target articles from the search, as well as any review articles concerning IUD use among our target population.

We selected studies that examined a group of young women using an IUD and assessed the relative risks of several outcomes for these women compared with either young women not using an IUD or older IUD users. We defined young women as those aged less than or equal to 25 years after initially searching for studies including women aged less than 20 years according to the WHO recommendation; we realized we would exclude many useful studies that included women 21–25 years. Our review included CuT380A, LNG-IUD, NovaT, Gynefix, Multiload Cu-250 and Multiload Cu-375, which we determined are currently approved and available by contacting international IUD experts. We included studies in which these IUDs were used in over 25% of the study IUD sample. When possible, we reported data by IUD type and excluded results reported for other IUDs not included in this review. For two recent US studies which included Cu-IUD or CuT IUD, we assumed this referred to CuT380A, the only Cu-IUD available recently in the United States. For studies that did not specify the type of Cu-IUD used, we examined study location and included the article if one of our preidentified types of Cu-IUDs was commonly used in that country.

Our outcomes of interest were IUD expulsion, perforation, pregnancy, PID (or infection, such as cervicitis, if PID was not reported), infertility or time to return to fertility, heavy bleeding or anemia, and removals or discontinuations due to any of these outcomes; articles had to report rates or relative measures of effect for each outcome of interest.

Ideally, we sought evidence that compared young women using IUDs with young women using another contraceptive method or no method. This comparison, however, is only possible for certain outcomes of interest and not possible for the IUD-specific outcomes of expulsions and perforations. For these outcomes, we selected older IUD users as the comparison group. Therefore, we selected primary research articles that directly answered the first key question: “Are young women with a Cu- or LNG-IUD at increased risk of expulsion or perforation compared with older women with a Cu- or LNG-IUD?”

For the outcomes of pregnancy, infection, infertility or return to fertility, bleeding, and removals or discontinuations due to any of these outcomes, we selected primary research articles that directly answered the second key question: “Are young women using a Cu- or LNG-IUD at increased risk of serious adverse events (specifically pregnancy, infection, infertility or return to fertility, bleeding, and removals or discontinuations due to any of these outcomes) compared with young women using other methods of contraception?” We also included indirect evidence that compared IUD use among younger women with older women and reported any of these outcomes.

Three authors (T.J., H.R. and K.C.) independently abstracted, summarized and assessed the data from each primary article. The quality of each article was independently evaluated using the US Preventive Services Task Force grading system [9]. When the quality assessment varied between authors, we decided the grade by consensus. We did not compute summary measures of association due to heterogeneity among the studies with respect to study design, populations and outcomes.

3. Results

The search strategy yielded 3169 articles of which 16 met our inclusion criteria [10–25]. Twelve studies answered our first key question and compared risk of expulsion or perforation among younger versus older women with a Cu- or LNG-IUD [10–13,16,17,19–22,24,25]; 11 studies reported expulsions (Table 1), and 4 reported perforations (Table 2). Eleven studies answered our second key question; 2 compared risk of adverse events among young IUD users with young nonusers [15,23], and 10 studies compared risk of adverse events among younger versus older IUD users [11–18,20–22]. Of these studies answering our second key question, nine studies reported pregnancies (Table 3), nine reported infections (Table 4), and eight reported heavy bleeding or removal for bleeding (Table 5). No studies meeting our inclusion criteria examined infertility or return to fertility. Three articles were published from the same 5-year randomized controlled trial (RCT) of two copper IUD types, NovaT and CopperT 200, which reported point estimates for our outcomes of interest at different time points [16–18]. For our purposes, this study examined our question with a prospective cohort design comparing adolescent IUD users with older users. The results from NovaT users, an IUD included in this review, were reported separately when possible; however, the multivariate analyses at 5 years combined NovaT and CopperT 200 data, and those results are presented together [16,17]. Two target articles were published in a language other than English and were translated for full data abstraction [10,22].

3.1. Expulsion

Twelve articles from 11 studies reported on IUD expulsion. These included three prospective cohort studies, seven retrospective cohort studies and one case–control study [10–13,16,17,19–22,24,25]. Studies generally compared samples of young women with varying age cutoffs (aged less than 20–25 years) with older women using LNG or Cu-IUDs or both in a variety of geographic locations.

Three prospective cohort studies and one case–control study reported in five articles found increased risk of expulsion for younger compared with older women [16,17,19,20,25]. All of these studies examined Cu-IUDs, and one also provided results for LNG-IUD. One of the three prospective cohort studies (Level II-2, good) examined 918 NovaT and CuT200 IUD users, of all ages, and found that the cumulative net rate of expulsion at year 5 was 9.3 per 100 NovaT users; although expulsion rates by age were not reported, the authors did report that the risk of expulsion decreased significantly with increasing age [adjusted risk ratio (aRR) 0.96 per year, p=.001], adjusted for previous IUD use and history of vaginal delivery [16,17]. The second prospective cohort study (Level II-2, poor) included 852 primiparous women aged less than 30 years presenting 6–8 weeks after vaginal delivery for CuT380A insertion [20]. At 1 month, the crude rate of expulsion among adolescents (aged 13–19 years) was 2.9% compared with 0.2% among older women [aged 20–30 years, crude odds ratio (OR) 12.16, 95% confidence interval (CI) 1.48–99.50, p=.001]. From 1 to 3 months, there were one expulsion in the adolescent group and none in the older group, and no report of expulsion was documented from 3 to 6 months. The most recently published prospective cohort study (Level II-2, fair) was a secondary analysis of data from the CHOICE project in the United States. This study reported an increased risk of expulsion for women aged 14–19

years compared with women 20–45 years using either the LNG-IUD or Cu-IUD over mean follow-up of 22.6 months [LNG-IUD: adjusted hazards ratio (aHR) 2.26, 95% CI 1.68–3.06; Cu-IUD: aHR 3.06, 95% CI 1.75–5.33, respectively] [19]. The cumulative expulsion rates of Cu-IUD and LNG-IUD were not significantly different at 3 months among women aged less than 20 years compared with those aged 20 years or older (3.5%, 95% CI 2.2–5.5; 2.5%, 95% CI 2.1–2.9, respectively) but were significantly higher at 6 (7.1%, 95% CI 5.2–9.7; 3.9%, 95% CI 3.4–4.5, respectively), 12 (10.5%, 95% CI 8.0–13.5; 5.7, 95% CI 5.1–6.4, respectively), 24 (16.4%, 95% CI 13.2–20.3; 7.7%, 95% CI 6.9–8.5, respectively) and 36 months (18.8%, 95% CI 15.1–23.4; 9.3%, 95% CI 8.3–10.4, respectively); p values were not reported. The one case–control study (Level II-2, good) identified examined factors associated with Cu-IUD expulsion among 70 cases and 1536 controls over 12 months of follow-up [25]. Women aged less than 20 years had an aHR of expulsion of 5.4 (95% CI 1.7–17.5) compared with women aged 35 years or older. The aHR found the risk of expulsion decreased significantly with increasing age (p<.001) after controlling for amount of menstrual flow and dysmenorrhea.

Of seven retrospective cohort studies, one examined the LNG-IUD, and four examined a mix of Cu-IUD and LNG-IUD users and reported no significant differences in expulsion between younger women and older women [11–13,21,24]; one study of the Cu-IUD (II-2, poor) reported decreasing rates of expulsion with increasing age, but no significance testing was performed [10]; one study reported higher crude rates of expulsion for younger women compared with older women using two different Cu-IUDs, but no significance testing was performed [22].

The first of these retrospective cohort studies (Level II-2, fair) compared 131 women aged less than 21 years with 697 women aged 21 years or more using the LNG-IUD. This study found a significant difference between groups in overall expulsion rates at 3 years (9.9% and 5.2%, respectively, p=.03); however, no significant association was found in multivariable analysis (aHR for women with follow-up 1.72, 95% CI 0.61–4.89) once adjusted for parity, race and marital status [13]. Another retrospective cohort study (Level II-2, poor) compared women aged less than 18 years (n=69) with women aged 18 years and older (n=164) using mostly LNG-IUD (11 women used CuT380A) with up to 8 years of follow-up [11]. Expulsion rates were 0.049 per person-year for those aged <18 years and 0.012 per person-year for those aged 18–21 years; the crude relative risk (cRR) of expulsion was not significant (cRR=4.09; no confidence interval reported; p=.22). The third study (Level II-2, good) compared expulsion rates among women age 13–19 (n=249), 20–24 (n=750) and 25–35 years (n= 1139) with a mean follow-up of 37 months. This study showed a significant difference in crude rates of either LNG- or Cu-IUD expulsions by age group that ranged from 5.1% to 8.0% (p=.03); however, in adjusted models, there was no significant difference among women aged 13–19 years compared with 20–24 years (aHR 0.79, 95% CI 0.47–1.35, p=.39) or compared with women aged 25–35 years (aHR 0.68, 95% CI 0.40–1.13, p=.14) after adjusting for race and IUD type [12]. Two retrospective cohort studies (Level II-2, fair to poor) reported crude rates of expulsion for younger women compared with older women (aged <21 years versus 21–35 years and aged 13–17 years versus 18–24 years) for Cu- and LNG-IUD users and found no significant differences between age groups with rates ranging from 2.7% to 8.8% over 1 and 6 years of follow-up [21,24]. A retrospective cohort study

(Level II-2, poor) that combined 938 NovaT and 717 Multiload 250 users reported cumulative 6-year rates of loss of IUD for those aged less than 20, 20–24, 25–29, 30–35 and 35+ years; loss of IUD was not further described. Point estimates decreased with increasing age from 13.2% for those less than 20 years to 3.0% for those 35+ years. Confidence intervals overlapped between contiguous groups but differed when comparing aged less than 20 years and age groups greater than 25 years; no p values were reported [22]. Finally, one retrospective cohort study (Level II-2, poor) described crude expulsion rates among NovaT and MultiLoad 250 users aged greater than 25 years compared with users 16–25 years over at least 2 years of follow-up [10]. Expulsion rates were lower among older women using NovaT or MultiLoad 250 IUDs (4.6% and 0%, respectively) compared with younger users (10.4% and 5.4%, respectively), although no significance testing was performed.

3.2. Perforation

Four retrospective cohort studies reported on perforation. Two were relatively small retrospective chart reviews of Level II-2, poor quality (233 women aged less than 21 using primarily LNG-IUD and followed for up to 7 years; 1132 women aged 13–24 years using CuT380A or LNG-IUDs and followed for up to 6 months). No perforations were reported in either study [11,24]. A retrospective analysis of insurance claims data (Level II-2, fair) found two perforations among 11,722 (0.02%) women aged 24 years and younger using the LNG-IUD or Cu-IUD and 36 perforations among 78,767 women aged 25 years and older (0.05%) [14]. No significance testing was reported. Finally, another retrospective study based on data obtained from medical chart review (Level II-2, fair) found no significant difference in perforations among 249 women aged 13–19 years (0%), 750 women aged 20–24 years (1%) and 1139 women aged 25–35 years (0%) (p=.09) after LNG or Cu-IUD insertion with mean follow-up of 37 months [12].

3.3. Pregnancy

Nine studies, reported in 11 articles, reported on pregnancy as an outcome. These included one RCT, one prospective cohort study and seven retrospective cohort studies [11–18,21–23]. Only two studies provided direct evidence by evaluating pregnancy rates among young IUD users compared with young women using other contraceptive methods. The first, an RCT (Level I, fair), randomized 193 nulliparous women aged 18–25 years to either the LNG-IUD or a combined oral contraceptive (COC) and found no pregnancies in either group over 12 months [23]. The second was a large retrospective cohort study (Level II-2, fair) that compared etonorgestrel (ENG) implant users with LNG-IUD users by age from nationwide insurance database information [15]. Among 15- to 19-year-olds, the authors found no differences within 12 months for ENG implant compared with LNG-IUD users in the odds of ectopic pregnancy (aOR 0.92, 95% CI 0.06–14.8) or odds of abnormal pregnancy or spontaneous abortion (aOR 1.29 95% CI 0.41–4.08), and a significantly decreased odds of normal pregnancy (aOR 0.40, 95% CI 0.21–0.75, respectively). Among 20- to 24-year-olds, the authors found no differences for ENG implant compared with LNG-IUD users in the odds of ectopic pregnancy (aOR 0.56, 95% CI 0.07–4.46) or normal pregnancy (aOR 0.68, 95% CI 0.41–1.12), and slightly increased odds of abnormal pregnancy or spontaneous abortion (aOR 2.24, 95% CI 1.05–4.79). This study reported similar rates of ectopic pregnancy (0%, 0.1%, 0.1%), abnormal pregnancy or spontaneous abortion (0.2% for all age

groups), and normal pregnancy (1.5%, 1.3%, 0.8%) for age groups of 15–19 years, 20–24 years and 25–44 years, respectively, but no statistical testing results were reported for these comparisons.

Seven studies (one prospective and six retrospective) provided indirect evidence by comparing pregnancy rates among younger IUD users with older IUD users. A prospective cohort study using RCT data (Level II-2, fair) found a significant decrease in pregnancy rate with increasing age among NovaT and CuT200 IUD users over 5 years (aRR 0.90 per year, p=.001, no confidence interval reported), adjusting for IUD type and country location [16,17]. Similar findings of decreasing pregnancy rates with increasing age groups were also reported at 3 years from the same study (Level II-2, poor), but no significance testing or multivariable analysis was performed [18]. Authors of a retrospective study (Level II-2, poor) from Denmark also reported 6-year cumulative rates of pregnancy among users of NovaT and Multiload 250 IUDs. Pregnancy rates declined across age groups, with higher rates for women aged less than 20 years (10.8%, 95% CI 5.0–22.6) compared with women aged 20–24 years (5.0%, 95% CI 3.0–8.3) and 35+years (0.9, 95% CI 0.2–3.4) [22]. However, five retrospective studies compared pregnancy rates among IUD users by age and found either no difference in pregnancy risk or a minimal increased risk for younger women. One retrospective study (Level II-2, fair) reported no pregnancies among 131 adolescent LNG-IUD users aged less than 21 years and 3 pregnancies among 697 (0.4%) adult LNG-IUD users aged 21 years or more; this difference was not statistically significant, and follow-up times were not reported for the majority of the sample [13]. One retrospective study obtaining data from medical chart review (Level II-2, poor) compared younger Cu-IUD and LNG-IUD users aged less than 18 years with users aged 18–21 years and found no pregnancies with an IUD in place in either group with mean follow-up of 37 months [11]. One large retrospective cohort study (Level II-2, fair) found no difference in risk of contraceptive failure among women using LNG- or Cu-IUD who were aged 20–24 vs. 13–19 years (aHR 0.98, 95% CI 0.30–3.13, p=.97) or 25–35 vs. 13–19 years (aHR 0.48, 95% CI 0.15–1.59, p=.23) [12]. One large retrospective cohort study (Level II-2, fair) used a national insurance claims database to examine several pregnancy outcomes among Cu-IUD and LNG-IUD users over 12 months [14]. There were no significant differences in odds of ectopic pregnancy, abnormal pregnancy or spontaneous abortion, or normal pregnancy between women aged 15–19 compared with 20–24 years. When compared with women aged 25–44 years, there were no significant differences in odds of ectopic pregnancy or abnormal pregnancy or odds of spontaneous abortion among women aged 15–19 years; however, there were slightly elevated odds of normal pregnancy among the younger age group (aOR 1.42, 95% CI 1.13–1.78). Finally, a retrospective cohort study (Level II-2, poor) reviewed charts up to 6 months after Cu-IUD or LNG-IUD insertion for 684 women and reported 1 pregnancy among 502 women (0.2%) aged 21–35 years compared with no pregnancy among women aged less than 21 years; no significance testing was reported [21].

3.4. Reported infection

Nine studies reported infection as an outcome, although studies used various terms and definitions for their outcomes [11,12,14,15,18,20–23]. Two studies, an RCT (Level I, fair) and a large retrospective cohort study (Level II-2, fair), provided direct evidence by

reporting PID rates among young women using IUDs compared with young women using other methods [15,23]. The RCT enrolled 193 nulliparous women aged 18–25 years and randomized 94 to LNG-IUD and 99 to COCs; no PID cases were reported among the total study population over 12 months [23]. The large retrospective cohort study reviewed nationwide insurance claim data from the United States and found no difference in PID rates within 12 months of contraception initiation among women aged 15–19 years using ENG implant (n=2388) compared with LNG-IUD (n=2204) (aOR 0.23, 95% CI 0.03–2.06); similarly, there was no difference in PID rates among women aged 20–24 years using ENG implant (n=2014) compared with LNG-IUD (n=8988) (aOR 0.32, 95% CI 0.04–2.42) [15]. Rates of PID were also reported for women aged 25–44 years (0.1%), aged 20–24 years (0.2%) and aged 15–19 years (0.2%) using LNG-IUD, but no significance testing or confidence intervals were reported.

The remaining seven studies provided indirect evidence and compared rates of infection among younger and older IUD users. Rates of PID were reported in five studies, while rates of infection were reported in two studies. One prospective cohort study (Level II-2, poor) of CuT380A users reported 2 cases of PID among 281 women (0.8%) aged 13–19 years within the week after insertion; this study reported no additional cases in this age group or among women aged 20–30 years (n=571) at 6 months [20]. The large retrospective insurance claims analysis (Level II-2, poor) found no difference in PID rates within 12 months of initiation of either a LNG- or Cu-IUD among 1835 women aged 15–19 years compared with 9887 women aged 20–24 years (aOR 1.36, 95% CI 0.38–4.82); similarly, there was no difference for the women aged 15–19 years compared with 78,767 women aged 25–44 years (aOR 1.44, 95% CI 0.65–3.15) [14]. One study using data from retrospective chart reviews (Level II-2, poor) of 2138 LNG- or Cu-IUD users found no significant difference in crude rates of PID among 249 women aged 13–19 years (PID rate: 3%), 750 women aged 20–24 years (2%) or 1139 women aged 25–35 years (1%) (p=.08) [12]. In another retrospective cohort study (Level II-2, poor), cumulative 6-year rates of IUD removal for PID requiring treatment were higher among women aged 20–24 years (15.4%, 95% CI 12.0–19.7) compared with women aged 35 years and older (6.2%, 95% CI 3.7–10.3), but rates of removal were similar for women aged less than 20 years compared with the two older groups (15.1%, 95% CI 8.7–25.5) [22]. Finally, one retrospective cohort study (Level II-2, poor) reported numbers of PID cases by chart review among 684 IUD users and reported one case among women aged 21–35 years and no cases among women aged less than 21 years for up to 6 months after IUD insertion [21].

The remaining two studies providing indirect evidence included the 5-year RCT from which we abstracted prospective comparative data on removals for infection at year 3 among copper IUD users [18,26,27] and a retrospective study comparing women aged less than 18 vs. 18–21 years using either the LNG- or Cu-IUD [11]. At year 3 of the prospective study (Level II-2, poor), the highest rate of removal for infection was reported among women aged 20–24 years (7.3%); rates were similarly low for those aged less than 20 years (2.8%) and those aged 25 years and older (2.5–3.0%); no significance testing was reported [18]. The retrospective study (Level II-2, poor) reported 5 infections among 69 women aged less than 18 years and 13 infections among 164 women aged 18–21 years, with a crude relative risk of 1.56 which was not significant; no p values or confidence intervals were reported [11].

3.5. Heavy bleeding or removal for bleeding

Ten articles from eight studies reported on heavy bleeding. Studies reported either bleeding rates or removal rates for bleeding, or removal for bleeding and/or pain [12,14–18,20–23]. Two of the studies provided direct evidence and compared bleeding rates or removal rates for bleeding for adolescent IUD users with adolescent users of other methods; six of the studies provided indirect evidence by comparing bleeding rates or removal rates for bleeding among IUD users of different age groups. No articles were identified that fit our inclusion criteria and reported anemia as an outcome.

The first study providing direct evidence was the RCT (Level I, fair) comparing 94 adolescent (aged 18–25 years) LNG-IUD users with 99 adolescent COC users; in this study, a significantly higher proportion of LNG-IUD users reported a decrease in bleeding compared with COC users (49.3% and 22%, respectively; p=.001), and a larger decrease in bleeding days was seen in the LNG-IUD group compared with the COC group (p=.001). The termination rate for bleeding in the LNG IUD group was 2.5% compared with 0 in the COC group. This difference was not statistically significant (p=.16) [23]. The second study (Level II-2, fair) providing direct evidence was a retrospective cohort study that examined nationwide insurance claims data, which reported rates of contraceptive removal within 30 days after abnormal bleeding [15]. Women aged 15–19 years and 20–24 years with ENG implant had increased odds of removal within 30 days after experiencing abnormal bleeding compared with LNG-IUD users of the same age (aOR 1.56, 95% CI 1.09–2.23; aOR 1.48, 95% CI 1.12–1.96, respectively). Rates of LNG-IUD removal within 30 days after abnormal bleeding were also reported for women aged 25–44 years (21.9%), aged 20–24 years (21.4%) and aged 15–19 years (19.7%); however, statistical testing or confidence intervals were not reported.

One prospective and one retrospective study provided indirect evidence by examining rates of bleeding for young women compared with older women using IUDs [14,20]. The prospective study (Level II-2, poor) compared two age groups of primiparous postpartum women who had a CuT380A placed 6–8 weeks after vaginal delivery [20]. Self-reported bleeding (spotting, breakthrough, menorrhagia or metrorrhagia) was significantly higher among women aged 13–19 years compared with women aged 20–30 years at 1 and 3 months (crude odds ratio (cOR) 1.46, 95% CI 1.02–2.07, p=.015; cOR 1.76, 95% CI 1.07–2.90, p=.004, respectively), but there was no significant difference at 6 months (OR 1.42, 95% CI 0.79–2.55, p=.230). One retrospective study (Level II-2, poor) examined insurance claim data for bleeding and compared 1835 women aged 15–19 years using either Cu-IUD or LNG-IUD with 9887 women aged 20–24 years or 78,767 women aged 25–44 years. The authors found no significant differences in excessive menstruation or uterine hemorrhage comparing the youngest group with those aged 20–24 years (aOR for excessive menstruation1.01, 95% CI 0.76–1.33; aOR for uterine hemorrhage 1.18, 95% CI 0.93–1.50) or those 25–44 (aOR for excessive menstruation 0.94, 95% CI 0.79–1.12; aOR for uterine hemorrhage: 1.14, 95% CI 0.98–1.32) [14].

The remaining four studies, three retrospective and one prospective, examined rates of IUD removal due to bleeding for younger compared with older women [12,16–18,21,22]. A retrospective study based on data from chart review (Level II-2, fair) reported significantly

different crude rates of removal for abnormal bleeding by age group (p=.03) among 2138 LNG- or Cu-IUD users aged 13–19 years (12%), aged 20–24 years (8.8%) and aged 25–35 years (10.2%) [12]. Another retrospective cohort study (Level II-2, poor) reported cumulative 6-year removal rates per 100 women for bleeding and/or pain that ranged from 12.7% (among women 35 years or older) to 14.1% (among women aged 20–24 years) to 20.5% (among women under 20 years old). No significant testing was reported [22]. The third retrospective cohort study (Level II-2, poor) examined removals for bleeding among 334 LNG- or Cu-IUD users with 6-month follow-up and reported that 7.1% of women aged less than 21 years and 5.0% of women aged 21–35 years had their IUD removed for bleeding; no p value was reported [21]. Prospective comparative data from an RCT (Level II-2, fair) examined removals for bleeding and/or pain and found that age was not significantly associated with these removals among NovaT and Copper T200 users over 5 years [16–18].

4. Discussion

The 16 studies included in this review provide direct and indirect evidence on whether young women who use IUDs are at increased risk of adverse events compared with similar-aged women using other contraceptive methods or compared with older women using IUDs.

For the outcome of expulsion, we examined 11 studies that compared younger women to older women using 4 different kinds of IUDs (Multiload 250, NovaT, LNG, TCu380A). All studies were of Level II-2 evidence, with three studies of good quality, three of fair quality and five of poor quality. In general, results across six studies suggested decreasing risk of expulsion with increasing age for Cu-IUD, results from two studies reported mixed results for LNG-IUD, and four studies did not find a significant difference in expulsion rates between younger and older groups, examining Cu- and LNG-IUDs together. Only one case–control study was designed with expulsion as the primary outcome, and no study was powered to detect a difference in expulsion between age groups. Parity was assessed and adjusted for in several of the studies. Quality otherwise varied, with poor studies often having small sample sizes, high attrition and no adjustments made for potential confounders including parity. Seven of the 11 studies reporting expulsion were retrospective cohort studies, and the majority ascertained the outcome from chart review which may be underestimated.

The direct evidence evaluating perforation came from four Level II-2 studies, all retrospective cohorts with sample sizes ranging from 233 to over 90,000 women and all with a very small number of reported events. The two smaller studies of poor quality had sample sizes of 233 and 1132 women using either CuT380A or LNG-IUDs. These two studies were also limited by loss to follow-up and limited by the diagnosis of perforation as a reported event rather than a sought-after diagnosis by ultrasound, possibly underestimating events. No perforations were reported from any women in these two studies with follow-up times of 6 months to 7 years [11,24]. The larger national sample from an insurance claims database [14] and the multicenter retrospective cohort study [12] were both of fair quality but were also limited by the potential underreporting of events as well as the inability to assess parity as a potential confounder for expulsion in the larger national study. Still, the perforation rate

for both LNG and Cu IUD users was extremely low, ranging from 0% to 0.1% regardless of age, among the samples of 2138 and 90,489 women with follow-up of 12 months and mean follow-up of 37 months.

Evidence on pregnancy risk among young women using IUDs is limited by the rare occurrence of pregnancy among IUD users. One study comparing young COC users to young LNG-IUD users reported no pregnancies, which differs from the higher typical-use failure rates of COCs [28]. Another study comparing adolescent ENG implant users to adolescent LNG IUD users reported a minimally increased risk for pregnancy outcomes among LNG-IUD users, although pregnancy was rare, which is similar to typical-use failure rates for both methods. The indirect studies that compared younger IUD users with older IUD users reported either no pregnancies or a slightly higher risk of pregnancy among younger IUD users. This may simply reflect decreasing risk of pregnancy among women of older reproductive age.

One of the largest obstacles to young women using IUDs is provider concern about pelvic infection, possibly leading to PID and infertility. There are several flaws in studies that have examined risk for infection among IUD users. These include the use of an inappropriate comparison group, the overdiagnosis of PID among IUD users and not controlling for confounders [4]. For this review, we included studies that stratified infection outcomes by age. Given the higher risk for STI in younger women, the most appropriate comparison group is one of younger women not using an IUD and not using a method that affects STI risk, as condoms do as a barrier method or COCs do with thickening of cervical mucus [6]. Two studies provided direct evidence of fair quality. The first was a Level I study that randomized young women to the IUD or COCs and found no cases of PID. The second was a Level II study that used nationwide insurance claims data and found no difference in odds for PID among ENG implant user or LNG-IUD users. The remaining six studies provided indirect evidence and were Level II-2, fair to poor quality. Infection was generally poorly defined, all used comparison groups of older IUD users, and none controlled for sexual behavior or condom use. No studies were identified that assessed infertility risk among young IUD users; however, it has been shown in a previous study that infertility secondary to tubal occlusion among nulligravid women is associated with antibodies to *Chlamydia trachomatis* and is not associated with previous copper IUD use [5].

The evidence for bleeding among young IUD users varied across the studies. The most useful data would assess whether heavy bleeding leads to other complications, such as anemia or discontinuation, particularly among Cu-IUD users. However, no data were identified that reported anemia as an outcome, and removal for bleeding may be influenced by provider practices and women's preferences as opposed to patients' ages. Among two direct studies of fair quality, one reported decreased odds of bleeding among young LNG-IUD compared with COC users, and another reported decreased odds of removal among young LNG IUD compared with ENG implant users [15,23]. Two studies providing indirect evidence of poor quality compared rates of bleeding for younger women with older women using IUDs, and four studies compared rates of removal for bleeding for different age groups. A large retrospective cohort study was limited by reporting only combined bleeding data for LNG and Cu IUD users, which would have opposite effects on bleeding profiles,

and found no significant difference in bleeding among young IUD users compared with older users [14]. The other study was of poor quality and examined primiparous women's report of any bleeding after insertion of Cu IUD at postpartum visit and found reports to be higher in younger women at 1 and 3 months but not at 6 months [20], which may likely have been affected by the postpartum status. The remaining studies looking at removals for bleeding found no to minimal differences between age groups but were limited by small sample sizes leading to wide confidence intervals or limited by no significance testing to demonstrate a true difference in rates.

5. Conclusion

Overall, this review does not support an association between the adverse outcomes of pregnancy, perforation, infection or bleeding and IUD use by young women aged less than or equal to 25 years. However, evidence suggests that young women are at increased risk for expulsion of Cu-IUDs and may be at increased risk for LNG-IUD expulsion compared with older women, although evidence is mixed and limited. While IUD expulsion is not a safety issue, these events may expose young women to an increased risk of unintended pregnancy if replacement contraception is not initiated. IUDs are safe for young women and provide highly effective reversible contraception.

Acknowledgments

⋆⋆ Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Appendix A.: Pubmed search terms:

(((((((“Intrauterine Devices”[Mesh] OR “Intrauterine Devices, Medicated”[Mesh] OR “Intrauterine Devices, Copper”[Mesh]) OR (“intrauterine devices”[MeSH Terms] OR (“intrauterine”[All Fields] AND “devices”[All Fields]) OR “intrauterine devices”[All Fields] OR (“intrauterine”[All Fields] AND “device”[All Fields]) OR “intrauterine device” [All Fields]) OR iud[All Fields] OR iucd OR ius OR “intrauterine system” OR “intrauterine systems” OR (intrauterine[All Fields] AND (“contraception”[MeSH Terms] OR “contraception”[All Fields])))) AND (((complication* OR expuls* OR perforation OR infection OR insertion OR anemia OR bleed* OR fertil* OR infertil* OR continuation OR discontinuation or remov*))))) AND (teen* OR adolescen*)))

Embase search terms:

((levonorgestrel or copper) and (IUD or IUCD or IUS or device or system or contraception)) or ((intrauterine and (device or contraception or system*)) or IUD or IUCD or IUS) and (complicat* or explus* or perforat* or infect* or insert* or anemia or bleed* or continu* or discontinu* or remov*) and (teen* or adolescen*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

- adolescen*

- anemia
- bleed*
- complicat*
- continu*
- contraception
- contraceptive
- copper
- copper intrauterine device
- device
- device*
- discontinu*
- explus*
- infect*
- insert*
- intrauterine
- intrauterine contraceptive device*
- intrauterine device
- iucd
- iud
- ius
- levonorgestrel
- perforat*
- remov*
- system
- system*
- teen*

CINAHL search terms:

(iud* or iucd* or ius* or intrauterine device* or intrauterine contraceptive device* or intrauterine system* OR (intrauterine AND contraception)) AND (complicat* or expuls* or perforat* or infect* or insert* or place* or injur* or continuation or discontinuation OR fertil* or infertil*) AND (adolescen* OR teen*)

POPLINE search terms:

(IUD OR IUCD OR IUS OR (intrauterine device) OR (intrauterine contraceptive device) or (intrauterine system) OR (intrauterine AND contraception)) AND (complicat* OR expuls* OR perforat* OR infect* OR insert* OR place* OR injur* OR continuation OR discontinuation OR fertil* OR infertil*) AND (adolescen* OR teen*)

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Table 1

Expulsion

Author, year, location, sources up of support	Study design, follow-Up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Albert, 1982 [10] Spain Source of support NR	Retrospective cohort chart review Follow-up of at least 2 years	Minor complications from use of 3216 Cu- IUDs Age 16–25: *n*=373 Age>25: *n*=854	ML Cu250 (*n*=237) Age 16–25: *n*=190 Age>25: *n*=47 Nova-T (*n*=990) Age 16–25: *n*=183 Age>25: *n*=807	Expulsion (total and partial)	Frequency of expulsion: ML Cu 250: Age 16–25: 10/190 (5.3%) Age >25: 0/47 (0%) p value NR Nova-T: Age 16–25: 19/183 (10.4%) Age >25: 37/807 (4.6%) p value NR	Outcome well defined	Potential confounders not assessed Only descriptive statistics reported for age; no measures of precision or association reported	II-2, poor
Alton, 2012 [11] United States Source of support NR	Retrospective cohort chart review, 3 sites Up to 7 years of follow-up Up to 80.88 person-years among women aged b18 years Up to 330.52 person-years among women aged 18–21 years	Women aged ≤ 21 years (range 11–21 years) having IUD inserted Age <18: *n*=69 Age 18–21: *n*=164	LNG-IUD (*n*=222) CuT380A (*n*=11)	Expulsions	Crude RR for expulsion alone (age <18 vs. 18–21): 4.1 (p=.22)	Multicenter trial, diverse population Rates reported in person-year to account for different follow-up	Small sample and few events; no information on study power All data from chart review; outcomes may be underestimated if women sought care from other sites High proportion of adolescents that were parous (82%)	II-2, poor
Aoun, 2014 [12] United States No financial disclosures	Retrospective cohort Mean follow-up 37±11 months (range 19–57 months)	Women aged 13–35 years who had LNG-IUD or Cu-IUD inserted for contraception (*n*=2138) Age 13–19: *n*=249 Age 20–24: *n*=750 Age 25–35: *n*=1139	LNG-IUD (*n*=1746) Cu-IUD (*n*=392)	Expulsion *n*=125	Adjusted hazard ratio for expulsion (95% CI) (reference group age 13–19): Age 20–24: 0.79 (0.47–1.35) p=.39 Age 25–35: 0.68 (0.40–1.13) p=.14	Multicenter Large sample size with sufficient power Reviewed charts from office, emergency department and hospitals including laboratory and imaging results Multivariable analysis adjusted for age, race and IUD type Excluded those with no follow-up	Age groups differed by parity, gravidity, marital status, insurance but not tested in multivariable model	II-2, good

Author, year, location, sources up of support	Study design, follow-Up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Behringer, 2011 [13] United States Doris Duke Charitable Foundation; NIH	Retrospective cohort 69.2% of sample (*n*=573) returned to study clinic at least once 47.2% of sample (*n*=391) ≥ 1 year of follow-up	Women aged 14–50 years who received LNG-IUD (*n*=828) Age ≤21: *n*=131 Age >21: *n*=697	LNG-IUD	Expulsion	Adjusted HR for expulsion (age ≤20 years vs. 21–30 years assuming continued use for women not seen for follow-up): 1.49 (95% CI: 0.76–2.92) Adjusted HR for expulsion (age ≤20 years vs. 21–30 years among women seen for follow-up): 1.72 (95% CI: 0.61–4.89)	Reported study power (although powered for outcomes by parity) Adjusted for age, race, parity and marital status and interaction terms Separately analyzed expulsions for all participants assuming those with loss to follow-up as continuers and analyzed expulsions only for participants who had follow-up (similar results were observed) Performed analysis with age as continuous and categorical variable	All data from chart review from single site; outcomes may be underestimated if women sought care from other sites High attrition: follow-up information unavailable for 31% of women who had IUDs inserted Powered to detect differences in discontinuation between adolescents and older women, not our outcome of interest, coupled with few reported events Unclear criteria for ascertaining the outcome Groups differed at baseline by race, marital status and parity High proportion of adolescents that were parous (82%)	II-2, fair
Luukkainen, 1983 [16], and Allonen, 1984 [17] Denmark, Finland and Sweden Population Council, International Development Research Centre of	Prospective cohort (single arm of data from RCT comparing two Cu-IUDs) 5 years (follow-up visits at 3, 6, 12, 24, 36, 48 and 60 months)	Women presenting for IUD insertion, (1865 interval and 322 postabortion insertions) randomized to Nova-T (*n*=918) or Cu T Nova-T: Age ≤19: *n*=75 Age 20–24: *n*=253 Age >24: *n*=590	Nova-T (*n*=918)	60-month cumulative net expulsion rates per 100 acceptors	60-month cumulative net expulsion rates per 100 Nova-T acceptors (9) Age <25: 8.2% Age 25–29: 12.3% Age 30–34: 5.9% Age 35+: 10.9%	Long follow-up (5 years) Multiple country sites, multiple providers Low loss to follow-up at 5 years (13.1%) Life table regression analysis, including screening for parity as potential confounder, included history of vaginal	Not powered to detect differences between age groups Multivariate analysis combined IUD results from two types of IUDs (one not of interest)	II-2, good

Author, year, location, sources up of support	Study design, follow-Up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Canada, Ford Foundation Rockefeller Foundation					Expulsion risk (estimate combines both IUDs) decreased with increasing age: Adjusted RR: 0.96 per year of age, p=.001 (5) Nova T expulsion rate at year 5 (all ages): 9.3 expulsions/100 acceptors	delivery and previous IUD use	Infrequent follow-up after first year (every 12 months) may have led to underreporting of some outcomes	
Madden, 2014 [19] United States The Susan Thompson Buffett Foundation, NICHD, NCRR, National Center for Advancing Translational Sciences	Secondary data analysis from prospective cohort Follow-up by telephone at 3 and 6 months then every 6 months for 2 or 3 years Mean follow-up 22.6±11 months	Women who received LNG-IUD or Cu-IUD during study period (5403) Age <20 years: *n*=529 Age 20–29 years: *n*=3519 Age 30–45 years: *n*=1355	LNG-IUD: (*n*=4219) Cu-IUD: (*n*=1184)	Cumulative expulsion rates at 3, 6, 12, 24, 36 months	Adjusted hazards ratio (95% CI) for age 14–19 years (reference group: age ≥ 20): LNG-IUD 2.26 (1.68–3.06) Cu-IUD 3.06 (1.75–5.33)	Large sample size with large number events with adequate power calculated to detect twofold difference Adjusted for age, race, obesity, marital status, low socioeconomic status, nulliparity, self-reported heavy periods and immediate postabortion placement	High loss to follow-up at 24 months (55.3%) Partial and complete expulsions combined, diagnostic criteria not reported Follow-up reports either self-reported or by office visit	II-2, fair
Rasheed, 2011 [20] Egypt Source of support not stated	Prospective cohort 1, 3, 6 months	Primiparous women age <30 at time of IUD insertion 6–8 weeks after vaginal delivery Adolescents (age 13–19): *n*=281 Adults (age 20–30): *n*=571	CuT380A	Expulsion	Expulsion OR (age 13–19 vs. age 20–30): 12.16 (95% CI: 1.48–99.50); p=.001	Ultrasound check for proper placement and at follow-up to check for expulsions All primiparous, so no concern about parity as potential confounder	Postpartum population only, less generalizable No assessment for potential confounders Single site High attrition and differential loss to follow-up at 6 months (66% adolescents and 85% adults lost) Small number of events, no power calculation	II-2, poor

Author, year, location, sources up of support	Study design, follow-Up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
							reported for any outcome	
Ravi, 2014 [21] United States American Academy of Family Physicians, NIH grant K23HD067247	Retrospective cohort Chart reviewed up to 6 months after insertion	All women aged ≤35 with IUD insertion in an NYC-area FQHC network (*n*=684) Age <21: *n*=182 Age 21–35: *n*=502	LNG-IUD (*n*=487) Cu-IUD (*n*=196)	Expulsion	Crude Rates of Expulsion among those with follow-up: Age <21: 8.8% (10/113) Age 21–35: 6.3% (14/221) p=.7 Subgroup analyses did not find difference between groups by device type, gravidity or parity	Multiple sites within FQHC network Participants with follow-up had similar baseline characteristics as those without follow-up, except for IUD payment Potential confounders assessed with subgroup analyses	Groups differed at baseline by race, ethnicity, parity, IUD payment and site of insertion All data from chart review; outcomes may be underestimated if women sought care from other sites Outcome not defined, diagnostic criteria not reported High attrition	II-2, fair
Skajaa, 1990 [22] Denmark Organon and Kabi Vitrum	Retrospective cohort 6 years Follow-up visit at 5 weeks, then annually; 820 women who stopped visiting were sent questionnaire	Women aged 14–47 who received IUD (*n*=1697) Age < 20: *n*=98 Age 20–24 years: *n*=454 Age 25–29: *n*=506 Age 30–35: *n*=337 Age ≥35: *n*=260	ML Cu250 (*n*=717) Nova-T (*n*=938)	Loss of the IUD	Cumulative 6-year complication rate per 100 women for loss of IUD (95% CI) Age < 20: 13.2 (7.4–23.1) Age 20–24: 7.5 (5.2–10.6) Age 25–29: 4.2 (2.6–6.8) Age 30–34: 2.6 (1.2–5.4) Age 35+: 3.0 (1.4–6.1) All: 5.0 (4.0–6.3)	Large sample size	Unclear follow-up rates and women-years Single site Outcome and diagnostic criteria not described Cumulative rates for each outcome did not assess or adjust for potential confounders such as parity, IUD type, previous IUD use	II-2, poor
Teal, 2015 [24] United States Source of funding NR	Retrospective cohort 6 months	All successful IUD insertions for women age 13–24 years at adolescent family planning clinic (*n*=1132) with 6-month IUD status known (*n*=796)	LNG-IUD CuT380A	Expulsion	24 expulsions reported: Age 13–17: 4.3% Age 18–24: 2.7% p=.31	Large sample	All data from chart review from single site; outcomes may be underestimated if women sought care from other sites High attrition	II-2, poor

Author, year, location, sources up of support	Study design, follow-Up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
							(able to ascertain IUD status at 6 months for 70%) Outcome and diagnostic criteria not described Potential confounders not assessed for these two age groups	
Zhang, 1992 [25] Multicenter international trial (13 sites) Family Health International; USAID	Nested case–control 12 months	Women age 18–40 years in trial comparing Copper T380A to other IUDs Total expulsion cases: *n*=70 Total controls: *n*=1536 Cases age <20: *n*=12 Controls age <20: *n*=92 Cases age ≥20: *n*=58 Controls age ≥20: *n*=1444	CuT380A TCu 200B TCu 220C	Expulsion	Adjusted HR for women <20 vs. women ≥ 35: 5.4 (95% CI: 1.7–17.5) Adjusted HRs by age had significant trend of decreasing risk with increasing age (p<.001)	Large sample size Authors combined 3 types of IUDs in analyses for larger sample (includes TCu-200B and TCu220C data, not IUDs of interest); no significant differences in expulsion by IUD type Multivariate analysis, adjusted for amount of menses flow and dysmenorrhea Frequent follow-up (1, 3, 6 months from insertion)	Could not examine by parity (only 0.5% nulliparous)	II-2, good

Table 2

Perforation

Author, year, location, sources of support	Study design, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Alton, 2012 [11] United States Source of support not stated	Retrospective cohort, 3 sites Up to 7 years follow-up: Up to 80.88 person-years among women age <18 years; Up to 330.52 person-years among women age 18–21 years	Women aged ≤ 21 years having IUD inserted Age <18 years: *n*=69 Age 18–21 years: *n*=164 Range: 11–21 years, Median age: 16 years	LNG-IUD (*n*=222) CuT380A (*n*=11)	Perforation	No perforations in either group	Multicenter trial	Small sample and few events; no information on study power All data from chart review; outcomes may be underestimated if women sought care from other sites No information on mean time to follow-up or on those lost from database	II-2, poor
Aoun, 2014 [12] United States No financial disclosures	Retrospective cohort Mean follow-up 37±11 months (range 19–57 months)	Women age 13–35 years who had LNG-IUD or Cu-IUD inserted for contraception (*n*=2138) Age 13–19 years: *n*=249 Age 20–24 years: *n*=750 Age 25–35 years; *n*=1139	LNG-IUD *n*=1746 Cu-IUD *n*=392	Perforation	Crude Rates: Age 13–19 years: 0/249 Age 20–24 years: 3/750 (1%) Age 25–35 years: 0/1139 p=. 09	Multicenter Reviewed charts from office, emergency department and hospitals including laboratory and imaging results Multivariate analysis adjusted for age, race and IUD type Excluded those with no follow-up	Small number of events No power calculation	II-2, fair
Berenson, 2013 [14] United States Society for Family Planning; NIH	Retrospective cohort (claims data) Nationwide US health insurance program 12 months (58% of those with IUD insertion also had 12 months of continuous insurance coverage and included in the analysis)	Women age 15–44 yearswith a claim for IUD insertion by procedure code (*n*=90,489) Age 15–19: LNG-IUD: *n*=1528 CuT IUD: *n*=307 Age 20–24: LNG-IUD: *n*=7860 CuT IUD: *n*=2027 Age 25–44: LNG-IUD: *n*=61,197 CuT IUD: *n*=17,570	LNG-IUD CuT IUD	Perforation	Crude Rates: 15–19 years: LNG-IUD: 0/1528 CuT IUD: 0/307 20–24 years: LNG-IUD: 2/7860 (0.0%) CuT IUD: 0/2027 25–44 years: LNG-IUD: 29/61,197 (0.0%) CuT IUD: 7/17,570 (0.0%)	Large database Several outcomes Multivariate analysis, adjusted for age, intrauterine device type, health care provider specialty, region and year of IUD insertion	Limited by diagnostic coding; potential underreporting of outcomes not captured in database Did not include parity as potential confounder No	II-2, fair

Author, year, location, sources of support	Study design, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
						Excluded women without 12 months of continuous insurance coverage	information on whether those not included in analysis were different from sample	
Teal, 2015 [24] United States Source of funding NR	Retrospective cohort 6 months	All successful IUD insertions for women age 13–24 years at adolescent family planning clinic (*n*=1132) with 6 month IUD status known (*n*=796)	LNG-IUD CuT380A	Perforation	No identified perforations	Large sample size	All data from chart review from single site; outcomes may be underestimated if women sought care from other sites High attrition (able to ascertain IUD status at 6 months for 70%) Outcome and diagnostic criteria not described Potential confounders not assessed for these two age groups	II-2, poor

NR= not reported; Cu IUD= copper intrauterine device; IUD= intrauterine device; LNG-IUD= levonorgestrel intrauterine device; LNG-IUS= levonorgestrel intrauterine system; NIH= National Institutes of Health

Table 3

Pregnancy

Author, year, location, sources of support	Study design, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Alton, 2012 [11] United States Source of support not stated	Retrospective cohort (chart review), 3 sites Up to 7 years follow-up Up to 80.88 person-years among women age <18 Up to 330.52 person-years among women age 18–21	Women aged ≤ 21 (range 11–21 years) having IUD inserted (*n*=233) Age <18: *n*=69 Age 18–21: *n*=164	LNG-IUD (*n*=222) CuT380A (*n*=11)	Pregnancy	No pregnancies with IUD in place (pregnancy data missing for 10 patients)	Multicenter trial (3 sites), diverse population	Small sample and few events; no information on study power No information on mean time to follow-up or on those lost from database All data from chart review; outcomes may be underestimated if women sought care from other sites	II-2, poor
Aoun, 2014 [12] United States No financial disclosures	Retrospective cohort Mean follow-up 37±11 months (range 19–57 months)	Women age 13–35 years who had LNG-IUD or Cu-IUD inserted for contraception (*n*=2138) Age 13–19: *n*=249 Age 20–24: *n*=750 Age 25–35: *n*=1139	LNG-IUD (*n*=1746) Cu-IUD (*n*=392)	Contraceptive Failure	Adjusted HR (95% CI) (reference group age 13–19): Age 20–24: 0.98 (0.30–3.13); p=.97 Age 25–35: 0.48 (0.15–1.59); p=.23	Multicenter Reviewed charts from office, emergency department and hospitals including laboratory and imaging results Multivariate analysis adjusted for age, race and IUD type Excluded those with no follow-up	Age groups differed by parity, gravidity, marital status, insurance but not tested in multivariate model No power calculation	II-2, fair
Behringer, 2011 [13] United States Doris Duke Charitable Foundation; NIH	Retrospective cohort 69.2% of sample (*n*= 573) returned to study clinic at least once 47.2% of sample (*n*=391) ≥1 year of follow-up	Women aged 14–50 years who received LNG-IUD (*n*=828) Age ≤21: *n*=131 Age> 21: *n*=697	LNG-IUD	Pregnancy	Frequency of method failure as reason for IUD removal among all women with insertion: No pregnancies among women age < 21 3 pregnancies among 697 women age ≥ 21 (0.4%) p=. 71	Analyzed all those with IUD insertion and those who came back for follow-up to assess potential bias through loss to follow-up for discontinuation outcome (similar results were observed)	All data from chart review from single site; outcomes may be underestimated if women sought care from other sites. Powered to detect differences in discontinuation between adolescents and older women,	II-2, fair

Author, year, location, sources of support	Study design, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
							not our outcome of interest, coupled with few reported events High proportion of adolescents that were parous (82%) Groups differed at baseline by race, marital status and parity	
Berenson, 2015 [15] United States Institute for Translational Sciences, University of Texas Medical Branch, Clinical and Translational Science Award; NIH	Retrospective cohort Nationwide US health insurance program 12 months	Women age 15–44 years with insurance claim for insertion of IUD (*n*=79,920) or ENG implant (*n*=7374) Age 15–19: ENG: *n*=2388 LNG: *n*=2204 Age 20–24: ENG: *n*=2014 LNG: *n*=8988	LNG-IUD	Pregnancy	Adjusted OR(95% CI) for complication with ENG implant vs. LNG-IUD: Age 15–19: Normal pregnancy: 0.40 (0.21–0.75); significant interaction of age and contraceptive method (p<.05) Ectopic pregnancy: 0.92 (0.06–14.8) Abnormal pregnancy or spontaneous abortion: 1.29 (0.41–4.08) Age 20–24: Normal pregnancy: 0.68 (0.41–1.12); significant interaction of age and contraceptive method Ectopic pregnancy: 0.56 (0.07–4.46)	Large sample size Reported both normal and abnormal/ectopic pregnancies Multivariate analyses performed for each outcome, adjusted for age at insertion, contraceptive type, provider type and year of insertion Excluded women without 12 months of continuous insurance coverage	Limited by diagnostic coding; potential underreporting of outcomes not captured in database Did not include parity as potential confounder	II-2, fair

Author, year, location, sources of support	Study design, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
					Abnormal pregnancy or spontaneous abortion: 2.24 (1.05–4.79)			
Berenson, 2013 [14] United States Society for Family Planning; NIH	Retrospective cohort Nationwide US health insurance program 12 months (58% of those with IUD insertion also had 12 months of continuous insurance coverage and included in the analysis)	Women age 15–44 with an insurance claim for IUD insertion (*n*=90,489) Age 15–19: LNG-IUD: *n*=1528 CuT IUD: *n*=307 Age 20–24: LNG-IUD: *n*=7860 CuT IUD: *n*=2027 Age 25–44: LNG-IUD: *n*=61,197 CuT IUD: *n*=17,570	LNG-IUD Cu-IUD	Pregnancy	Ectopic Pregnancy: Adjusted OR for ectopic pregnancy (women age 15–19 vs. age 20–24): 0.57 (95% CI: 0.07–4.48) Adjusted OR for ectopic pregnancy (women age 15–19 vs. age 25–44): 0.76 (95% CI: 0.20–2.85) Abnormal Pregnancy or Spontaneous Abortion: Adjusted OR for abnormal pregnancy/ spontaneous abortion for women age 15–19 vs. age 20–24: 0.86 (95% CI: 0.30–2.46) Adjusted OR for abnormal pregnancy/ spontaneous abortion for women age 15–19 vs. age 25–44: 1.05 (95% CI: 0.54–2.06) Normal Pregnancy: Adjusted OR for normal pregnancy for women age 15–19 vs. age 20–24: 1.28 (95%	Large database Able to look at types of pregnancies Multivariate analysis, adjusted for age, intrauterine device type, health care provider specialty, region and year of IUD insertion Excluded women without 12 months of continuous insurance coverage	Limited by diagnostic coding; potential underreporting of outcomes not captured in database Did not include parity as potential confounder No information on whether those not included in analysis were different from sample	II-2, fair

Author, year, location, sources of support	Study design, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
					CI: 0.89–1.86) Adjusted OR for normal pregnancy for women age 15–19 vs. age 25–44: 1.42 (95% CI: 1.13–1.78)			
Luukkainen, 1983 [16], and Allonen, 1984 [17] Denmark, Finland and Sweden Population Council, International Development Research Centre of Canada, Ford Foundation, Rockefeller Foundation	Prospective cohort (data from RCT comparing two Cu-IUDs) 5 years, yearly visits	Women presenting for IUD insertion, randomized to Nova-T (*n*=918) or Cu T (*n*=947) inserted postmenstrual or postabortion (*n*=322) Nova-T: Age ≤19: *n*=75 Age 20–24: *n*=253 Age>24: *n*=590	Nova-T (*n*=918)	60-month cumulative net pregnancy rates per 100 acceptors	60-month cumulative pregnancy rates per 100 NovaT acceptors: Age <25: 3.0%; Pearl Index 1.3 Age 25–29: 2.6%; Pearl Index 0.9 Age 30–34: 1.1%; Pearl Index 0.4 Age 35+ years: 0.8%; Pearl Index 0.3 Pregnancy rate d ecreased with age for both devices combined in analysis (9) (adjusted RR 0.90 per year of age, p=.001) (5)	Long follow-up Multicenter trial Multiple providers Low loss to follow-up over 5 years (13.1%) Life Table regression analysis, including screening for parity as potential confounder and included IUD type and country in final model	Not powered to detect differences between age groups Infrequent follow-up after first year (every 12 months) may have led to underreporting of some outcomes	II-2, fair
Nygren, 1981 [18]	Prospective cohort (data from RCT two IUDs) 3 years	Women presenting for IUD insertion, randomized to Nova-T (*n*=916) or Cu T inserted postmenstrual Nova T: Age <20 years old: *n*=~73 (~8%) Age 20–24 years: *n*=~257 (~28%) >24 years: *n*=~586 women (~64%)	Nova-T	36-month net cumulative pregnancy rates by age Number of pregnancies at 36 months	Pregnancy rates (number of pregnancies): Age <20: 1.5% (*n*=1) Age 20–24: 3.0% (*n*=7) Age 25–29: 2.1% (*n*=5) Age 30–34: 1.1% (*n*=2) Age>35: 0.8% (*n*=1)	Multicenter trial Multiple providers Women not seen after insertion were not included in study Low LTFU 11.4%	Graphical display of age and parity breakdown No statistical testing for age or parity comparisons reported	II-2, poor
Ravi, 2014 [21] United States American Academy of Family Physicians,	Retrospective cohort Chart reviewed up to 6 months after insertion	All women age ≤35 with IUD insertion in an NYC-area FQHC network (*n*=684) Age <21: *n*=182 Age 21–35: *n*=502	LNG-IUD (*n*=487) Cu-IUD (*n*=196)	Pregnancy	One pregnancy reported among older age group (23-year-old woman) using Cu-IUD	Multiple sites within FQHC network Participants with follow-up had similar baseline	Groups differed at baseline by race, ethnicity, parity, IUD payment and site of insertion All	II-2, poor

Author, year, location, sources of support	Study design, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
NIH grant K23HD067247						characteristics as those without follow-up, except for IUD payment	data from chart review; outcomes may be underestimated if women sought care from other sites High attrition	
Skajaa, 1990 [22] Denmark	Retrospective cohort 6 years Follow-up visit at 5 weeks, then annually	Women aged 14–47 who received IUD (*n*=1697) Age <20: *n*=98 Age 20–24: *n*=454 Age 25–29: *n*=506 Age 30–35: *n*=337 Age ≥35: *n*=260	Multiload Cu250 (*n*=717) Nova-T (*n*=938)	Removals due to pregnancy with IUD in place	Cumulative 6-year complication rate per 100 women for pregnancy (95% CI) Age <20: 10.8 (5.0–22.6) Age 20–24: 5.0 (3.0–8.3) Age 25–29: 3.9 (2.4–6.5) Age 30–34: 2.6 (1.3–5.5) Age ≥35: 0.9 (0.2–3.4) All: 3.7 (2.8–5.0)	Large sample size	Unclear follow-up rates and women-years Single site Cumulative rates for each outcome did not assess or adjust for potential	II-2, poor
Suhonen, 2004 [23] Finland, Sweden Source of support NR	RCT 12 months	Nulliparous women age 18–25 (median age 21 years) randomized to LNG-IUD or COCs (*n*=193) LNG-IUD: *n*=94 COC (30 mcg EE/ 150 mcg desogestrel): *n*=99	LNG-IUD	Pregnancy	No pregnancies reported in either group	Multiple sites Similar loss to follow-up: 19/94 (20.2%) attrition in IUD and 27/99 (27.3%) in COC group	Determination of adequate randomization not reported, potential confounders uncertain Few events, powered on anticipated continuation rates, mostly likely lacking in power for other outcomes	I, fair

EE, ethinyl estradiol; LNG-IUS, levonorgestrel intrauterine system; LTFU, long-term follow-up.

Table 4

Infection

Author, year, sources of support	Study design, location, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Alton, 2012 [11] United States Source of support not stated	Retrospective cohort, 3 sites Up to 7 years follow-up Up to 80.88 person-years among women aged <18 years Up to 330.52 person-years among women aged 18–21 years	Women aged ≤21 years (range 11–21 years) having IUD inserted Age <18 years: *n*=69 Age 18–21 years: *n*=164	LNG-IUD (*n*=222) CuT380A (*n*=11)	Infection	18 infections (7.7% of patients) reported (5 infections in women b18 years; 13 infections in women <18–21 years) 2 cases PID, both with history of STI (ages not reported) Crude RR infection for women <18 years vs. 18–21 years: 1.56 (NS, p value not given)	Multicenter trial Rates reported in person-year to account for different follow-up	Small sample and few events; no information on study power Age not included in multivariate model for infection outcome (not significant) Outcome not clearly described, diagnostic measures not reported All data from chart review; outcomes may be underestimated if women sought care from other sites Did not assess sexual behaviors, condom use as potential confounders	II-2, poor
Aoun, 2014 [12] United States No financial disclosures	Retrospective cohort Mean follow-up 37±11 months (range 19–57 months)	Women age 13–35 years who had LNG-IUD or Cu-IUD inserted for contraception (*n*=2138) Age 13–19 years: *n*=249 Age 20–24 years: *n*=750 Age 25–35 years; *n*=1139	LNG-IUD *n*=1746 Cu-IUD *n*=392	PID	Crude Rates: Age 13–19 years: 8/249 (3%) Age 20–24 years: 17/750 (2%) Age 25–35 years: 15/1139 (1%) p=.08	Multicenter Reviewed charts from office, emergency department and hospitals including laboratory and imaging results Multivariate analysis adjusted for age, race and IUD type Excluded those with no follow-up	Did not assess potential confounders such as sexual behavior or history or condom use Small number of events No power calculation	II-2, poor
Berenson, 2015 [15] United States Institute for Translational Sciences, University of Texas Medical Branch, Clinical and	Retrospective cohort Nationwide US health insurance program 12 months	Women age 15–44 years with insurance claim for insertion of IUD (*n*=79,920) or ENG implant (*n*=7374) Age 15–19 years: ENG: *n*=2388 LNG: *n*=2204 Age 20–24 years: ENG: *n*=2014 LNG: n=8988	LNG-IUD	PID	aOR(95% CI) comparing having complication for women with ENG implant vs. those for women with	Large sample size Multivariate analyses performed for each outcome, adjusted for age at insertion, contraceptive type, provider type and	Limited by diagnostic coding; potential underreporting of outcomes not captured in database Did not include parity as	II-2, fair

Author, year, sources of support	Study design, location, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Translational Science Award; NIH					LNG-IUD: Age 15–19 years: 0.23 (0.03–2.06) Age 20–24 years: 0.32 (0.04–2.42)	year of insertion Excluded women without 12 months of continuous insurance coverage	potential confounder	
Berenson, 2013 [14] United States Society for Family Planning; NIH	Retrospective cohort (health insurance claims data) Nationwide US health insurance program 12 months (58% of those with IUD insertion also had 12 months of continuous insurance coverage and included in the analysis)	Women age 15–44 years with a claim for IUD insertion by procedure code (*n*=90,489) Age 15–19: LNG-IUD: *n*=1528 CuT IUD: *n*=307 Age 20–24: LNG-IUD: *n*=7860 CuT IUD: *n*=2027 Age 25–44: LNG-IUD: *n*=61,197 CuT IUD: *n*=17,570	LNG-IUD CuT IUD	PID	aOR for PID (women age 15–19 years vs. 20–24 years): 1.36 (95% CI: 0.38–4.82) aOR for PID (women 15–19 age years vs. 25–44 years): 1.44 (95% CI: 0.65–3.15)	Large database Several outcomes Multivariate analysis, adjusted for age, intrauterine device type, health care provider specialty, region and year of IUD insertion Excluded women without 12 months of continuous insurance coverage	Limited by diagnostic coding; potential underreporting of outcomes not captured in database Did not include parity, sexual behavior or condom use as potential confounder No information on whether those not included in the analysis were different from sample	II-2, poor
Nygren, 1981 [18]	Prospective cohort (data from RCT two IUDs) 3 years (follow-up from Luukkainen 1979, Allonen, 1980) 21,146.5 woman-months of use	Women presenting for IUD insertion, randomized to Nova-T (*n*=916) or Cu T (*n*=945) inserted postmenstrual Nova T users: Age <20 years old: ~73 (~8%) Age 20–24 years: ~257 (~28%) >24 years: ~586 women (~64%)	Nova-T (*n*=916)	36-month net removal rate for infection, by age	Removal rate for infection: Age <20: 2.8 (*n*=2) Age 20–24: 7.3 (*n*=17) Age 25–29: 2.5 (*n*=6) Age 30–34: 2.6 (*n*=5) Age >35: 3.0 (*n*=4) p values NR	Multicenter trial Multiple providers Women not seen after insertion were not included in study Low loss to follow-up 11.4%	Graphical display of results pertaining to age and parity, no statistical testing for age or parity comparisons reported Outcome not clearly described, diagnostic measures not reported	II-2, poor
Rasheed, 2011 [20] Egypt Source of support not stated	Prospective cohort 1, 3, 6 months	Primiparous women <30 years old at time of IUD insertion 6–8 weeks after vaginal delivery Age 13–19: *n*=281 Age 20–30: *n*=571	CuT380A	Evidence of PID or removal for PID	Crude PID rates at 1 month: Age 13–19: 2/244 (0.8%) (both cases occurred in first week after insertion) Age 20–30: 0/413 No PID data reported at 3 or 6 months	Ultrasound check for proper placement and at follow-up for displacements and expulsions All primiparous, so no concern about parity as potential confounder	No assessment of potential confounders such as STI history, sexual behavior or condom use Outcome not clearly described, diagnostic measures not reported Postpartum population only, less generalizable	II-2, poor

Author, year, sources of support	Study design, location, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
							Single site High attrition and differential loss to follow-up at 6 months (66% adolescents and 85% adults lost) Small number of events, no power calculation reported for any outcome	
Ravi, 2014 [21] United States American Academy of Family Physicians, NIH grant K23HD067247	Retrospective cohort Chart reviewed up to 6 months after insertion	All women age ≤35 years with IUD insertion in an NYC-area FQHC network (*n*=684) Age <21: *n*=182 Age 21–35: *n*=502	LNG-IUD (*n*=487) Cu-IUD (*n*=196)	PID	One case of PID in older age group	Multiple sites within FQHC network Participants with follow-up had similar baseline characteristics as those without follow-up, except for IUD payment	Groups differed at baseline by race, ethnicity, parity, IUD payment and site of insertion All data from chart review; outcomes may be underestimated if women sought care from other sites Outcome not clearly described, diagnostic criteria not reported High attrition	II-2, poor
Skajaa, 1990 [22] Denmark	Retrospective cohort 6 years Follow-up visit at 5 weeks, then annually	Women aged 14–47 who received IUD (*n*=1697) Age < 20 years: *n*=98 Age 20–24 years: *n*=454 Age 25–29 years: *n*=506 Age 30–35: *n*=337 Age 35+ years: *n*=260	Multiload Cu250 (*n*=717) Nova-T (*n*=938)	Removals due to PID requiring treatment	Cumulative 6-year complication rate per 100 women for PID (95% CI): Age < 20 years: 15.1 (8.7–25.5) Age 20–24 years: 15.4 (12.0–19.7) Age 25–29 years: 13.0 (10.1–16.8) Age 30–34 years: 9.5 (6.7–13.5) Age 35+ years: 6.2 (3.7–10.3) All: 11.9 (10.3–13.8)	Large sample size	Unclear follow-up rates and women-years and denominators used for analyses Single site Outcome not clearly described, diagnostic measures not reported Cumulative rates for each outcome did not assess or adjust for potential confounders such as parity, IUD type, previous IUD use, sexual behavior and history or condom use	II-2, poor

Author, year, sources of support	Study design, location, follow-up	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Suhonen, 2004 [23] Finland, Sweden Source of support not stated	RCT 12 months	Nulliparous women age 18–25 years (median age 21 years) randomized to LNG-IUD or COCs (*n*=193) LNG-IUD: *n*=94 COC (30 mcg EE/150 mcg desogestrel): *n*=99	LNG-IUD	Infection	No PID reported in either group	Multiple sites Parity similar between groups Similar loss to follow-up: 19/94 (20.2%) attrition in IUD and 27/99 (27.3%) in COC group	Determination of adequate randomization not reported, potential confounders uncertain Outcome not clearly described, diagnostic measures not reported Few events, powered on anticipated continuation rates, mostly likely lacking in power for other outcomes	I, fair

COC: combined oral contraceptive; Cu IUD= copper intrauterine device; EE= ethinyl estradiol; IUD= intrauterine device; LNG-IUD= levonorgestrel intrauterine device; LNG-IUS: levonorgestrel intrauterine system; NIH= National Institutes of Health; NR: not reported; NS= not significant; OC= oral contraceptive; OR= odds ratio; PID= pelvic inflammatory disease; RCT= randomized controlled trial; RR= relative risk; STI= sexually transmitted infection

Table 5

Bleeding

Author, year, location, sources up of support	Study design, follow-	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Aoun, 2014 [12] United States No financial disclosures	Retrospective cohort (chart review) Mean follow-up 37±11 months (range 19–57 months)	Women age 13–35 years who had LNG-IUD or Cu-IUD inserted for contraception (*n*=2138) Age 13–19 years: *n*=249 Age 20–24 years: *n*=750 Age 25–35 years; *n*=1139	LNG-IUD *n*=1746 Cu-IUD *n*=392	Removal of either IUD for abnormal bleeding	Crude Rates: Age 13–19 years: 30/249 (12%) Age 20–24 years: 66/750 (8.8%) Age 25–35 years: 116/1139 (10.2%) p=.03	Multicenter Reviewed charts from office, emergency department and hospitals including laboratory and imaging results Assessed potential confounders Multivariate analysis adjusted for age, race and IUD type Excluded those with no follow-up	Age groups differed by parity, gravidity, marital status, insurance but not tested in multivariate model No power calculation or significance testing to determine difference in proportion who discontinued due to bleeding by age	II-2, fair
Berenson, 2015 [15] United States Institute for Translational Sciences, University of Texas Medical Branch, Clinical and Translational Science Award; NIH	Retrospective cohort Nationwide US health insurance program 12 months	Women age 15–44 years with claim for insertion of IUD (*n*=79,920) or ENG implant (*n*=7374) Age 15–19 years: ENG: *n*=2388 LNG: *n*=2204 Age 20–24 years: ENG: *n*=2014 LNG: *n*=8988	LNG-IUD	Removal within 30 days after abnormal bleeding	Adjusted OR (95% CI) comparing having removal within 30 days after abnormal bleeding for women with ENG implant vs. those for women with LNG-IUD: Age 15–19 years: 1.56 (1.09–2.23) Age 20–24 years: 1.48 (1.12–1.96)	Large sample size Able to look at types of pregnancies Multivariate analyses performed for each outcome, adjusted for age at insertion, contraceptive type, provider type and year of insertion Excluded women without 12 months of continuous insurance coverage	Limited by diagnostic coding; potential underreporting of outcomes not captured in database Did not include parity as potential confounder	II-2, fair
Berenson, 2013 [14] United States Society for Family Planning; NIH	Retrospective cohort (claims data) Nationwide US health insurance program 12 months	Women age 15–44 years with a claim for IUD insertion by procedure code (*n*=90,489) Age 15–19: LNG-IUD: *n*=1528 Cu IUD: *n*=307 Age 20–24: LNG-IUD: *n*=7860 Cu IUD: *n*=2027 Age 25–44: LNG-IUD: *n*=61,197 Cu IUD: *n*=17,570	LNG-IUD Cu-T	Excessive menstruation Uterine hemorrhage	Excessive menstruation: Adjusted OR for excessive menstruation (women age 15–19 years vs. 20–24 years): 1.01 (95% CI: 0.76–1.33) Adjusted OR for excessive menstruation (women age 15–19 years vs. 25–	Large database Several outcomes Multivariate analysis, adjusted for age, intrauterine device type, health care provider specialty, region and year of IUD insertion Excluded women without 12 months of continuous insurance coverage	Limited by diagnostic coding; potential underreporting of outcomes not captured in database Did not include parity as potential confounder Only 58% of those with IUD insertion also had 12 months of	II-2, poor

Author, year, location, sources up of support	Study design, follow-	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
					44 years): 0.94 (95% CI: 0.79–1.12) Uterine hemorrhage: Adjusted OR for uterine hemorrhage (women 15–19 years vs. 20–24 years): 1.18 (95% CI: 0.93–1.50) Adjusted OR for uterine hemorrhage (women 15–19 years vs. age 25–44 years): 1.14 (95% CI: 0.98–1.32)		continuous insurance coverage and included in the analysis; no information on whether those not included were different Combined LNG and IUD users for bleeding analysis by age	
Luukkainen, 1983 [16] and Allonen, 1984 [17] Denmark, Finland and Sweden Population Council, International Development Research Centre of Canada, Ford Foundation, Rockefeller Foundation	Prospective cohort (data from RCT comparing two Cu IUDs) 5 years, yearly visits	Women presenting for IUD insertion, randomized to Nova-T (*n*=918) or Cu T inserted postmenstrual or postabortion (*n*=322) Nova-T: Age ≤ 19: *n*=75 Age 20–24: *n*=253 Age>24: *n*=590	Nova-T	Cumulative net rates of removals for bleeding/pain per 100 NovaT acceptors	60-month cumulative removal rates for bleeding/pain per 100 acceptors: Age <25 years: 27.1% Age 25–29 years: 26.1% Age 30–34 years: 27.4% Age 35+ years: 25.0% Age was not significantly associated with removal rates for bleeding/pain for both IUD types combined	Long follow-up Multiple country sites and providers Low loss to follow-up over 5 years (13.1%) Life table regression analysis, including screening for parity as potential confounder, included parity, number of abortions, country and previous IUD use	Not powered to detect differences between age groups Infrequent follow-up after first year (every 12 months) may have led to underreporting of some outcomes	II-2, fair
Nygren, 1981 [18]	Prospective cohort (data from RCT two IUDs) 3 years	Women presenting for IUD insertion, randomized to Nova-T (*n*=916) or Cu T (*n*=945) inserted postmenstrual Nova T: Age <20 years: ~73 (~8%) Age 20–24 years: ~257 (~28%) N24 years: ~586 women (~64%)	Nova-T	36-month cumulative net removal rate for bleeding and/or pain (absolute number of events)	Net removal rate for bleeding/pain: Age <20: 24(*n*=17) Age 20–24: 22.8(*n*=53) Age 25–29: 21.8(*n*=53) Age 30–34: 19.2 *n*= (36) Age>35: 18.1(*n*=24)	Multicenter trial Multiple providers Women not seen after insertion were not included in study Low LTFU 11.4%	Graphical display of results pertaining to age and parity, no statistical testing for age or parity comparisons reported	II-2, poor

Author, year, location, sources up of support	Study design, follow-	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
Rasheed, 2011 [20] Egypt Source of support not stated	Prospective cohort 1, 3, 6 months	Primiparous women b30 years old at time of IUD insertion 6–8 weeks after vaginal delivery Adolescents (age 13–19): *n*=281 Adults (age 20–30): *n*=571	Cu T380A	Bleeding or removals	Bleeding OR (adolescents vs. adults) at 1 month: 1.46 (95% CI: 1.02–2.07); p=.034 Bleeding OR (adolescents vs. adults) at 3 months: 1.76 (95% CI: 1.07–2.90); p=.030 Bleeding OR (adolescents vs. adults) at 6 months: 1.42 (95% CI: 0.79–2.55); p=.230	All primiparous, so no concern about parity as potential confounder	Postpartum population only, less generalizable No assessment for potential confounders Single site High attrition and differential loss to follow-up at 6 months (66% adolescents and 85% adults lost) Bleeding complications could include spotting, breakthrough, menorrhagia or metrorrhagia	II-2, poor
Ravi, 2014 [21] United States American Academy of Family Physicians, NIH grant K23HD067247	Retrospective cohort Chart reviewed up to 6 months after insertion	All women age ≤35 years with IUD insertion in an NYC-area FQHC network (*n*=684) Age <21 years: *n*=182 Age 21–35 years: *n*=502	LNG-IUD (*n*=487) Cu-IUD (*n*=196)	Removals for bleeding	Crude rates of removal for bleeding among those with follow-up within 6 months (*n*=334): Age < 21 years: 8/113 (7.1%) Age 21–35 years: 11/221 (5.0%) p value not reported	Multiple sites within FQHC network Participants with follow-up had similar baseline characteristics as those without follow-up, except for IUD payment	Groups differed at baseline by race, ethnicity, parity, IUD payment and site of insertion All data from chart review; outcomes may be underestimated if women sought care from other sites High attrition Participants may have had removal for multiple reasons and unclear who had removal for both pain and bleeding	II-2, poor
Skajaa, 1990 [22] Denmark	Retrospective cohort 6 years Follow-up visit at 5 weeks and annually	Women aged 14–47 who received IUD between 1981–1982 (*n*=1697) Age < 20 years: *n*=98 Age 20–24 years: *n*=454 Age 25–29 years: *n*=506 Age 30–35: *n*=337 Age 35+ years: *n*=260	Multiload (*n*=717) Nova-T (*n*=938)	Removals due to bleeding and/or pain not previously present	Cumulative 6-year complication rate per 100 women for bleeding and/or pain (95% CI) Age < 20 years: 20.5 (12.5–32.5) Age 20–24	Large sample size	Unclear follow-up rates and women-years and denominators used for analyses Single site Cumulative rates for each outcome did not assess or adjust for	II-2, poor

Author, year, location, sources up of support	Study design, follow-	Population, intervention	Type(s) of IUD	Outcomes of interest	Results	Strengths	Weaknesses	Grade
					years: 14.1 (10.9–18.2) Age 25–29 years: 15.7 (12.3–19.8) Age 30–34 years: 14.3 (10.6–19.1) Age 35+ years: 12.7 (8.9–17.9) All: 14.8 (13.0–16.9)		potential confounders such as parity, IUD type, previous IUD use No significance testing reported	
Suhonen, 2004 [23] Finland, Sweden Source of support not stated	RCT 12 months	Nulliparous women age 18–25 years (median age 21 years) randomized to LNG IUD or COCs (*n*=193) LNG-IUD: *n*=94 COC (30 mcg EE/ 150 mcg desogestrel): *n*=99	20 mcg LNG daily release IUS	Median number of days of bleeding and spotting; termination rates during 12 months	Number of days of bleeding decreased for both groups; more significantly in LNG IUS group (p=.001) Significantly higher rate of self-reported decrease in bleeding reported by LNG users (49.3%) than OC users (22%) (p=.001) Termination rate for bleeding per 100 over 12 months: LNG-IUS: 2/19 terminations COC: 0/27 terminations (p=. 16)	Multiple sites Parity similar between groups Low loss to follow-up: (19/94) attrition in IUD and 27/99 in COC group	Determination of adequate randomization not reported, potential confounders uncertain Few events, powered on anticipated continuation rates, mostly likely lacking in power for other outcomes Self-reported outcome	I, fair

NR: not reported; COC: combined oral contraceptive; Cu IUD : copper intrauterine device; EE= ethinyl estradiol; IUD= intrauterine device; LNG-IUD= levonorgestrel intrauterine device; LNG-IUS: levonorgestrel intrauterine system; LTFU= long-term follow-up; NIH= National Institutes of Health; OC= oral contraceptives; OR= odds ratio; PID= pelvic inflammatory disease; RCT= randomized controlled trial; STI= sexually transmitted infection