Copper containing, framed intra-uterine devices for contraception (Review)

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ABSTRACT

Background
Intrauterine devices (IUD) are safe and effective methods of long term reversible contraception. The design, and copper content as well as placement of the copper on IUDs could affect their effectiveness and side-effect profile.

Objectives
We compared different copper IUDs for their effectiveness and side effects.

Search strategy
Multiple electronic databases were searched with appropriate key words and names of the IUDs known to be in the market. We searched the reference lists of papers identified and contacted trialists when possible. There was no language restriction.

Selection criteria
Randomised controlled trials comparing different IUDs were considered. Trials needed to report on clinical outcomes.

Data collection and analysis
Data on outcomes and trial characteristics were extracted in duplicate and independently by two reviewers. Meta-analysis results are expressed as rate difference (RD) using a fixed-effects model with 95% confidence interval (CI). In the presence of significant heterogeneity a random-effects model was applied.

Main results
We included 35 trials, resulting in 18 comparisons of 10 different IUDs in approximately 48,000 women. TCu380A was more effective in preventing pregnancy than MLCu375 (RD 1.70%, 95% CI 0.07% to 2.95% after 4 years of use). TCu380A was also more effective than MLCu250, TCu220 and TCu200. There tended to be fewer pregnancies with TCu380S compared to TCu380A after the first year of use, a difference which was statistically significant in the fourth year (RD -1.62%, 95% CI -3.00% to -0.24%). This occurred despite more expulsions with TCu380S (RD 3.50%, 95% CI 0.36% to 6.63% at 4 years). MLCu375 was no more effective than TCu220 at 1 year of use, or MLCu250 and NovaT up to 3 years. Compared to TCu380A or TCu380S, none of the IUDs showed any benefits in terms of bleeding or pain, or any of the other reasons for early discontinuation. None of the trials that reported events at insertion found one IUD easier to insert than another or caused less pain at insertion. There is no evidence that uterine perforation rates vary by type of device. There are minimal randomised data on IUD use in nulliparous women.

Authors' conclusions
TCu380A or TCu380S appear to be more effective than other IUDs. No IUD showed consistently lower removal rates for bleeding and pain in comparison to other IUDs. There is no evidence that any particular framed copper device is better suited to women who have not had children.

PLAIN LANGUAGE SUMMARY

The most commonly used intrauterine devices (IUDs) (or coils) are made up of a T-shaped or horseshoe-shaped frame surrounded by thin copper wires. Some IUDs have copper on the arms of the T. The main mechanism of action is to prevent fertilisation. The shape of the device and the amount and placement of the copper affects performance. The T-shaped IUDs with copper on the arms (TCu380A and TCu380S) are the most effective, have the longest duration of action and are the IUDs of choice. No IUD showed consistently lower removal rates for bleeding and pain in comparison to other IUDs. There is no evidence that any particular framed copper device is better suited to women who have not had children.

BACKGROUND

The IUD is the most widely used reversible method of contraception in the world today, used by an estimated 100 million women (WHO 1997). Around 13% of couples use an IUD, more in the developing world than developed (United Nations 2006). Thus this review has direct relevance to millions of users. Developed in the beginning of the nineteenth century, intrauterine devices (IUDs or IUCDs) became popular for contraceptive use from the 1960s onwards (WHO 1987, Tietze 1970). The earlier IUDs were non-medicated and consisted only of what is nowadays referred to as the frame of the IUD, the frame being made of plastic material. These IUDs have been replaced by the more effective copper-bearing devices over the years. Intrauterine copper devices exist in different shapes, mainly framed ones (T or horseshoe shaped), and frameless ones. The framed devices stay in place in the uterine cavity due to the extended horizontal 'arms' whereas the frameless ones are anchored to the wall of the uterine fundus.

Copper-bearing IUDs consist usually of a plastic core body, surrounded by copper wires; some devices have a silver core to delay fragmentation of copper and increase their lifespan. Earlier devices contained copper around the vertical stem only. Further development lead to the addition of extra copper, and for the T-frame adding copper sleeves to the horizontal arms with the aim to provide copper surface close to the fundus and therefore improve the effectiveness (Sivin 1979A). The generally recommended duration of use is between 3-10 years, depending on the device, but large follow-up studies have shown that some IUDs can be used for up to 12 years providing highly effective contraception (WHO 1997). Devices with longer duration of action are preferred as they reduce the need for re-insertion and insertion-related problems.

Discontinuation of contraceptive methods is a major factor in unwanted fertility (Blanc 1999). Discontinuations of intrauterine device use are less common, apart from implants, than for other methods, partly perhaps because cessation of use requires a deliberate decision to have the device removed (Ali 1999, Trussell 2004, Blanc 1999). The continuation rates with IUDs are reported around 70% after three years of use (UNDP 2004, WHO 1994).

The contraceptive mechanism of copper IUDs is mainly to prevent fertilisation by inhibiting sperm mobility, stimulating a cytotoxic inflammatory reaction that is spermicidal. Further, it changes the intrauterine environment to make it more hostile for implantation (Mishell 1998). The effectiveness of copper IUDs is comparable to other long acting reversible contraceptives, such as injectables (Trussell 2004). Failure rates are highest earlier during its use and seem to be positively correlated with the surface area of copper in the endometrial cavity (Tatum 1972, WHO 1997).

Sometimes IUDs are difficult to insert, although complications during insertion, such as cervical laceration or uterine perforation are rare (WHO 1997). Expulsion has been reported to occur mostly during the first year of use (WHO 1994); it may occur more frequently in nulliparous compared to multiparous women, and it has been claimed to depend on the form and frame of the device (WHO 1994, Sastrawinata 1991). However, a Cochrane systematic review showed there was insufficient evidence to state that frameless devices reduce the problem of early expulsion compared to framed ones (O'Brien 2005). Increased or prolonged vaginal bleeding has been described as the most common side-effect (Mishell 1998) and could be related to the copper content of the IUD, therefore raising concern that this may decrease the tolerability and compliance with high copper content devices. Smaller devices with less copper content aim to minimise side effects and to provide an alternative for women with smaller sized uterus, but may be less effective. Other side effects reported are abdominal pain, especially during menstruation, and vaginal discharge (Sastrawinata 1991).

The possible association between use of IUDs in general and pelvic inflammatory disease (PID) has been a concern, and it has led to a decrease in IUD use at the time, mainly in the USA (Mishell 1998). An analysis of data from WHO's IUD clinical trials showed that PID in IUD users is related to the time since insertion and to the background risk for sexually transmitted diseases. No significant differences were found among different types of copper containing IUDs (Farley 1992).

The optimal IUD choice has important public health implications as it concerns millions of women worldwide. This review focuses on the framed IUDs and their effectiveness and side effects; frameless IUDs are reviewed elsewhere (O'Brien 2005).

OBJECTIVES

The objective of this review is to compare different framed copper IUDs for their effectiveness, acceptabiliity and side effects.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomised controlled trials. Trials needed to report on clinical outcomes.

Types of participants

Participants were women using copper IUDs for contraception, regardless of timing of insertion: immediate postabortion/post-partum and unrelated to pregnancy.

Types of intervention

Any framed copper IUD.

Types of outcome measures

Effectiveness:
pregnancy rates (failures)
ectopic pregnancy rates
Side effects: side/adverse effects as reason for discontinuation:

- prolonged/heavy menstrual bleeding and
- intermenstrual bleeding
- pain
- bleeding and pain combined
- infection
- total medical removal rates

Expulsion rates
Non-medical (personal) removal rates
Overall discontinuation rates
Events at insertion:

- failed or difficult insertions
- cervical injuries

Perforation rates

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

Reports were located using the Cochrane Fertility Regulation trials search strategy.

We searched MEDLINE/PUBMED, EMBASE, The Cochrane Central Trials register, POPLINE, LILACS, PASCAL. Reference lists of identified trials were searched. We also searched two most widely used registers of ongoing controlled trials (clinicaltrials.gov and Current Controlled Trials meta-register). The following search strategies were applied:

MEDLINE/PUBMED: (Intrauterine devices, copper OR ((IUD* OR IUCD*) AND (Copper OR Cu))) AND (efficacy OR effective* OR pregnancy OR side effects OR expulsion OR PID OR pelvic inflammatory disease OR hemorrhage) AND (clinical trials OR comparative study OR multicenter study OR cross over studies OR follow up studies). Textwords: Multiload 375, MLCu375, MLCu 375, Multiload 250, MLCu250, MLCu 250, Copper T 380, CopperT380A, CuT380, CuT 380, TCu 380, TCu 380A, CuT380A, TCu 380S, GyneT 380, NovaT380, Copper 7, NovaT, NovaT 200, Copper T 200, Copper T 220,TCu 220, CuT 220, MonaLisa, Shanghai V, ParaGard, Gravigard, Gynelle 375, Sertalia, UT 380.

EMBASE: S1 intrauterine devices S2 'intrauterine contraceptive device' S3 IUD? OR IUCD? S4 intrauterine(W)device S5 S1 OR S2 OR S3 OR S4 S6 copper S7 'copper' S8 S5 AND S7 S9 S8 AND PY=2003:2006 S10 'clinical trial' S11 S9 AND S10

The Cochrane Central Trials Register: Intrauterine device AND (copper OR cu), IUD* AND (copper OR cu), IUCD* AND (copper OR cu)

POPLINE: (IUD*/IUCD*/intrauterine device* & (copper/cu))/iud copper releasing & (efficacy/ effect*/pregnancy/side effect*/expulsion*/PID/pelvic inflammatory disease/hemorrhage/haemorrhage/bleeding)& clinical trials

LILACS: (iud or iuds or IUCD or iucds) and copper [Words] or intrauterine devices, copper or dispositivos intrauterinos de cobre or dispositivos intra-uterinos de cobre [Words]

WWW.CLINICALTRIALS.GOV: iud or iuds or iucd or intrauterine device or intrauterine devices [ALL-FIELDS]

Current Controlled MetaRegister: (1): (iud or iuds or iucd or iucds or intrauterine device%) and (copper or cu); (2): "intrauterine devices, copper" or "intrauterine device, copper" or ((copper or cu) AND (IUD% or IUCD % or Intrauterine device%)); (3): "copper iud" or "copper iuds" or "copper intrauterine device" or "copper intrauterine devices" or "intrauterine devices, copper"

There were no language preferences for selecting the trials. The last search was performed on 08 May 2006. For this update we have added one new trial (Haugen 2007).

METHODS OF THE REVIEW

Data extraction

Identified titles and abstracts were assessed whether they fulfilled the inclusion criteria and full text articles were retrieved for those eligible or unsure. Quality assessment and data extraction were done independently by two of the authors using a specially designed data extraction form. Baseline characteristics such as setting, age group, parity, previous contraceptive use, previous infection, time of insertion (e.g. post abortion, post partum), were recorded. Data on IUD specification, including size, shape, have been extracted from the original papers. Further information on the Bahamondes 1999 trial was provided by the author. Copper dose refers to the copper surface area of the IUD.

Quality assessment

The quality assessment took into account the description of randomisation and allocation procedure and loss-to-follow-up rate.

A score has been assigned for allocation concealment, using the following criteria:

(A) adequate concealment of allocation (such as central randomisation; use of numbered, sealed opaque envelopes)

(B) unclear whether concealment of allocation is adequate

(C) inadequate concealment of allocation (such as alternation)

(D) concealment of allocation not used

Only trials scoring A or B were included in the review.

Analysis

Survival (time-to-event) methods are used in contraception studies that involve long periods of observation and take into account varying lengths of time that women remain in a study. Kaplan-Meier or daily life-table estimates are commonly used in IUD studies (Farley 1986). Monthly (actuarial) life-table estimates have also been used extensively in the past (Tietze 1973). Farley has shown that the results obtained with both methods are very similar (Farley 1986) and for the purposes of this review are treated the same and combined in the meta-analyses. Both methods give estimated probabilities of event over a specific time period, which are expressed as percentages or rates per 100 women.

In IUD studies reasons for discontinuation 'compete' with each other in the sense that if a woman discontinues from the study because the IUD is expelled, for example, or because of excessive bleeding, she is no longer at risk of pregnancy in that interval. Based on how these competing events are handled, two types of rates can be derived in life-table analysis in contraception studies. Most studies report adjusted, or non-competing single decrement life-table rates, in which the rates are calculated after adjusting ('censoring') for discontinuations for other reasons (also called cumulative 'net' probability rates by statisticians (Farley 1986), and 'gross' cumulative rates by demographers (Tietze 1973)). Adjusted rates are theoretical and not observable, and provide a pure estimate for each reason for comparison with other IUDs. The advantage of the adjusted rate is that an excess rate for one reason, for example expulsion, will not influence discontinuations rates for other reasons. Adjusted rates are used when looking at single events, such as pregnancies or expulsions, in isolation to compare events rates among different devices, as the influence of other events, such as discontinuations for bleeding, is removed.

Crude rates, or competing multiple decrement life-table rates, on the other hand, are discontinuation rates for an event without adjusting for other events (also called 'net' rates by Tietze). Crude rates provide an estimate of overall IUD performance, showing the relative importance of different reasons for discontinuation, which are additive. Crude rates give systematically lower estimates. In this review Wilson 1992 was the only one to use multiple decrement life tables.

For individual studies we subtracted the rates for the comparison IUDs to get the rate difference, and calculated the standard error of the difference from the square root of the sum of the square of each standard error in Excel (Version 11.2, 2005). Outcomes were pooled in RevMan (Version 4.2, 2005) using the inverse variance method. When there was substantial heterogeneity (I^2 statistic greater than 50%), we used the random effects model.

The meta-analysis graphs indicate the direction of effect at the bottom of the graph. If the rate difference (RD) is positive, and the outcome is undesirable (e.g. pregnancy, discontinuation), the result favours the second IUD listed in the graph.

Trials that met the inclusion criteria but for which results could not be included in the meta-analyses, due to the way their results were presented, are listed in Table 02.

DESCRIPTION OF STUDIES

See also Table of Included Studies.

The review includes 35 trials that enrolled 48,000 women, generating 18 different comparisons of 10 different IUDs. Seventeen of the 18 comparisons are presented in the meta-analyses, one comparison is listed in table 2 only. Follow-up publications of a trial are listed in table 1 and are referred to by their original report (i.e. first publication) throughout the text.

Time of recruitment: Most of the trials started recruitment during the 1980s, eight trials in the 1970s [Goh 1983, McCarthy 1983A, McCarthy 1983C, Sivin 1979A, Sivin 1979B, WHO 1982, WHO 1983A, WHO 1983B] and two in the 1990s [Bahamondes 1999, Haugen 2007] and two trials did not state the dates of recruitment [Chen 2003, Petersen 1991].

Duration of trials: Most of the trials had a follow-up for one or two years. Seven trials had a follow-up of three years [Baveja 1989, Champion 1988, Van Kets 1995, WHO 1990A, Wilson 1992], one trial over four years [Sivin 1990], two trials five years [Bahamondes 1999, Haugen 2007], one trial seven years [WHO

1990B], two trials 10 years [WHO 1994, Chen 2003] and one with 12 years of follow-up [WHO 1990C].

Settings: 21 trials were multicentric: nine studies were in developing countries [Baveja 1989, Chen 2003, Champion 1988, Cole 1985C, Farr 1994A, Farr 1994B, Farr 1994C, Ho 1992, Sastrawinata 1991], four in industrialised countries [Haugen 2007, Saure 1985, Sivin 1979A, Sivin 1979B] and nine included centres from developing and developed countries' [Goh 1983, Sivin 1990, WHO 1982, WHO 1983A, WHO 1983B, WHO 1990A, WHO 1990B, WHO 1990C, WHO 1994]. Most single centre trials were conducted in industrialised countries [Batar 1987, Bratt 1988, Luukkainen 1979, McCarthy 1983A, McCarthy 1983C, McCarthy 1985, Petersen 1991, Van Kets 1995].

Trial size: The number of women enrolled ranged from 200 [Shrestha 1995] to more than 3000 [Sivin 1979A, WHO 1990B, WHO 1994]. Eighteen trials had more than 1000 participants, and seven trials more than 2,000.

Participants: Mean age and parity for the comparison groups were provided for all trials, except two [McCarthy 1983A, McCarthy 1983C]. Two trials mentioned that the comparison groups were similar regarding age and parity, but without actual data [McCarthy 1985, Petersen 1991]. Eleven trials included only parous women [Arowojolu 1995, Bahamondes 1999, Baveja 1989, Farr 1994A, Haugen 2007, Ho 1992, WHO 1982, WHO 1990A, WHO 1990B, WHO 1990C, WHO 1994], four trials included only women with 'proven fertility' [McCarthy 1983A, McCarthy 1983C, McCarthy 1985, Sivin 1990]. One trial was conducted in nulliparous women [Petersen 1991]. All other trials included nulliparous or parous women, or the parity was not stated [Chen 2003].

Person performing the insertion: Twelve trials specified the person inserting the IUD as 'experienced' either gynaecologists, physicians, nurses or midwives [Arowojolu 1995, Bahamondes 1999, Bratt 1988, Chen 2003, Farr 1994A, Farr 1994C, Ho 1992, McCarthy 1985, Petersen 1991, Sastrawinata 1991, Saure 1985, Wilson 1992]. Haugen [Haugen 2007] reported that the general practitioners were 'trained'. The rest of the trials did not specify who inserted the devices and what experience they had.

IUDs used: TCu380A has been the IUD most studied in trials: TCu380A in 17 trials, TCu380S in three trials, TCu220 in 12 trials, TCu200 in seven trials, MLCu375 in 10 trials, MLCu250 in 10 trials, NovaT in seven trials, NovaT380 in one trial and, Cu7 in six trials. Most trials compared two different copper IUDs; four trials used a three-arm comparison [Arowojolu 1995, Baveja 1989, Goh 1983, Wilson 1992].

Timing of insertion: Insertions were performed only immediately after surgical abortion in four trials [McCarthy 1983C, McCarthy 1985, WHO 1983A, WHO 1990A] and in one trial after miscarriage [WHO 1983B]. In one trial the insertions were performed as interval and postabortion procedures [Baveja 1989]. Five trials did not state the time of insertion [Sivin 1979A, Sivin 1979B, Sivin 1990, WHO 1982, WHO 1994], and the insertion was performed as an interval procedure, unrelated to pregnancy, in the rest of the trials.

Sponsorship: Five trials clearly stated that the trial was sponsored by a manufacturing company [Arowojolu 1995, Batar 1987, Haugen 2007, McCarthy 1985, Sivin 1990]. Ten trials were conducted by international organizations: WHO, UNFPA, Population Council without stating additional sponsorship [Baveja 1989, Sivin 1979A, Sivin 1979B, WHO 1982, WHO 1983A, WHO 1983B, WHO 1990A, WHO 1990B, WHO 1990C, WHO 1994]. Five trials were conducted by Family Health International (FHI) and/or the United States Agency for International Development (USAID) without stating further sponsorship [Champion 1988, Farr 1994A, Farr 1994B, Farr 1994C, Sastrawinata 1991]. One trial, conducted by the Population Council stated Industry sponsorship [Bahamondes 1999]. The rest of the included trials did not state the source of sponsorship.

Analyses used in trials: All the trials reported single-decrement, adjusted, cumulative rates, except for Wilson 1992 who reported multiple-decrement rates. Four trials presented results also according to age and parity [Sivin 1979A, Sivin 1979B, Sivin 1990, WHO 1982], two trials according to length of endometrial cavity and position of the uterus [Petersen 1991, Sivin 1990].

Devices used in the included trials: Copper T380A (TCu380A), TCu380 Slimline (TCu380S), CopperT220 (TCu220) and Copper T200 (TCu200) IUDs have a T-shaped polyethylene frame, measuring 36 mm long and 32 mm wide. A monofilament thread is tied at the distal end of the stem, allowing for removal of the device. The TCu380A has copper wire on the vertical stem with a surface area of 320 mm^2, and 30 mm^2 of copper on sleeves in the middle of each of the horizontal arms. The TCu380S has the copper sleeves at the ends of the horizontal arms, embedded into the arms. The TCu220 has copper collars on the vertical stem and horizontal arms, amounting to a total of 220 mm^2. The TCu200 has a copper wire along the vertical stem with a surface area of 200 mm^2.

Multiload 375 (MLCu375) and Multiload 250 (MLCu250) are horseshoe-shaped devices with copper wires around the plastic vertical stem amounting to either 375 mm^2 or 250 mm^2. The arms are down-curved, with a 'saw-like' appearance.

Nova T has a copper surface area of 200 mm^2 and NovaT380 has a surface of 380 mm^2. The copper coil has a silver wire core and is on the vertical stem. The horizontal arms are rounded at the end and face slightly downwards once inserted, giving the device a more curved shape compared to the straight arms of the T-devices. The distal end of the vertical stem forms a loop to which the thread is attached.

Copper 7 (Cu 7): consists of a vertical and one horizontal arm, giving it the shape of the number '7'. The copper wire is around the stem and has a total copper surface of 200 mm^2.

The Cu-Safe 300 has a slightly thinner frame, with the horizontal arms being 23 mm wide and the ends are bent downwards and inwards. A copper wire is wound around the stem and amounts to about 300 mm^2 of copper surface.

Excluded studies (see Table of Excluded Studies):
Thirty-five papers were excluded: 11 for quality issues (e.g. no allocation concealment); six because they were not randomised controlled trials; 12 because they were duplicate publications, and six because the IUD tested is no longer in use or they are other IUDs.

METHODOLOGICAL QUALITY

Randomisation procedure: Randomisation was described as computer generated for 16 trials [Bahamondes 1999, Cole 1985B, Cole 1985C, Farr 1994A, Farr 1994B, Farr 1994C, Haugen 2007, Sastrawinata 1991, Shrestha 1995, WHO 1982, WHO 1983A, WHO 1983B, WHO 1990A, WHO 1990B, WHO 1990C, WHO 1994, Wilson 1992] and a 'random number table' was used in one trial [McCarthy 1983A]. Sivin [Sivin 1990] used linear congruent method for randomisation, and van Kets [Van Kets 1995] prepared a random list for each investigator. Haugen [Haugen 2007] randomised in blocks of ten. Baveja [Baveja 1989] also used constrained randomisation, with equal number of women assigned to each device and separate random permutation for each centre. Several issues with the Baveja trial suggest caution in interpretation of its results. It is not clear what 'constrained' randomisation exactly means, there is imbalance in numbers allocated to high versus low copper IUD groups and one centre dropped out after recruiting more than 150 women and the data for those women are not available. In the Arowojolu trial [Arowojolu 1995], women randomly and blindly picked up an envelope. The rest of the included trials did not further specify the randomisation process.

Allocation concealment: Allocation concealment was rated 'A' for 14 trials and 'B' (unclear) for the rest (see table of included studies). A number of the latter reported the use of sealed envelopes, but did not specify that the envelopes were sealed or opaque, so concealment could not be assumed.

Blinding: Double blinding was described for two trials without further information [Arowojolu 1995, Petersen 1991]. Four trials stated single (patient) blinding [Champion 1988, Sivin 1979A, Sivin 1979B, Sivin 1990], three trials stated that the outcome assessment was blinded [Petersen 1991, Sivin 1979A, Sivin 1979B] and the rest of the included trials did not mention blinding.

Loss to follow-up: Five trials did not report on loss-to-follow-up during the study period [Arowojolu 1995, Champion 1988, Petersen 1991, Shrestha 1995, WHO 1994]. About half of the included trials (16) reported the number of women excluded after randomisation [Bahamondes 1999, Baveja 1989, Bratt 1988, Chen 2003, Champion 1988, Cole 1985B, Cole 1985C, Farr 1994A, Farr 1994B, Farr 1994C, Haugen 2007, Sastrawinata 1991, WHO 1982, WHO 1990A, WHO 1990B, WHO 1990C, WHO 1994].

RESULTS

The review includes 18 comparisons of 10 different IUDs. Data from trials that could not be incorporated into the meta-analyses, because the standard errors were not published, are presented in Table 02.

Comparisons:
1. MLCu375 vs TCu380A
Three multicentre trials (7048 women) were included in this meta-analysis [Cole 1985C, Sastrawinata 1991, WHO 1994]. The TCu380A was more effective in preventing pregnancy than the MLCu375 at all time intervals to 10 years. The rate difference (RD) at 1, 2, 6 and 10 years was 0.60% (95% CI 0.13% to 1.06%), 1.10% (95% CI 0.29% to 1.90%), 1.52% (95% CI 0.08% to 2.95%) and 1.90% (95% CI 0.12% to 3.59%) respectively. The six and 10-year data were from one trial (WHO 1994). There tended to be more expulsions with MLCu375 with longer duration of use, and those were statistically significant from the fourth year of follow-up. The rate difference at 10 years was 3.50% (95% CI 0.44% to 6.56%). However, the ectopic pregnancy rate was lower with MLCu375, although this was statistically significant only after 10 years of follow-up, and the rate difference was small (RD -0.70%; 95% CI -1.33% to -0.07%).

There was no significant difference in removals for bleeding and/or pain in the first two years. However, in the large WHO trial there were fewer removals for bleeding alone with MLCu375 in the fourth and sixth year of use (RD -1.80%; 95%CI -3.61% to 0.01% and RD -3.16%; 95% CI -5.61% to -0.71%, respectively). There were also fewer removals because of excessive bleeding and pain in this trial in the same years. Both are reflected in the reduced total medical removal rate in these years with MLCu375 (RD -2.60%; 95% CI -4.96% to -0.24% and RD -3.75%; 95% CI -6.82% to -0.68% respectively). There are no data published for individual menstrual-related reasons for later years, but the differences appear to have been reduced or eliminated, as by the tenth year of follow-up in the WHO trial, there was no difference in total medical removals (RD -0.60%; 95% CI -4.62% to 3.42%).
There are two other reports of trials comparing the same IUDs but the data could not be incorporated in the meta-analyses. Champion 1988 presented two and three -year follow-up data from some of the centres included in Cole 1985C, which showed similar results to the earlier years. The small Arowojolu [1995] trial found no significant difference in pregnancy rates and expulsions,

as no significant difference in removals for bleeding or pain (see Table 02). Data from this trial, and other trials which could not be incorporated into the meta-analyses because the standard errors were not published, are presented in Table 02.

2. MLCu250 vs TCu380A

One trial compared these devices [Farr 1994A], reporting on outcomes after 1 year of use only. There were fewer pregnancies in the group receiving TCu380A compared to the MLCu250 after 1 year (RD 1.00%, 95%CI 0.24% to 1.76%). There were no statistically significant differences in expulsion, discontinuation for bleeding and pain or other medical or non-medical reasons between the devices.

3. TCu380S vs TCu380A

Two large trials were included in this comparison (2564 women). One trial lasted four years [Sivin 1990] and the other five years [Bahamondes 1999]. There tended to be fewer pregnancies with TCu380S after the first year, which was statistically significant in the fourth year (RD -1.62%, -3.00% to -0.24%). There were more expulsions with TCu380S (RD 2.86%, 95% CI 1.04% to 4.68% at 1 year, and 3.50%, 95% CI 0.36 to 6.63% at 4 years). There were no statistical differences in removal rates for bleeding and/or pain, PID or other medical reasons for discontinuation.

4. TCu220 vs TCu380A

Three trials (4647 women) were included in this meta-analysis [Baveja 1989, Farr 1994B, WHO 1990C]. One year results for pregnancy showed significant heterogeneity in the two trials reporting this outcome [Baveja 1989, Farr 1994B]. Similarly, there was heterogeneity between WHO 1990C and Baveja 1989 at year three. In the Baveja trial there tended to be fewer pregnancies with TCu220, while in the other two trials there tended to be more. The WHO 1990C trial reported additional follow-up results at 5, 7, 8, 10 and 12 years, all consistently showing higher pregnancy rates with TCu220. There were no statistically significant differences for ectopic pregnancy, expulsion, perforation or discontinuation either due to bleeding, pain, infection, or all use related discontinuations between the comparison groups. In the Chen 2003 trial there were no differences in reported pregnancies or removals for bleeding and/or pain, but there were more expulsions with TCu380A at 5 and 10 years of follow-up.

5. TCu200 vs TCu380A

Four trials (6372 women) were included in this comparison [Baveja 1989, Farr 1994A, Shrestha 1995, Sivin 1979A] with maximum follow-up of 3 years. Here again, the Baveja 1989 trial introduced heterogeneity, with fewer pregnancies in the TCu380A group in the other three trials but not in the Baveja trial. When the trials were combined (using random effects model), there were more pregnancies in the TCu200 group at 1 year (RD 1.42%, 95% CI 0.09% to 2.76%), but at 2 years there was no statistically significant difference between the groups (RD 2.32%, 95% CI -1.18% to 5.82%). Only one trial reported results after 3 years of use [Baveja 1989], showing no difference between the groups. There were fewer discontinuations due to bleeding and pain in the TCu200 group after 1 and 2 years (RD -1.9%, 95% CI -3.27% to -0.53% and RD -3.38%, 95% CI -5.33% to -1.44%) but no difference after 3 years of use. There was no statistically significant difference in the number of expulsions, perforations, infections, other medical or non-medical reasons and overall continuation or discontinuation rates between the groups.

6. Cu-Safe 300 vs TCu380A

One small trial involving 600 women with a follow-up to 3 years was included in the review [Van Kets 1995]. The trial was too small to detect an excess pregnancy rate of 1% with Cu-Safe300 at 3 years (95% CI -3.10% to 5.10%). There was a tendency towards more expulsions and towards fewer removals for bleeding and pain with Cu-Safe 300 with both almost reaching statistical significance. The trial report states these latter results are statistically significant, but this is not consistent with the published results.

7. Cu7 vs TCu380A

Cole 1985B found no statistically significant difference in one year rates for pregnancies or expulsions, or removals for bleeding and/or pain, or other medical reasons (see Table 02)

8. NovaT380 vs TCu380S

One study [Haugen 2007)] compared these devices in 1005 women. There was twice the number of pregnancies in the NovaT380 group, statistically significant at the end of the first year of use (RD 1.40%, 0.30% to 2.50% at year 1, RD 2.30%, -0.64% to 5.24% at year 5). The overall expulsion rates were similar, although there were fewer partial expulsions with NovaT380. There were no statistically differences in removal rates for bleeding, pain, dysmenorrhoea PID or other medical reasons, and overall discontinuation rates were similar.

9. TCu220 vs MLCu375

One trial with a follow-up of one year was included in this comparison [Ho 1992]. There was no difference in the number of pregnancies, expulsions, discontinuations due to medical reasons or continuation rates between the comparison groups.

10. MLCu250 vs MLCu375

This comparison includes two small trials with a follow-up of three years [Bratt 1988, Wilson 1992]. There were no statistically significant differences between the groups for pregnancy after one year (RD 0.50%; 95% CI -1.97% to 0.93%), two years (RD 0.02%; 95% CI -2.45% to 2.50%) and three years (RD 0.79; 95% CI -2.19 to 3.78) or expulsions. The two studies were heterogenous for discontinuations for bleeding and pain. The combined results (random effects model) showed no statistical difference between the devices, and there was no statistical difference in discontinuation for PID, other medical reasons, planned pregnancy and other personal reasons.

11. Nova T vs MLCu375

Three trials involving a total of around 2400 women were included in this comparison with follow-up of up to three years [Bratt 1988,

Saure 1985, Wilson 1992]. The combined rate differences for pregnancy and discontinuation for bleeding and pain were not statistically significant different between the two groups for 1, 2 or 3 years of follow-up. There was no statistically significant difference in rates for discontinuation due to PID, other medical or personal reasons or all discontinuations.

12. MLCu250 vs TCu220

One trial reported outcomes for one and two years [Goh 1983 A]; and another trial at three years [WHO 1990A]. There tended to be more pregnancies with MLCu250, but statistically significant at the end of the second year only (RD 2.20%; 95% CI 0.18% to 4.22%). The results were similar for both groups for expulsions and removals for different medical and personal reasons.

13. Nova T vs TCu220

One large trial (3728 women) was included [WHO 1990B], reporting on outcomes at three and five years of use. Pregnancy rates were statistically significant less in the TCu220 group after three and five years of use (RD 2.1%, 95% CI 0.75% to 3.63% and RD 5.5%, 95% CI 2.78% to 8.22%). Discontinuation for non-medical reasons and overall discontinuation rates were also statistically significant less in the TCu220 group after five years of use (RD 5.5%, 95%CI 1.89% to 9.11% and RD 3.7%, 95% CI 0.09% to 7.31%, respectively). Rates for expulsion, ectopic pregnancy, discontinuations due to bleeding and pain or other medical reasons were similar for both groups.

14. Cu 7 vs TCu220

Four trials were included, reporting on outcomes over two years of use [Goh 1983, WHO 1982, WHO 1983A, WHO 1983B]. In the TCu220 group, there were fewer pregnancies, expulsions and use related discontinuations. The rates for perforation, ectopic pregnancy, discontinuation due to bleeding and pain, PID or other medical reasons were not statistically different for both groups.

15. TCu220 vs TCu200

One large trial was included [Sivin 1979B], reporting on outcomes to two years of use. There were fewer pregnancies in the group using TCu220 at the end of two years of use (RD -3.2%, 95% CI -5.04% to -1.36%). No significant differences in rates for expulsion, discontinuation due to bleeding and pain, other medical or personal reasons and overall discontinuation were shown between the groups.

16. Nova T vs TCu200

There was one trial included in this comparison [Luukkainen 1979]. There were significantly less pregnancies in the Nova T group after 1, 2 and 3 years of use (RD -1.5%, 95%CI -2.81% to -0.19%; RD -2.6%, 95%CI -4.44% to -0.76%; RD -4.2%, 95%CI -6.59% to -1.81%). There were significantly more expulsions with Nova T by the end of the third year of use (RD 2.9%, 95%CI 0.11% to 5.69%). The rates for discontinuation due to bleeding and pain, PID, other medical or non-medical reasons and overall continuation were similar for the two groups.

17. MLCu250 vs NovaT

Two trials were included [Bratt 1988, Wilson 1992] reporting on outcomes up to three years. The combined results were similar for both groups for pregnancy (RD 0.94. 95%CI -1.88% to 3.76% at 3 years) , perforation, different reasons for discontinuation and continuation rates.

18. MLCu250 vs Cu 7

Two small trials were included reporting on outcomes up to one [Petersen 1991] and two years of use [Goh 1983]. In the Goh trial (564 women) there were less pregnancies, expulsions and overall use related discontinuations in the MLCu250 group after one year of use. Pregnancy rates continued to be lower in the second year, but the difference was not statistically significant different. All use related discontinuations, discontinuation due to bleeding and pain, PID and other medical reasons were similar at two years of use for both groups. Expulsions at two years of use continued to be less frequent in the MLCu250 group (RD -4.50%, 95% CI -7.75% to -1.25%). Petersen 1991 compared MLCu375 and Cu7 with shorter version of each device in a trial in 236 nulligravidae. The continuation rate was higher with MLCu375 (table 2).

DISCUSSION

This review includes all IUD trials to date that compared standard framed IUDs. Five alternative plastic frames were assessed. Most frames have versions with different copper loads or placement. Our review has demonstrated that the frame and amount and position of copper all play a part in performance. The T-shaped devices, when carrying a surface area of 380mm^2 of copper performed better than other contenders. In general, the comparative analyses suggest higher effectiveness and similar side-effect profile with high copper IUDs compared to low copper ones although some variability exists in different comparisons. In this discussion we focus on the IUDs that are used widely.

Cumulative pregnancy rates for the different IUDs vary between 0.5-2.2% for the smaller (less than 300mm^2 of copper) and 0.1-1.0% for the devices with a higher copper load after the first year of use (Table 04) and are 5.8% for the TCu220 compared to 2.2% for the TCu 380A after 12 years of use. The comparative analyses suggest a higher effectiveness and similar side-effect profile with IUDs having larger copper surface areas compared to those with smaller areas, although some variability exists in different comparisons.

TCu380A and TCu380S have the lowest pregnancy rates in the trials. They also have the longest duration of use, which minimises the need for replacement and the attendant problems.

Comparison 1: MLCu375 vs TCu380A

TCu380A is the superior of these two devices, although the differences were not large. There was a small excess in pregnancies with MLCu375, from around 1% at the end of one year of use to 2% at

ten years. MLCu375 also had a higher expulsion rate, appearing from the third year of use. Most of the data comparing these two devices come from one trial [WHO 1994], and 54% of women taking part in this ongoing trial are in China [WHO 2004b] (see Table 05). The pregnancy rate in both arms of this trial is significantly higher amongst the Chinese participants compared to non-Chinese, at least part of which will be explained by the much reduced loss-to-follow-up at Chinese centres (TCu380A 5.8% and MLCu375 6.8%, and 25.9% and 21.8% in non-Chinese at 10 years). The pregnancy rate at ten years of use was 70% higher with MLCu375 compared to TCu380A in the Chinese centres where there was a low loss rate, but similar in the non-Chinese centres with the high loss rate. The low loss rate in the Chinese cohort and the high quality of the WHO trial generally, supports the conclusion that TCu380A performs better than MLCu375.

Removal for bleeding and pain are generally the main reasons for use-related removals in IUD trials. There is a suggestion that troublesome bleeding and pain may be less of a problem with MLCu375, as was found in the WHO trial at four and six years. No data on these outcomes is available for later years, but the similarity in total medical removals at 10 years of follow-up suggest that any benefit did not persist and may have been due to chance.

The simplicity of the insertion technique for MLCu375 and the smaller diameter of the insertion tube, may make this IUD appropriate in some circumstances. But if insertions are easier with MLCu375, this was not shown in the large WHO 1994 trial. There were five reported failed insertions with MLCu375 and three with TCu380A (p=0.46).

Comparison 3: TCu380S vs TCu380A

The one device that performed as well, if not better than TCu380A, was the modified version of the same device, TCu380S, in which the copper sleeves on the arms are flush with, and at the ends of the plastic arms. The pregnancy rate difference tended to favour TCu380S after the first year, reaching statistical significance in the fourth year of use. This occurred despite more expulsions with TCu380S. Apart from this, the modified version performed similarly to its progenitor. The validity of both of the trials making this comparison is unlikely to have been affected by selection bias as the allocation was concealed in both. The blinding of the women in the Sivin 1990 trial should have partially prevented other potential biases from funding of the trials by the manufacturer of TCu380S.

Anecdotal evidence suggests some clinicians find it easier to load the narrower arms of the modified device into the inserter tube, as the whole of the arms and not just the tips can fit into the inserter tube. Some also find that a modification of the inserter tube for TCu380S, in which the device is pushed through the tube from below, eases the loading, but this insertion tube has a slightly wider diameter.

Comparison 4: TCu220 vs TCu380A

TCu220 differs from TCu380A in that the copper coil on the stem of the TCu380A frame is replaced by copper sleeves, which have a smaller total copper surface area. This difference in copper load may be the reason for its lower effectiveness in preventing pregnancy. In this review it was apparent from the fifth year of use. Apart from that, the two IUDs performed similarly, notably with no difference in removals for bleeding and pain, despite the difference in copper load. Most of the data in the later years for this comparison comes from one trial [WHO 1990C], which had high, though similar, loss-to-follow-up rates, which reduces our confidence in the conclusion that TCu380A is the superior IUD. The pregnancy rate in the Baveja 1989 trial tended to be lower with TCu220 compared to TCu380A. This may be due to chance, as the pregnancy rate with TCu220 in this trial was unusually low, while the rate for TCu380A was high when compared to the performance of these IUDs in other trials in this review. Also, the possibility of selection bias has to be considered, as the methods used to conceal allocation in the Baveja trial were not described.

Comparison 8. NovaT380 vs TCu380S

In the Haugen 2007 study, the sample size was based on removal rates for bleeding and pain, and the study was underpowered to detect a clinically significant doubling of pregnancy rates with NovaT380 compared to TCu380S. Apart from the difference in efficacy, these devices performed similarly. While there were fewer partial expulsions with NovaT380, the overall expulsion rates did not differ. IUD expulsions, partial or complete, are important primarily if they result in pregnancy. Expulsions that result in pregnancy are recorded as pregnancies. There were fewer pregnancies with TCu380A. Three other trials in this review compared expulsion rates with NovaT and copper T framed devices. The expulsion rates were similar in Batar 1987 and WHO 1990B and higher with NovaT in the Luukkainen 1979 trial.

Comparison 10: MLCu250 vs MLCu375

Trials using these two devices are easy to blind throughout the course of the trial as the devices are very similar and have the same coloured strings. Unfortunately, this does not appear to have been done in either of the two included studies. In none of the outcomes reviewed were there any differences in performance between these devices, either in the individual trials or in the meta-analyses. The one exception was removals for bleeding and pain in the Bratt 1988 trial, which found a statistically lower rate of removals with the lower copper load device at one year, different from Wilson [Wilson 1992] who found no difference between the devices. The data does not support using the lower copper-load device to minimise problems with excessive bleeding or pain. Importantly, the two trials terminated at three years duration, after which time any improved efficacy in preventing pregnancy with a higher copper load device, and any excess removals for bleeding and pain, might have become apparent. If a Multiload device is preferred, the data gives no support to use the one with less copper, MLCu250, when MLCu375 has been shown to provide effective long-term contraception.

Comparison 11: NovaT vs MLCu375

Poor reporting of the trials making this comparison means that we do not know whether the women received the type of device to which they had been randomly allocated, making selection bias possible. Some of these studies may have been funded by a manufacturer, and tight research methods are particularly important. The direction of any possible bias is unknown. Loss-to-follow-up rates were low in the Wilson trial (Wilson 1992), and are not given in Saure 1985 and Bratt 1988. In the three trials, the two devices performed similarly, and there were no differences in outcomes in the meta-analyses.

Problems at insertion

Interestingly, despite the 5 different frames, different IUD insertion tubes and different insertion techniques, there were no differences in reported problems at insertion. Sixteen trials reported insertion failure rates. On average in one in 300 insertions failed, and there were no differences between the devices.

At a theoretical level, the NovaT, Multiload and Cu-Safe devices, which are narrower at insertion, could be easier to insert. Eight trials reported failed insertion with a Multiload compared to a T-shaped device. In none of the trials was there a statistically significant difference in failure to insert. Three trials reported the numbers requiring dilation when either a Multiload or a T-shaped device was used. There was no difference in the rates. Two trials comparing a NovaT to a T-shaped device found no difference in the number of insertions that were reported as 'difficult', or in which the insertion failed. Wilson 1992 was the only trial that found a difference at insertion. There were more insertions recorded as difficult with NovaT compared to the two Multiload devices combined, but there was no difference in the number of failed insertions. There were no differences in reported pain at insertion in the seven trials that reported this outcome. Likewise there was no difference between the devices in six trial that reported the numbers of perforations, and the six trials that reported cumulative perforation rates, some up to 12 years, showed no statistical difference in perforation rates. The trial data reported here suggest no type of device is easier to insert or causes less pain at insertion than another. However, almost all of the women included in the trials were multiparous, so this may or may not apply to women who have not had children.

Nulliparous women

Increasingly, women who have not had children are choosing an IUD as their preferred method of contraception. WHO Medical Eligibility Criteria for Contraceptive Use advises that nulliparous women can generally use the method [WHO 2004a]. The optimum IUD for these women is unknown, however. Most of the trials include only parous women, and most trials that do include women who have not had children have not published a subgroup analysis to determine performance in nulliparous women. Sivin reported separated data for nulliparous and parous women in the trials comparing TCu380A to TCu200 and TCu220 to TCu200 [Sivin 1979A, Sivin 1979B]. The performance of the IUDs did not appear to vary by parity. The Petersen trial included nulliparous women only, but is too small and inadequately reported to provide valid information [Petersen 1991]. We were unable to include the Otero-Flores (Otero-Flores 2003) trial because of the apparent unreliability of the reporting (Sivin 2004). There is insufficient evidence to address whether a shorter stem offers any advantage in nulliparous women.

Choice of IUD

The International Planned Parenthood Federation recommends that 'only one type of IUD be used in any service delivery setting; at the most, two with similar insertion techniques may be used. This specialization will help the staff inserting the devices to maintain a high level of skill.' On the evidence reviewed here, which includes all randomised trials of framed IUDs, TCu380A or TCu380S should be the device of first choice, but there seems to be no place for a second device with a similar insertion technique, as this would suggest TCu200 or TCu220, which offer no advantage over their sister devices.

Quality of trials

The quality of reporting in many of the trials was poor. Only about one quarter of included trials reported secure allocation concealment; most trials did not specify the randomisation procedures or adhered to the intention to treat principle. Few trials provided definitions for their outcomes, such as PID, expulsion (e.g. WHO 1983A). In case of expulsion it may include cases of small displacement in one trial and entire expulsion in others. The continuation rates in the long-term WHO studies were good (< 77% after 3 years; 25-30% after 8 years) giving more stability to the results.

Many of the trials last for one or two years, which is shorter than the expected use of the devices, which limits the value of those trials when choosing an IUD. Trials should last for at least three years.

AUTHORS' CONCLUSIONS

Implications for practice

TCu380A is the preferred IUD over MLCu375, MLCu250, TCu220, TCu200 and Cu-Safe300. Indirect evidence suggests that it performs superiorly to NovaT and Cu7. TCu380S may be preferred to TCu380A for those who find it difficult to load the TCu380A, as it is at least as effective at TCu380A, although it may have a higher expulsion rate. None of the IUDs were easier to insert than another, so this review does not support selecting one over another to facilitate insertion. There is no evidence that any particular framed copper device is better suited to nulliparous women.

Implications for research

It is unlikely that new IUDs will be much more effective than TCu380A in short-term use. Contending IUDs will need to be studies in large number over a long period of time. Well-conducted randomised trials comparing devices which are smaller at insertion and smaller in-situ with TCu380A or TCu380S could identify more suitable IUDs for nulliparous women or those with a tight cervical canal. In common with other systematic reviews in this field, we appeal for transparency in reporting trials and adherence to CONSORT guidelines, and ask journal peer reviewers to ensure that authors follow the guidelines.

POTENTIAL CONFLICT OF INTEREST

None declared

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	**Arowojolu 1995**
Methods	women picked up an envelope ' blindly' and 'randomly'; non-competing single decrement life-table rates
Participants	300 women at the University College Hospital Ibadan, Nigeria. inclusion criteria: inclusion criteria of the manufacturer for each device; women needed to have a desire for contraception > 12 months; insertion during menstruation
Interventions	group 1:TCu380A (n=100) group 2: MLCu 250 (n=100) group 3: MLCu 375 (n=100) follow-up for 1 year
Outcomes	problems during insertion, side effects, continuation/discontinuation
Notes	no standard errors given. See table 2
Allocation concealment	B – Unclear

Study	**Bahamondes 1999**
Methods	computer randomisation; each device was sealed in an opaque envelope; non-competing single decrement life-table rates

Characteristics of included studies (*Continued*)

Participants	1568 women at the School of Medicine, CAMPINAS, Brazil were enrolled between March 1993 and March 1994. Inclusion criteria: parous women, at risk of pregnancy, no history of PID; insertions during the first 7 days of a menstrual period by gynaecologist or nurse or resident or medical student in training
Interventions	group 1: TCu380A (n=806) group 2: TCu380S (n=762) follow-up for 5 years
Outcomes	pregnancy rates, expulsion, discontinuation due to bleeding/pain, PID, other medical or personal reasons
Notes	post randomisation exclusion due to protocol violation mentionned, but numbers not stated. High expulsion rate reported for both groups may be due to the definition used (location > 20 mm distance from the fundus) by most local gynaecologists; the author provided unpublished data
Allocation concealment	A – Adequate

Study	**Batar 1987**
Methods	randomised, randomisation not described; sealed sequentially numbered envelopes; non-competing single decrement life-table rates
Participants	1738 women were enrolled at two family planning clinics in Budapest and Debrecen, Hungary between February 1982 and February 1983. Inclusion criteria: no contraindications for copper IUD insertions during first 7 days of menstrual cycle or =/> 6 weeks post-partum/post-abortion.
Interventions	group 1: Nova T (n= 855) group 2: TCu200 (n= 883) follow-up for 2 years
Outcomes	pregnancy rates, expulsion, side effects as reason for discontinuation
Notes	40% of participants were IUD users before; no standard errors given. See table 2
Allocation concealment	B – Unclear

Study	**Baveja 1989**
Methods	randomisation with equal number of women per device; separate randomisation for each centre; numbered, sealed envelopes; non-competing single decrement life-table rates
Participants	1430 women from 14 human reproduction research centres in India were analysed; 44 post-randomisation exclusions (10-14-20 women from three groups were excluded because the inclusion criteria were not met); enrolment from 1983 - 1986 inclusion criteria: 18-40 years; proven fertility; regular menstrual pattern; at risk of pregnancy
Interventions	group 1: TCu380A (n=444) group 2: TCu220C (n= 510) group 3: TCu200B (n=520) follow-up for 3 years
Outcomes	pregnancy rates, side effects as reason for discontinuation, non-medical reasons for discontinuation, expulsions
Notes	power calculation done for n=2400; sample size could not be achieved due to lack of supply of devices; 1 centre dropped out after 154 cases were enrolled - data was unavailable for analysis; 80% interval insertions; loss-to-follow-up stated; around 80% of interval insertions (> 6 weeks postpartum or-abortion) in all groups; women were similar with regard to age (25-26 years), gravidity (2.5-2.6), height (151-152 cm), weight (47-48 kg)
Allocation concealment	B – Unclear

Study	**Bratt 1988**
Methods	randomised trial, not further specified; non-competing single decrement life-table rates
Participants	600 women; at Trondheim University Hospital, Norway; recruitment between January 1980 - August 1981
Interventions	group 1: MLCu375 (n= 200) group2: MLCu250 (n= 200) group 3: Nova-T (n=200) follow-up for 3 years
Outcomes	pregnancy rates, expulsion, discontinuation due to bleeding/pain, PID, other medical or personal reasons
Notes	66% of insertions during menstruation; 34% during puerperium
Allocation concealment	B – Unclear

Characteristics of included studies (*Continued*)

Study	**Champion 1988**
Methods	computer generated randomisation, sealed, opaque envelopes (personal communication); prepared by FHI; women were blinded; non-competing single decrement life-table rates
Participants	885 women; multicentre trial: Rijeka and Belgrade, Yugoslavia; Panama City, Panama; enrolment from September 1980 to December 1981. Inclusion criteria: 18-40 years, healthy and sexually active. Exclusion criteria: uterine abnormalities, PID, anemia, history of menorrhagia or hypermenorrhoea.
Interventions	group 1: TCu380A (n=441) group2: MLCu375 (n=444) follow-up for 3 years
Outcomes	pregnancy rates, expulsion, discontinuation for bleeding and pain, other medical or personal reasons, continuation rates, events during insertion
Notes	no standard errors given; majority parous, data not given
Allocation concealment	A – Adequate

Study	**Chen 2003**
Methods	randomisation, not further specified; ACA not used; blinding not used
Participants	mulicentre trial; 2699 parous women from 7 township family planning clinics in townships in China inclusion criteria: 20-29 years, parous, regular menstruation or lactating, Hb: =/> 90g/L, PAP smear =/< II, IUCD as the only contraceptive method
Interventions	group 1: uterine cavity shaped device Cu 300 (n=899) group 2: TCu220C (n=900) group 3: TCu380A (n= 900) follow-up for 10 years
Outcomes	pregnancy rate, expulsion, perforations, side effects, removal rate for bleeding/pain, continuation rates
Notes	experienced providers inserted all devices; events rather than rates published
Allocation concealment	B – Unclear

Study	**Cole 1985B**
Methods	computer generated randomisation; sealed, opaque envelopes (personal communication); non-competing single decrement life-table rates
Participants	366 women; 2 centres in England and the Philippines; healthy , sexually active women; interval insertions; enrolment from January 1981 - January 1983
Interventions	group1: TCu380A (n=181) group 2: Cu7 (n=183)
Outcomes	pregnancy rate, expulsion, discontinuation due to bleeding and pain, other medical and personal reasons, perforation, failed insertion
Notes	no standard errors given - see table 2; complications: 1 perforation in each group
Allocation concealment	A – Adequate

Study	**Cole 1985C**
Methods	computer generated randomisation; sealed, opaque envelopes (personal communication); non-competing single decrement life-table rates
Participants	1499 women recruited between September 1980 to June 1982; multicentre international trial; 5 centres in Yugoslavia, Panama, Costa Rica and Egypt. inclusion criteria: healthy, sexually active women, last pregnancy terminated =/> 40 days; IUD as sole contraceptive method. 22 women excluded post-randomisation (inclusion criteria not met)
Interventions	group 1: TCu 380Ag (n=737) group 2: MLCu375 (n=740) follow-up for 1 year
Outcomes	pregnancy rates, expulsion, discontinuation due to bleeding/pain, other medical or personal reasons, insertion problems

Characteristics of included studies (*Continued*)

Notes	median age: TCu 380Ag: 26.7 years, MLCu 375: 27.5 years median of total life births: TCu 380Ag: 1.8, MLCu 375: 1.9 Insertion problems reported: failed insertion: TCu 380Ag: 0.1%, MLCu375: 0.1% one clinic performed the randomisation at the time of recruitment; all others at the time of insertion dilatation: TCu 380Ag: 4.1%, MLCu 375: 3.9% cervical laceration: TCu 380Ag: 1.6%, MLCu375: 1.5% moderate pelvic pain: TCu 380Ag: 1.1%, MLCu 375: 1.1%; no standard errors given.
Allocation concealment	A – Adequate

Study	**Farr 1994A**
Methods	computer generated randomisation; sealed, opaque envelopes (personal communication); same protocol used for Farr 1994B and Farr 1994C; non-competing single decrement life-table rates
Participants	1678 women recruited between 1985-1989; multicentre international trial; 6 developing country centres: Cameroon, Chile, Egypt, El Salvador, Mexico, Pakistan inclusion criteria: 18-40 years, healthy, sexually active, normal PAP smear, no failed insertion. breastfeeding status was determined on admission; all parous
Interventions	"group 1: TCu380A (n= 847) group 2: TCu 200 (n= 831) follow-up at 1,3,6,12 months"
Outcomes	accidental pregnancy rates, problems at insertion, expulsions, side effects, side effects as reason for discontinuation, continuation rates.
Notes	
Allocation concealment	A – Adequate

Study	**Farr 1994B**
Methods	see Farr 1994A
Participants	901 women randomised; 4 family planning clinics in Mexico and the Philippines inclusion criteria: see Farr 1994A
Interventions	included in analysis: group 1: TCu380A (n=427) group 2: TCu220C (n=430)
Outcomes	accidental pregnancy rates, expulsion, side effects as reason for discontinuation
Notes	
Allocation concealment	A – Adequate

Study	**Farr 1994C**
Methods	see Farr 1994A
Participants	2146 women enrolled; 4 family planning clinics in Sri Lanka (Colombo and Galle), Thailand (Bangkok) and Malaysia (Penang) inclusion criteria: 18-40 years, sexually active, last pregnancy terminated =/> 40 days abnormal PAP-smear, no current of PID, no failed insertion attempt 103 cases did not meet the inclusion criteria and were excluded from the analysis
Interventions	"included in analysis: group 1:TCu380A (n= 1008) group 2: ML 250 (n= 1035) follow-up for 12 months"
Outcomes	accidental pregnancy rates, expulsion, discontinuation due to side effects
Notes	the trial is part of a series of trials conducted by FHI in developing countries from 1985-1989 all insertions were performed by physicians at the time of insertion: 46.3% of women in the Cu380A group were using contraception during the month preceeding IUD insertion; 47.3% in the ML 250 group 50% of women were breastfeeding in the Cu380A group and 66% in the ML 250 group
Allocation concealment	A – Adequate

Study	**Goh 1983**
Methods	random allocation, randomisation not described; loss-to-follow-up mentioned; non-competing single decrement life-table rates

Characteristics of included studies (*Continued*)

Participants	1199 women were recruited; multicentre study at 3 University centres (Singapore, Kuala Lumpur, Medan) three - arm trial, inclusion criteria: 19-35 years; sexually active; parous; IUD as only contraceptive method; no abnormalities on general and gynaecological examinations; =/>4 weeks post-abortion; =/> 8 weeks post-partum; ability to attend the follow-up exclusion criteria: 'standard ' contraindications for Cu-IUD
Interventions	included in analysis: group 1: MLCu250 (n=278) group 2: TCu220C (n=286) group 3: Cu7 (n=261) follow-up for 2 years
Outcomes	accidental pregnancy rates, expulsions, discontinuation, reasons for discontinuation, continuation rates
Notes	
Allocation concealment	B – Unclear

Study	**Haugen 2007**
Methods	computer generated, blocks of 10, random list; sealed envelopes; power calculation given; primary efficacy parameter removal rates for bleeding/pain; non-competing single decrement life-table rates
Participants	years recruited 1993-1995. 1005 women parous, 18-45 yrs, 13 general practices in Norway
Interventions	Group 1: TCu380S (n=470) Group 2: NovaT380 (n=487) Follow-up for 5 years.
Outcomes	Difficult insertions, failed insertion, pregnancy rates, full expulsion, partial expulsion, bleeding, pain, dysmenorrhea, PID, other medical reasons, personal reasons, planning pregnancy, no longer need for contraception, wish to change method, other personal, lost to follow up, planned termination at 60 months (continued use), haemoglobin. Data at 1, 3 and 5 years.
Notes	60% used IUD before; chlamydia screening at insertion; pregnancy confirmation by test, histology or birth; bleeding and pain defined; 48 exclused from analysis, reasons given.
Allocation concealment	B – Unclear

Study	**Ho 1992**
Methods	randomly assigned, randomisation not described; non-competing single decrement life-table rates
Participants	768 women enrolled for the 2 IUDs included in the review; MCH Hospitals in Guangzhou, Jiangmen and Family Planning Centres in Donguan, Zhongshan and Shenzhen, China. Inclusion criteria: 18-40 years, parous, no previous use of IUD, uterine cavity =/> 6 cm, day 3-7 of menstrual cycle. All insertions performed by experienced physicians.
Interventions	group 1: MLCu 375 (n=384) group 2: TCu220C (n=384) follow-up for 1 year
Outcomes	pregnancy rates, discontinuation due to medical reasons, use related discontinuation
Notes	preliminary results - later data not found
Allocation concealment	B – Unclear

Study	**Luukkainen 1979**
Methods	list of random numbers, randomisation not described; double-blind; non-competing single decrement life-table rates
Participants	1843 women were enrolled between 1975-1977; multicentre international trial; centres in Denmark (Department of Gynaecology of the Bispebjerg Hospital), Finland (4 clinics), Sweden (Department of Obstetrics and Gynaecology, University of Uppsala)
Interventions	group 1: Nova T (n=907) group 2: TCu200 (n= 936) follow-up for 1 year
Outcomes	accidental pregnancy rates, expulsion, reasons for discontinuation, continuation rates
Notes	166 immediate postabortion insertions in the Nova T group, 156 in the CopperT200 other insertions during menstruation
Allocation concealment	B – Unclear

Characteristics of included studies (*Continued*)

Study	**McCarthy 1983A**
Methods	random number table; sealed envelopes consecutively numbered gross and net cumulative rates
Participants	491 women were recruited between 1974 - 1977 at the Department of Obstetrics and Gynaecology, National University of Singapore. Inclusion criteria: healthy volunteers less than 40 years, proven fertility. Exclusion criteria: recent history of PID, venereal disease, suspected malignancy, congenital uterine abnormality, irregular bleeding, uterine fibroids.
Interventions	group 1: MLCu250 (n=192) group 2: Cu7(n= 299) follow-up for 2 years
Outcomes	pregnancy rates, expulsion, discontinuation due to bleeding/pain, other medical or personal reasons
Notes	loss-to-follow-up: n= 44; no standard errors given. See table 2
Allocation concealment	B – Unclear

Study	**McCarthy 1983C**
Methods	random number table; sealed envelopes consecutively numbered; non-competing single and multiple decrement life-table rates
Participants	549 women were recruited between September 1977 and November 1978 at the Department of Obstetrics and Gynaecology, National University of Singapore. Inclusion criteria: healthy volunteers less than 40 years, proven fertility. Exclusion criteria: recent history of PID, venereal disease, suspected malignancy, congenital uterine abnormality, irregular bleeding, uterine fibroids.
Interventions	group 1: MLCu375 (n=275) group 2: MLCu250 (n=274)
Outcomes	pregnancy rates, expulsion, discontinuation due to bleeding/pain, other medical or personal reasons
Notes	loss-to-follow-up: n= 28; no standard errors given. See table 2
Allocation concealment	B – Unclear

Study	**McCarthy 1985**
Methods	randomised allocation, randomisation not described; non-competing single and muptiple decrement life-table rates
Participants	400 women were enrolled between September 1981 and November 1982 at the Kandang Kerbau Hospital, Singapore all insertions were immediately post-abortion inclusion criteria: 16-40 years, proven fertility, sexually active, IUD as only contraceptive method IUD inserted by doctor who performed the abortion
Interventions	group 1: MLCu 250 (n= not reported) group 2: Nova T (n= not reported) follow-up for 2 years
Outcomes	pregnancy, expulsion, discontinuation due to bleeding/pain, other medical or personal reasons
Notes	supported by IPPF and Schering follow-up was described as ongoing (until 4 years) - data not retrieved more Malay than Chinese women received the Nova-T loss-to-follow-up: 0.6% (MLCu250) and 2.7% (Nova T) after 2 years; no standard errors given. See table 2.
Allocation concealment	B – Unclear

Study	**Petersen 1991**
Methods	randomised, randomisation not described; patient & assessment blinding; non-competing single decrement life-table rates
Participants	236 nulliparous women; family planning clinic Herlev University Hospital, Copenhagen, Denmark; all insertions postmenstrual
Interventions	group 1: ML 250 (n=61) group 2: ML 250 short (n=50) group 3: Cu 7(gravigard) (n=55) group 4: Cu 7-mini (mini-gravigard) (n=62) follow-up for 12 months
Outcomes	problems during insertion, expulsion, discontinuation due to bleeding/pain, PID
Notes	hysterometry on all participants; no standard errors given. See table 2

Characteristics of included studies (*Continued*)

Allocation concealment	B – Unclear

Study	**Sastrawinata 1991**
Methods	computer-generated random allocation; sealed numbered envelopes; non-competing single decrement life-table rates
Participants	2992 women were enrolled at 6 centres in Indonesia (BKS PENFIN) between January 1986 and February 1987. Inclusion criteria: healthy, sexually active women without contraindications for IUD between 18-40 years, no IUD use in the previous month; > 40 days after last pregnancy
Interventions	group 1: TCu380A (n=946) group 2: MLCu375 (n=948) (group 3: LLD n=943; not included) follow-up for 2 years
Outcomes	pregnancy rates, ectopic pregnancy rates, expulsion, discontinuation due to bleeding/pain, other medical or personal reasons
Notes	study supported by FHI
Allocation concealment	A – Adequate

Study	**Saure 1985**
Methods	insertions were performed in a pre-randomised order; non-competing single decrement life-table rates
Participants	795 insertions were performed at 3 primary health care centres and 5 private outpatient clinics in Finland by skilled general practitioners or gynaecologists. Exclusion criteria: generally accepted contraindications, nulliparous women < 20 years; all insertions during menstruation, parous
Interventions	group 1: MLCu375 (n=385) group 2: Nova-T (n=410) (group3: Fincoid n=397; not included) follow-up for 2 years
Outcomes	pregnancy rates, expulsion, discontinuation due to bleeding/pain, PID, other medical or personal reasons
Notes	
Allocation concealment	B – Unclear

Study	**Shrestha 1995**
Methods	computer-generated random numbers; sealed envelopes; blinding not stated; non-competing single decrement life-table rates
Participants	200 women at the Maternity Hospital Thapathali,Kathmandu, Nepal; inclusion criteria: 18-40 years, sexually active, =/> 40 days after termination of last pregnancy
Interventions	group 1: TCu380A (n=100) group 2: TCu200 (n= 100) follow-up for 2 years
Outcomes	accidental pregnancy rates, expulsion and removal rates, insertion related complaints/complications, post-insertion IUD related complications
Notes	part of FHI study from 1985-1989 > 80% of participants were breastfeeding at the time of enrolment
Allocation concealment	B – Unclear

Study	**Sivin 1979A**
Methods	random assignment; double-blinding with records kept outside clinics at the Population Council; non-competing single decrement life-table rates
Participants	3530 women were enrolled between 1972 and 1975 in the United States
Interventions	group 1: TCu380A (n=1679) group 2: TCu200 (n=1851) follow-up for 2 years
Outcomes	pregnancy rates, expulsion, discontinuation bleeding/pain, other medical or personal reasons
Notes	trial performed by the Population Council

Characteristics of included studies (*Continued*)

Allocation concealment	B – Unclear

Study	**Sivin 1979B**
Methods	see Sivin 1979A
Participants	2111 women; enrolled between 1972 and 1975 in the United States
Interventions	group 1: TCu220C (n=1097) group 2: TCu200 (n=1014) follow-up for 2 years
Outcomes	pregnancy rates, expulsion, discontinuation bleeding/pain, other medical or personal reasons
Notes	trial performed by the Population Council
Allocation concealment	B – Unclear

Study	**Sivin 1990**
Methods	randomisation by linear congruent method; devices were placed into numbered, sealed, opaque envelopes; patients were blinded; power calculation given; non-competing single decrement life-table rates
Participants	996 women; multicentre international trial in 5 centres: Assiut (Egypt), Uppsala (Sweden), Santiago (Chile), Santo Domingo (Dominican Republic), Campinas (Brazil); time period of recruitment not stated inclusion criteria: women of reproductive age, < 41 years, proven fertility, no contraindications for IUD use
Interventions	group 1: TCu380A (n=298) group 2: TCu380S (n= 698) follow-up for 4 years
Outcomes	pregnancy rates, expulsion, discontinuation due to bleeding/pain, PID, other medical or personal reasons
Notes	"supported by Ortho Pharmaceuticals Ltd, Canada 21.5% and 22.8% were breast feeding at admission; modifications made to device after this study; authors say that the unusually low expulsion rate with TCu380A may have been due to experience with the device "
Allocation concealment	A – Adequate

Study	**Van Kets 1995**
Methods	randomisation list prepared for each investigator; non-competing single decrement life-table rates
Participants	600 women enroled at the University Hospital Gent, Belgium between December 1988 - May 1992; inclusion criteria: between 18-45 years, at risk of pregnancy, without contraindications for IUD. Insertions =/> 6 weeks after last pregnancy had ended - at any time of the menstrual cycle
Interventions	group 1: TCu380A (n=300) group 2: Cu-Safe 300 (n=300) follow-up for 3 years
Outcomes	pregnancy rates, expulsion, discontinuation due to bleeding/pain, other medical or personal reasons
Notes	
Allocation concealment	B – Unclear

Study	**WHO 1982**
Methods	randomly allocated, randomisation not described; non-competing single decrement life-table rates
Participants	2970 women were enrolled between 1976-1978; multicentre international trial, 9 centres: Shatby Maternity Hospital Alexandria-Egypt, Siriray Hospital Bangkok - Thailand, Freie Universität Berlin - Germany, Postgraduate Institute of Medical Education and Research Chandigarh - India, USSR Academy of Medical Sciences Leningrad - USSR, King's College Hospital London - UK, University of Southern California Medical Center Los Angeles - USA, General Hospital Medical Center Manila - Philippines, University Medical School Szeged - Hungary. inclusion/exclusion criteria mentioned but not described
Interventions	group 1: TCu220C (n=984) group 2: Copper 7 (n=994) group 3: Lippes Loop D (not included) follow-up for 2 years
Outcomes	pregnancy rates, expulsions, perforation, discontinuation due to bleeding/pain, intermenstrual bleeding, other medical or personal reasons, continuation rates

Characteristics of included studies (*Continued*)

Notes	
Allocation concealment	B – Unclear

Study	**WHO 1983A**
Methods	computer-generated random table; sealed envelopes; Chiang's actuarial method was used for analysis analysis; non-competing single decrement life-table rates for women continuing after 48h;
Participants	1563 women were enrolled between 1975 and 1978; multicentre study - 8 centres: Havana -Cuba, Ljubljana - Yugoslavia, London - UK, Lusaka - Zambia, New Delhi - India, Seoul - Korea, Singapore, Szeged - Hungary. all insertions post-abortion - immediately after evacuation of the uterus; 96,2% of insertions after 1st trimester termination;
Interventions	group1: TCu 220 (n=790) group 2: Cu 7 (n=773) group 3: Lippes Loop (not included) follow-up for 2 years
Outcomes	pregnancy rates, ectopic pregnancy, expulsion, perforation, discontinuation due to bleeding/pain, other medical or personal reasons, continuation rates
Notes	loss-to-follow ups were excluded from the analysis criteria for definition of PID: history of recurrent PID, pelvic abscess, postabortal/puerperial PID, episode of PID within the last 12 months diagnostic criteria: a)oral temperature >38C before vaginal examination, b)suprapubic tenderness with guarding, c)tenderness on moving of the cervix during vaginal examination, d) adnexal tenderness/adnexal mass (a+ b had to present for the diagnosis
Allocation concealment	A – Adequate

Study	**WHO 1983B**
Methods	computer-generated random table; sealed envelopes; Chiang's actuarial method was used for analysis analysis; non-competing single decrement life-table rates for women continuing after 48h
Participants	711 women; see WHO 1983A
Interventions	group 1: TCu220C (n=353) group 2: Cu 7 (n=358) group 3: Lippes Loop (not included) follow-up for 2 years
Outcomes	pregnancy rates, ectopic pregnancy, expulsion, perforation, discontinuation due to bleeding/pain, PID, other medical or personal reasons, continuation rates
Notes	see WHO 1983A
Allocation concealment	A – Adequate

Study	**WHO 1990A**
Methods	computer-generated random list, block size of six/ten, sealed envelopes; ACA performed; data management centrally at WHO/Geneva; non-competing single decrement life-table rates
Participants	2043 women; multicentre international trial between 1978 - 1984: centres in Bangkok-Thailand, Beijing, Shanghai, Wuhan-China, Chandigarh-India, Hanoi-Vietnam, Havana-Cuba, Leningrad-Russia, Ljubljana-Yugoslavia, Lusaka-Zambia, Manila-Philippines, Moscow-Russia, New Delhi-India, Santiago-Chile, Seoul - South Korea, Singapore, Szeged-Hungary, Tunis-Tunesia, Yerevan-Armenia exclusion criteria: nulliparous women, history of PID/ectopic pregnancy, undiagnosed vaginal bleeding, less than 6 weeks since last pregnancy, genital tract malformations, known/supected genital malignancy, multiple myoma, anaemia, history of hydatiform mole,
Interventions	group 1: MLCu 250 (n=1033) group 2: T220C (n=1011) follow-up for 3 years
Outcomes	pregnancy rates, expulsions, complications, discontinuation rates, side effects, side effects as reason for discontinuation, failure of insertion

Characteristics of included studies (*Continued*)

Notes	final data presented for study 1 trial 2 &3 are ongoing; final data for trial 2 are presented in WHO 1997 Nova T was discontinued in 1989 due to statistically significant higher pregnancy rates compared to TCu 220C
Allocation concealment	A – Adequate

Study	**WHO 1990B**
Methods	computer-generated random list, block size of six/ten, sealed envelopes; ACA performed; data management centrally at WHO/Geneva; non-competing single decrement life-table rates
Participants	3728 women; multicentric (see WHO 1990A)recruitment between 1982-1986
Interventions	group 1: TCu220C (n=1881) group 2: Nova T (n= 1847) (group 3: 2 mcg levonorgestrel-releasing IUD, not included) follow-up for 5 years
Outcomes	pregnancy rates, expulsions, complications, discontinuation rates, side effects, side effects as reason for discontinuation, failure of insertion (in ATR)
Notes	excess pregnancy rates with NovaT after 5 years of use in all participating centres and recommendation to remove the device
Allocation concealment	A – Adequate

Study	**WHO 1990C**
Methods	computer-generated random list, block size of six/ten, sealed envelopes; ACA performed; data management centrally at WHO/Geneva; non-competing single decrement life-table rates
Participants	2793 women; multicentric (see WHO 1990A), recruitment between 1981-1984
Interventions	group 1: TCu380A (n=1396) group 2: TCu 220C (n=1397) follow-up for 12 years
Outcomes	pregnancy rates, expulsions, complications, discontinuation rates, side effects, side effects as reason for discontinuation
Notes	
Allocation concealment	A – Adequate

Study	**WHO 1994**
Methods	computer-generated random list, randomisation in blocks of ten; sealed envelopes; ACA; non-competing single decrement life-table rates
Participants	3655 women, recruited between November 1989 and February 1992; multicentre international trial; 19 participating centres in Thailand, China, Benin, Hungary, Slowenia, Russia, Chile, Uzbekistan, Armenia exclusion criteria: nulliparous women, history of PID/ectopic pregnancy, undiagnosed vaginal bleeding, less than 6 weeks since last pregnancy, genital tract malformations, known/supected genital malignancy, uterus myomatosous, anaemia, history of hydatiform mole
Interventions	group 1: TCu380A (n=1823) group 2: MLCu375 (n=1832) follow-up for 10 years
Outcomes	intrauterine/ectopic pregnancy rates, expulsion, perforation, continuation rates, failure of insertion
Notes	interim analysis (up to 10 years) awaiting full publication
Allocation concealment	A – Adequate

Study	**Wilson 1992**
Methods	random assignment of the devices; operators were assigned according to a computer randomised basis; competing multiple decrement life-table rates

Participants	3-arm trial, women in New Zealand, recruitment between November 1982 to July 1988 exclusion criteria: previous ectopic pregnancy, abnormal uterine bleeding, past history of PID, cervical dysplasia, uterine fibroids, uterine cavity size < 6 or > 9 cm
Interventions	group 1:MLCu 375 (n=586) group 2: MLCu 250 (n=596) group 3: Nova T (n=608) follow-up for 3 years
Outcomes	pregnancy rates, expulsion, discontinuation due to bleeding/pain, PID, other medical or personal reasons, difficulty at insertion
Notes	
Allocation concealment	B – Unclear

ACA - available case analysis

Characteristics of excluded studies

Study	Reason for exclusion
Altman 1981	no allocation concealment used
Apelo 1989	data included in Cole 1985B
Audebert 1986	follow-up study of a single cohort
Bratt 1987	duplicate publication (Bratt 1988)
Chi 1990A	data included in Farr 1994A, B, and C
Chowdhury 1979	comparison between Lippes loop and copper IUD
Cole 1985A	duplicate publication (Cole 1985C)
Confino 1983	IUDs were compared in ' alternately and randomly chosen ' patients
DeCastro 1986	methods not stated
DeCastro 1987	methods not stated
Diaz 1992	retrospective cohort
Ditchik 1984	comparison between Lippes loop, Dalkon shield and Cu7
Farr 1996	follow-up of a single cohort
Fylling 1987	randomisation process unclear; allocation not concealed
Gao 1986	allocation concealment not used
Goh 1985	double publication (Goh 1983A, Goh 1983B, Goh 1983C)
Gu 1992	comparison between steel and copper device - not in scope of review
Hutapea 1984	double publication (Goh 1983A, Goh 1983B, Goh 1983C)
Jarvela 1986	this is a summary of studies that are already included (Nordic studies)
Kandil 1991	methods not stated
Ladehoff 1983	methods not stated
Lai 1991	comparison between metal and copper IUDs
Lim 1985	duplicate publication (McCarthy 1983C)
Luukkainen 1979A	study is a subgroup of patients already included in another trial (Luukkainen 1979)
Luukkainen 1979B	French publication of Luukkainen 1979
McCarthy 1983B	data included in Goh 1983
Nielsen 1980	duplicate publication (Luukkainen 1979)
Otero-Flores 2003	analysis incorrect; unable to use data
Reinprayoon 1998	data included in Farr 1994C

Characteristics of excluded studies (*Continued*)

Rivera 1999	results of only one group from a RCT
Roy 1979	randomisation according to hospital number; no allocation concealment; devices were studied during different time periods
Shih 1984	not a randomised controlled trial
WHO1983C	comparison between 2 copper IUDs and a progesterone IUD; results for the copper IUDs are combined
Wilson 1982	not a randomised controlled trial
Zhang 1994	allocation concealment not used

Lippes loop and Dalkon shield are not manufactured anymore

ADDITIONAL TABLES

Table 01. Follow-up trials

initial trial	follow-up report(s)
Sivin 1990	Sivin 1991(2 years), Sivin 1993 (4 years)
WHO 1990C	WHO 1997 (8,10,12 years)
WHO 1994	WHO 2003 (up to 10 years)
Luukkainen 1979	Allonen 1980 (2 years), Nygren 1981 (3 years), Nielsen 1982 (4 years), Luukkainen 1983 (5 years)

Table 02. Other included studies

Study	Comparison	Pregnancy	bleeding&pain	expulsion
Arowojolu 1995	MLCu250 vs MLCu 375 vs TCu380A	1 year: TCu 380A:1.1%; MLCu375:0%; MLCu 250: 2.1%		1 year: TCu380A: 4.1%; MLCu375: 0%; MLCu250:3.1%
Batar 1987	NovaT vs TCu200 vs	2 years: RD -1.5	2 years: RD 0.1	2 years: RD -1.2
Champion 1988	MLCu 375 vs TCu380A	2 years: RD 0.7; 3 years: RD 1.2	2 years:RD -0.2; 3 years: RD 2.6	2 years: RD 1.1; 3 years: RD 1.1
Chen 2003	TCu220 vs TCu380A	10 years: TCu 220: 46/900; TCu380: 38/900	10 years (bleeding): TCu220 42, TCu380A: 50	10 years: TCu 220: 44; TCu380A: 83
Cole 1985B	TCu380 vs Cu-7	1 year: RD 3.2	1 year: RD 1.1	1 year: RD 0.7
Luukkainen 1983	NovaT vs TCu200	5 years: RD -3.6	5 years: RD 3	5 years: RD 2.1
McCarthy 1983A	Cu 7 vs MLCu250	2 years: RD -0.2	2 years: RD 0.5	2 years: RD 11.1
McCarthy 1983C	MLCu250 vs MLCu375	2 years: RD -0.4	2 years: RD - 3.5	2 years: RD 1.1
McCarthy 1985	NovaT MLCu250	2 years: RD 3.9	2 years: RD 3	2 years: RD 1.4
Nielsen 1982	NovaT vs TCu200	4 years: RD -3.2	4 years: RD 1.1	4 years: RD 1.9
Petersen 1991	MLCu250 vs MLCu250(short) vs Cu-7 vs Cu-7 (short)		1 year: MLCu250(short): 13.8%, MLCu250: 11.5%, Cu-7: 16.4%, Cu-7 (short): 11.3%	1 year: MLCu250(short): 10.3%, MLCu250: 6.6%, Cu-7: 12.7%, Cu-7 (short): 9.7%

Table 03. Trials describing problems during insertion

Study	Failure of insertion	Cervical laceration	Perforation

Champion 1988	n=1 (MLCU375 group)	n=8 (4 each group)	
Cole 1985C	<1% both groups		none
Farr 1994A		<1% both groups	none
Farr 1994B		<1% both groups	none
Farr 1994C		<1% both groups	none
Ho 1992		none	
Sivin 1990	<1% both groups		
WHO 1982		n=1 (TCu220); n=2 (Cu 7)	
WHO 1983A	none		none
WHO 1983B	none		none
WHO 1990A	n=1 (TCu220); n=0 (MLCu250)		
WHO 1990B	n=1 (TCu220); n=0 (TCu380)		
WHO 1990C	n=2 (TCu220); n=1 (NovaT)		
WHO 1994	n=3 (TCu380), n=5 (MLCu375)		
Wilson 1992	=/<1% for all groups		

Table 04. Pregnancy and expulsion rates for IUDs after 1 year of use (per 100 women)

IUD	pregnancy	expulsion
TCu380A	0.0-1.0	2.4-8.2
TCu220	0.8-2.2	0-6.4
TCu200	0-6.2	3.9-10.3
Cu-Safe 300	1.5	3.6
TCu380S	0.2-0.3	2.6-7.3
Nova T	0.6-2.0	4.3
MLCu375	0.3-1.2	1.9-5.6
MLCu250	0.5-2.1	1.6-3.7
Cu 7	1.9-4.4	6.1-8
NovaT380	1.4	

Table 05. WHO 1994: 10 year follow-up : Chinese vs non-Chinese centres

Outcome	Chinese centres	non-Chinese centres
MLCu375vs TCU380A: Pregnancy	Rate: 6.7 vs 4;	Rate: 2.1 vs 2.1
MLCu375 vsTCu380A: Expulsions	Rate: 16.3 vs 11.4	Rate: 9.8 vs 9.9

Table 05. WHO 1994: 10 year follow-up : Chinese vs non-Chinese centres (*Continued*)

Outcome	Chinese centres	non-Chinese centres
MLCu375 vs TCu380A: total medical discontinuations	Rate: 17.5 vs 20.1	Rate: 53.8 vs 52
MLCu375 vs TCu380A: Continuation	Rate: 52.8 vs 57.5	Rate: 15.2 vs 14.9
MLCu375 vs TCu380A: Loss-to-follow-up	Rate: 6.8 vs 5.8	Rate: 21.8 vs 25.9

ANALYSES

Comparison 01. MLCu375 vs TCu380A

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Ectopic pregnancy			rate difference (Fixed) 95% CI	Subtotals only
03 Expulsion			rate difference (Random) 95% CI	Subtotals only
04 Discontinuation: bleeding and pain			rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: planned pregnancy			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: other personal reasons			rate difference (Fixed) 95% CI	Subtotals only
08 Continuation			rate difference (Fixed) 95% CI	Subtotals only
09 Discontinuation: total medical			rate difference (Fixed) 95% CI	Subtotals only
10 Discontinuation: infection/PID			rate difference (Fixed) 95% CI	Subtotals only

Comparison 02. MLCu250 vsTCu380A

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Fixed) 95% CI	Subtotals only
04 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: non-medical reasons			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: all			rate difference (Fixed) 95% CI	Subtotals only

Comparison 03. TCu380S vs TCu380A

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Fixed) 95% CI	Subtotals only

04 Discontinuation: PID	rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: other medical reasons	rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: planned pregnancy	rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: other personal reasons	rate difference (Fixed) 95% CI	Subtotals only
08 Continuation	rate difference (Fixed) 95% CI	Subtotals only
09 Discontinuation: all	rate difference (Fixed) 95% CI	Subtotals only

Comparison 04. Cu220 vs TCu380A

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Random) 95% CI	Subtotals only
02 Ectopic pregnancy			rate difference (Fixed) 95% CI	Subtotals only
03 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
04 Perforation			rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: bleeding and pain			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: intermenstrual bleeding			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: infection/PID			rate difference (Fixed) 95% CI	Subtotals only
08 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Subtotals only
09 Discontinuation: total medical			rate difference (Fixed) 95% CI	Subtotals only
10 Discontinuation: non-medical reasons			rate difference (Fixed) 95% CI	Subtotals only
11 Discontinuation: total use related			rate difference (Fixed) 95% CI	Subtotals only
12 Discontinuation: all			rate difference (Fixed) 95% CI	Subtotals only
13 Continuation			rate difference (Fixed) 95% CI	Subtotals only

Comparison 05. TCu200 vs TCu380A

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Random) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Perforation			rate difference (Fixed) 95% CI	Subtotals only
04 Discontinuation: bleeding and pain			rate difference (Random) 95% CI	Subtotals only
05 Discontinuation: intermenstrual bleeding			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: infection/PID			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Subtotals only
08 Discontinuation: non-medical reasons			rate difference (Fixed) 95% CI	Subtotals only
09 Discontinuation: all			rate difference (Fixed) 95% CI	Subtotals only
10 Continuation			rate difference (Fixed) 95% CI	Subtotals only

11 Discontinuation: planned pregnancy			rate difference (Fixed) 95% CI	Subtotals only
12 Discontinuation: other personal reasons			rate difference (Fixed) 95% CI	Subtotals only

Comparison 06. Cu-Safe 300 vs TCu380A

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Fixed) 95% CI	Subtotals only
04 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Totals not selected
05 Discontinuation: planned pregnancy			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: other personal reasons			rate difference (Fixed) 95% CI	Subtotals only

Comparison 08. NovaT380 vs TCu380S

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Random) 95% CI	Subtotals only
02 Expulsion (full)			rate difference (Fixed) 95% CI	Subtotals only
03 Expulsion (partial)			rate difference (Fixed) 95% CI	Subtotals only
04 Discontinuation: bleeding			rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: pain			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: other personal reasons			rate difference (Fixed) 95% CI	Subtotals only
08 Discontinuation: Infection/PID			rate difference (Fixed) 95% CI	Subtotals only

Comparison 09. TCu220 vs MLCu375

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: total medical			rate difference (Fixed) 95% CI	Subtotals only
04 Discontinuation: total use related			rate difference (Fixed) 95% CI	Subtotals only
05 Continuation			rate difference (Fixed) 95% CI	Subtotals only

Comparison 10. MLCu250 vs MLCu375

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Random) 95% CI	Subtotals only
04 Discontinuation: PID			rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: planned pregnancy			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: other personal reasons			rate difference (Fixed) 95% CI	Subtotals only
08 Continuation			rate difference (Fixed) 95% CI	Subtotals only

Comparison 11. NovaT vs MLCu375

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Random) 95% CI	Subtotals only
02 Expulsion			rate difference (Random) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Random) 95% CI	Subtotals only
04 Discontinuation: PID			rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: planned pregnancy			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: other personal reasons			rate difference (Fixed) 95% CI	Subtotals only
08 Discontinuation: all			rate difference (Fixed) 95% CI	Subtotals only
09 Continuation			rate difference (Fixed) 95% CI	Subtotals only

Comparison 12. MLCu250 vs TCu220

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Fixed) 95% CI	Subtotals only
04 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: medical total			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: non-medical reasons			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: total use related			rate difference (Fixed) 95% CI	Subtotals only
08 Discontinuation: all			rate difference (Fixed) 95% CI	Subtotals only

Comparison 13. NovaT vs TCu220

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Ectopic pregnancy			rate difference (Fixed) 95% CI	Subtotals only
04 Discontinuation: bleeding and pain			rate difference (Random) 95% CI	Subtotals only
05 Discontinuation: intermenstrual bleeding			rate difference (Fixed) 95% CI	Subtotals only
06 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Totals not selected
07 Discontinuation: medical total			rate difference (Fixed) 95% CI	Subtotals only
08 Discontinuation: all			rate difference (Fixed) 95% CI	Subtotals only
09 Continuation			rate difference (Fixed) 95% CI	Subtotals only
10 Discontinuation: non-medical reasons			rate difference (Fixed) 95% CI	Subtotals only

Comparison 14. Cu 7 vs TCu220

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Random) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Perforation			rate difference (Fixed) 95% CI	Subtotals only
04 Discontinuation: bleeding and pain			rate difference (Random) 95% CI	Subtotals only
05 Discontinuation: intermenstrual bleeding			rate difference (Fixed) 95% CI	Subtotals only
06 Ectopic pregnancy			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: infection/PID			rate difference (Fixed) 95% CI	Subtotals only
08 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Totals not selected
09 Discontinuation: non-medical reasons			rate difference (Fixed) 95% CI	Subtotals only
10 Discontinuation: all			rate difference (Fixed) 95% CI	Subtotals only
11 Continuation			rate difference (Fixed) 95% CI	Subtotals only
12 Discontinuation: total use related			rate difference (Fixed) 95% CI	Subtotals only
13 Discontinuation: total medical			rate difference (Fixed) 95% CI	Subtotals only

Comparison 15. TCu220 vs TCu200

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Random) 95% CI	Subtotals only
04 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Totals not selected

05 Discontinuation: all		rate difference (Fixed) 95% CI	Subtotals only
06 Continuation		rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: planned pregnancy		rate difference (Fixed) 95% CI	Subtotals only
08 Discontinuation: other personal reasons		rate difference (Fixed) 95% CI	Subtotals only

Comparison 16. NovaT vs TCu200

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Random) 95% CI	Subtotals only
04 Discontinuation: infection/PID			rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Totals not selected
06 Discontinuation: non-medical reasons			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: planned pregnancy			rate difference (Fixed) 95% CI	Subtotals only
08 Continuation			rate difference (Fixed) 95% CI	Subtotals only

Comparison 17. MLCu 250 vs NovaT

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Random) 95% CI	Subtotals only
04 Discontinuation: infection/PID			rate difference (Fixed) 95% CI	Subtotals only
05 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Totals not selected
06 Continuation			rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: planned pregnancy			rate difference (Fixed) 95% CI	Subtotals only
08 Discontinuation: other personal reasons			rate difference (Fixed) 95% CI	Subtotals only
09 Perforation			rate difference (Fixed) 95% CI	Subtotals only

Comparison 18. MLCu 250 vs Cu 7

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pregnancy			rate difference (Fixed) 95% CI	Subtotals only
02 Expulsion			rate difference (Fixed) 95% CI	Subtotals only
03 Discontinuation: bleeding and pain			rate difference (Random) 95% CI	Subtotals only
05 Discontinuation: other medical reasons			rate difference (Fixed) 95% CI	Totals not selected

06 Discontinuation: non-medical reasons	rate difference (Fixed) 95% CI	Subtotals only
07 Discontinuation: all use related	rate difference (Fixed) 95% CI	Subtotals only

INDEX TERMS

Medical Subject Headings (MeSH)

Contraception [*instrumentation]; *Intrauterine Devices, Copper [adverse effects]; Randomized Controlled Trials

MeSH check words

Female; Humans

COVER SHEET

Title	Copper containing, framed intra-uterine devices for contraception
Authors	Kulier R, O'Brien PA, Helmerhorst FM, Usher-Patel M, D'Arcangues C
Contribution of author(s)	RK wrote the review protocol and the review results. POB conducted the analysis and co-wrote the review. FH and RK did the data extraction. All authors critically reviewed and made intellectual contributions to the review text.
Issue protocol first published	2005/3
Review first published	2006/3
Date of most recent amendment	22 August 2007
Date of most recent SUBSTANTIVE amendment	20 August 2007
What's New	We added one new trial (Haugen 2007). We included unpublished data from the Bahamondes (1999) trial. We made a number of textual changes.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	14 August 2007
Date authors' conclusions section amended	Information not supplied by author
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GRAPHS AND OTHER TABLES

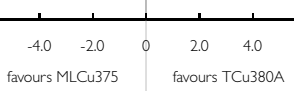
Analysis 01.01. Comparison 01 MLCu375 vs TCu380A, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 01 Pregnancy

Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
Cole 1985C	0.50 (0.45)		28.1	0.50 [-0.38, 1.38]
Sastrawinata 1991	1.00 (0.45)		28.1	1.00 [0.12, 1.88]
WHO 1994	0.40 (0.36)		43.9	0.40 [-0.31, 1.11]
Subtotal (95% CI)			100.0	0.60 [0.13, 1.06]
Test for heterogeneity chi-square=1.15 df=2 p=0.56 I^2 =0.0%				
Test for overall effect z=2.50 p=0.01				
02 2 years				
Sastrawinata 1991	1.50 (0.72)		32.5	1.50 [0.09, 2.91]
WHO 1994	0.90 (0.50)		67.5	0.90 [-0.08, 1.88]
Subtotal (95% CI)			100.0	1.10 [0.29, 1.90]
Test for heterogeneity chi-square=0.47 df=1 p=0.49 I^2 =0.0%				
Test for overall effect z=2.67 p=0.008				
03 3 years				
WHO 1994	1.30 (0.50)		100.0	1.30 [0.32, 2.28]
Subtotal (95% CI)			100.0	1.30 [0.32, 2.28]
Test for heterogeneity: not applicable				
Test for overall effect z=2.60 p=0.009				
04 4 years				
WHO 1994	1.70 (0.64)		100.0	1.70 [0.45, 2.95]
Subtotal (95% CI)			100.0	1.70 [0.45, 2.95]
Test for heterogeneity: not applicable				
Test for overall effect z=2.66 p=0.008				
05 6 years				
WHO 1994	1.52 (0.74)		100.0	1.52 [0.07, 2.97]
Subtotal (95% CI)			100.0	1.52 [0.07, 2.97]
Test for heterogeneity: not applicable				



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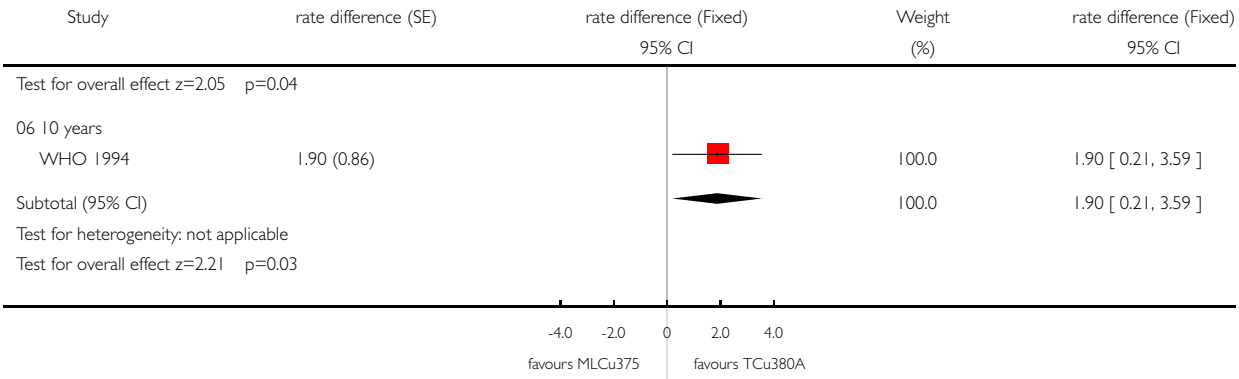
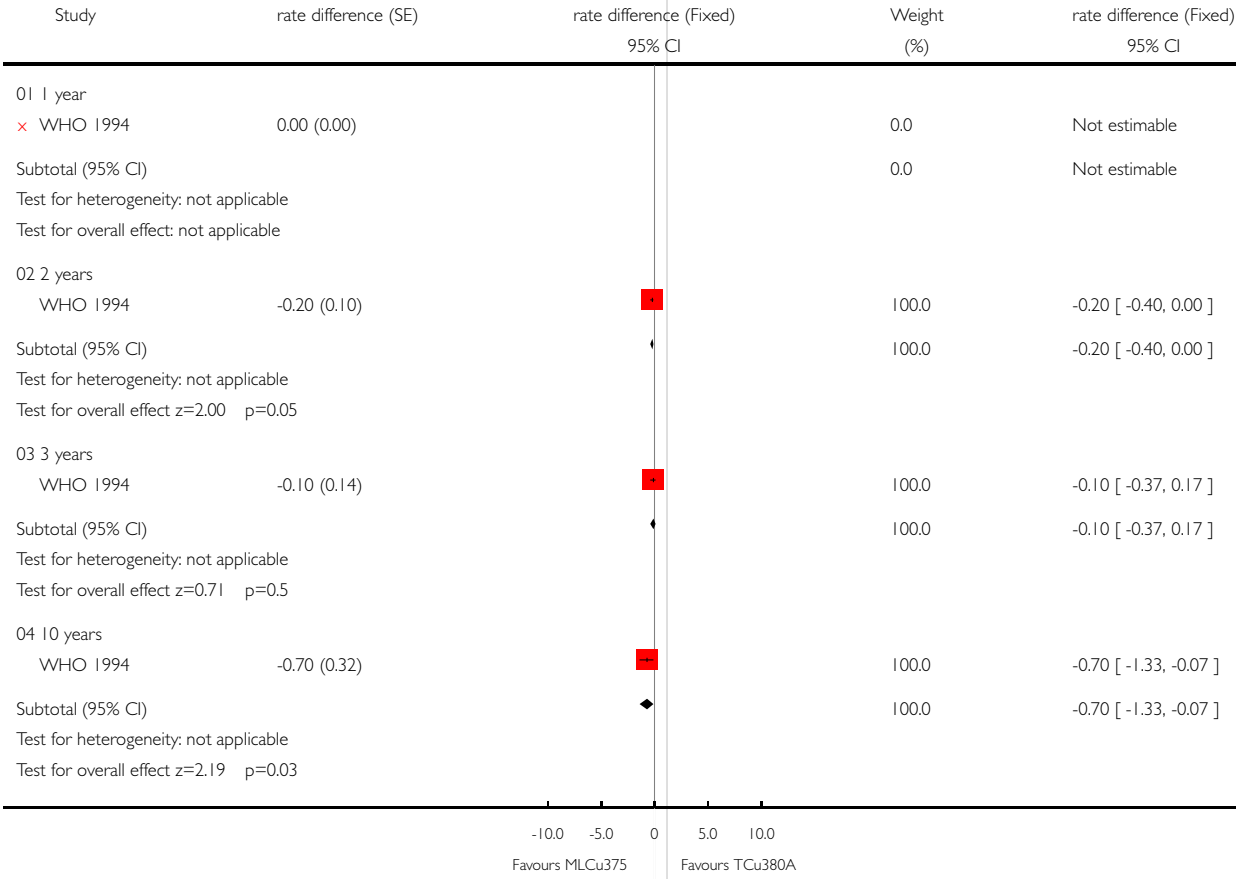


Analysis 01.02. Comparison 01 MLCu375 vs TCu380A, Outcome 02 Ectopic pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 02 Ectopic pregnancy

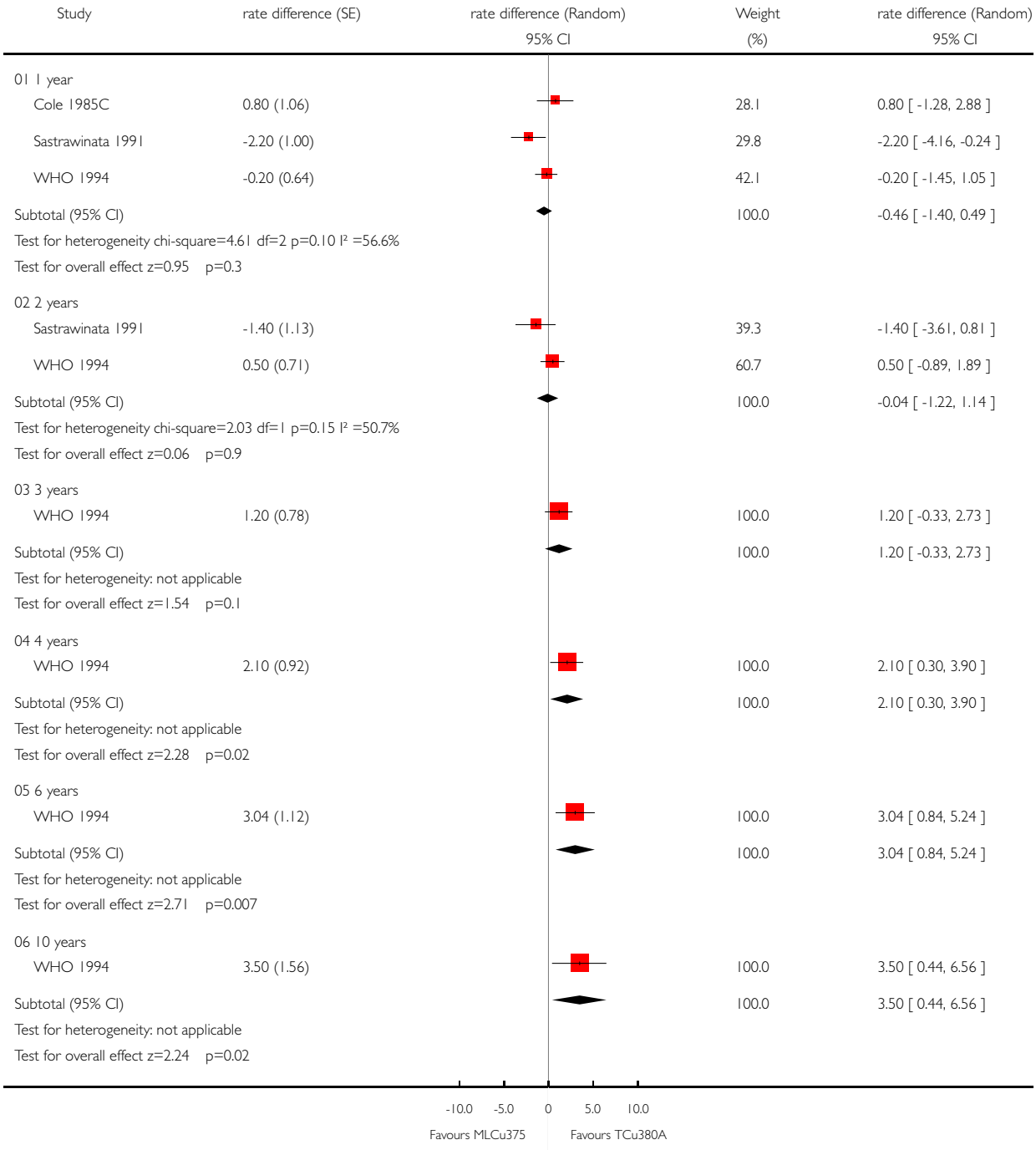


Analysis 01.03. Comparison 01 MLCu375 vs TCu380A, Outcome 03 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 03 Expulsion

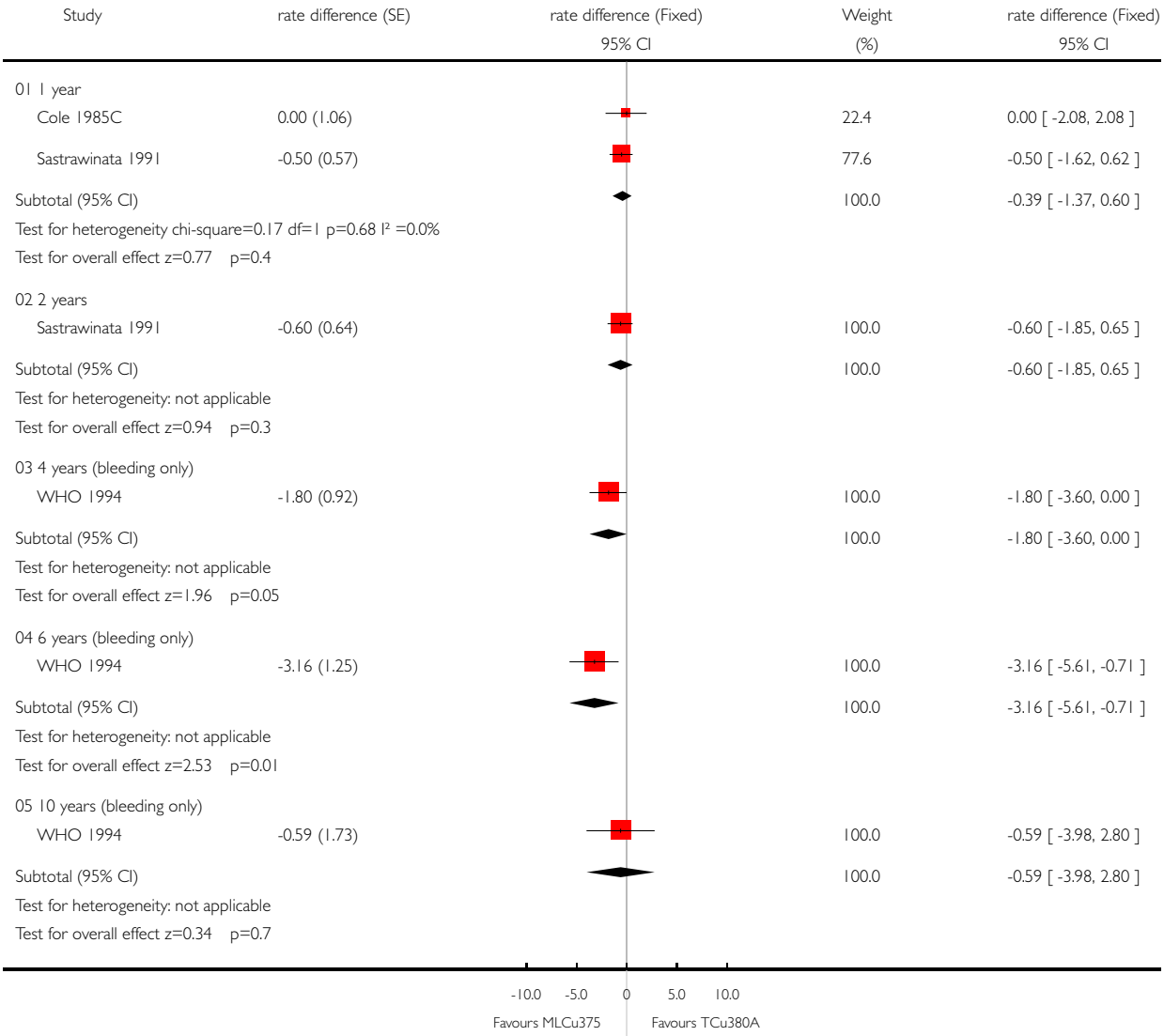


Analysis 01.04. Comparison 01 MLCu375 vs TCu380A, Outcome 04 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 04 Discontinuation: bleeding and pain

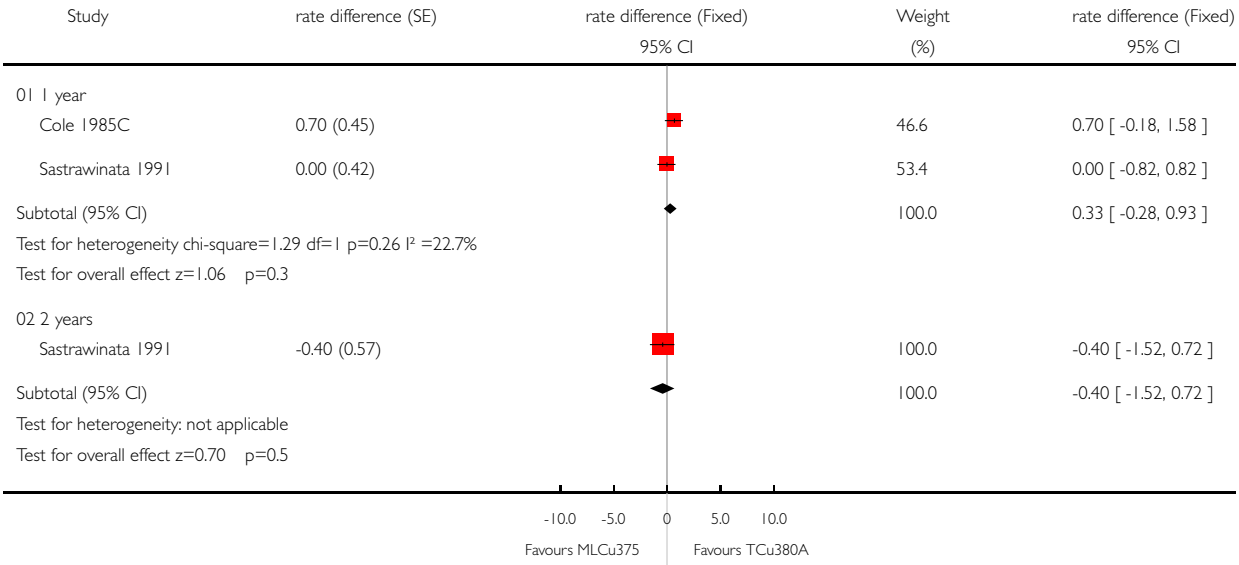


Analysis 01.05. Comparison 01 MLCu375 vs TCu380A, Outcome 05 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 05 Discontinuation: other medical reasons

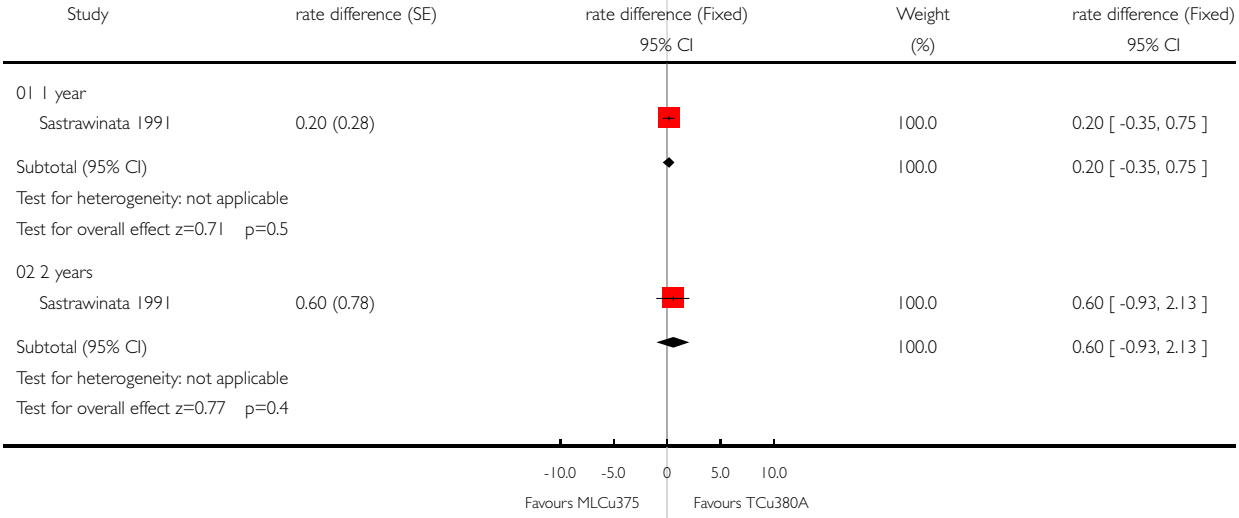


Analysis 01.06. Comparison 01 MLCu375 vs TCu380A, Outcome 06 Discontinuation: planned pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 06 Discontinuation: planned pregnancy

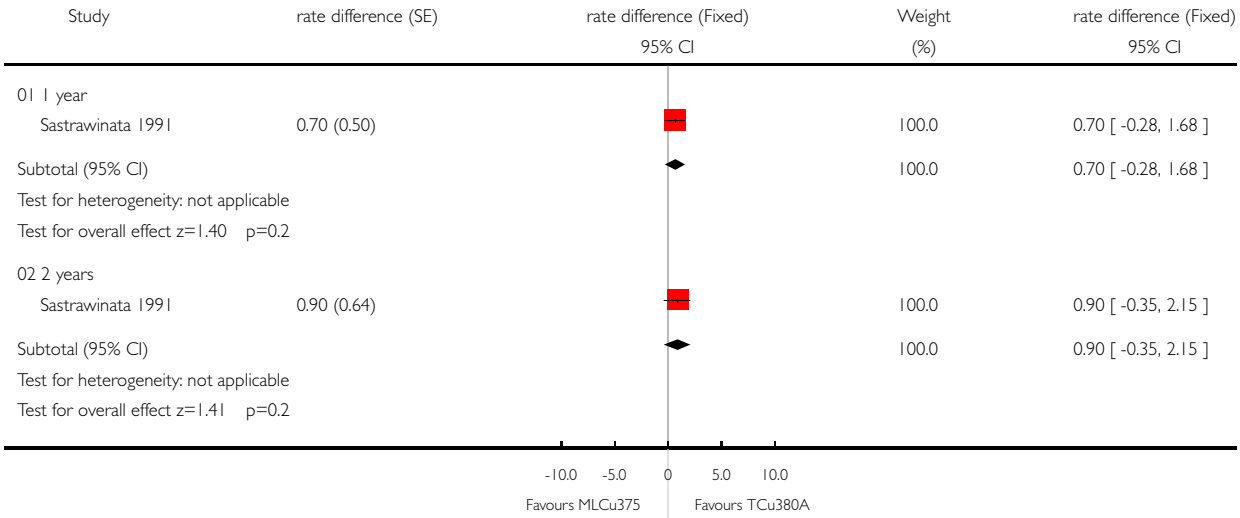


Analysis 01.07. Comparison 01 MLCu375 vs TCu380A, Outcome 07 Discontinuation: other personal reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 07 Discontinuation: other personal reasons

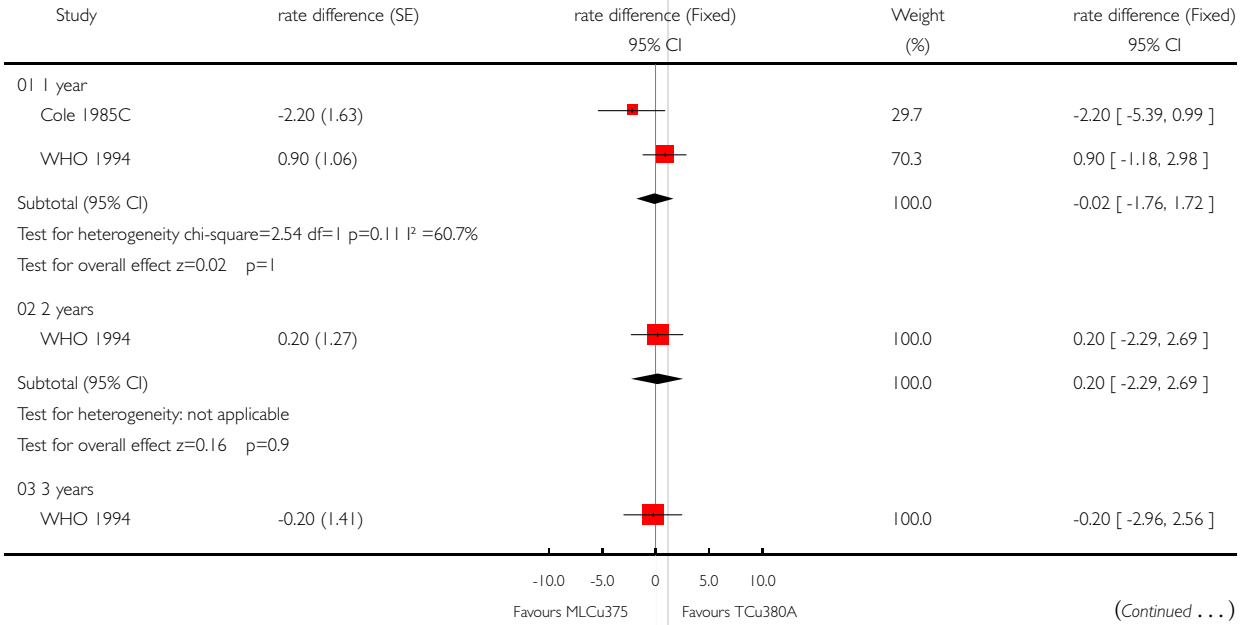


Analysis 01.08. Comparison 01 MLCu375 vs TCu380A, Outcome 08 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 08 Continuation



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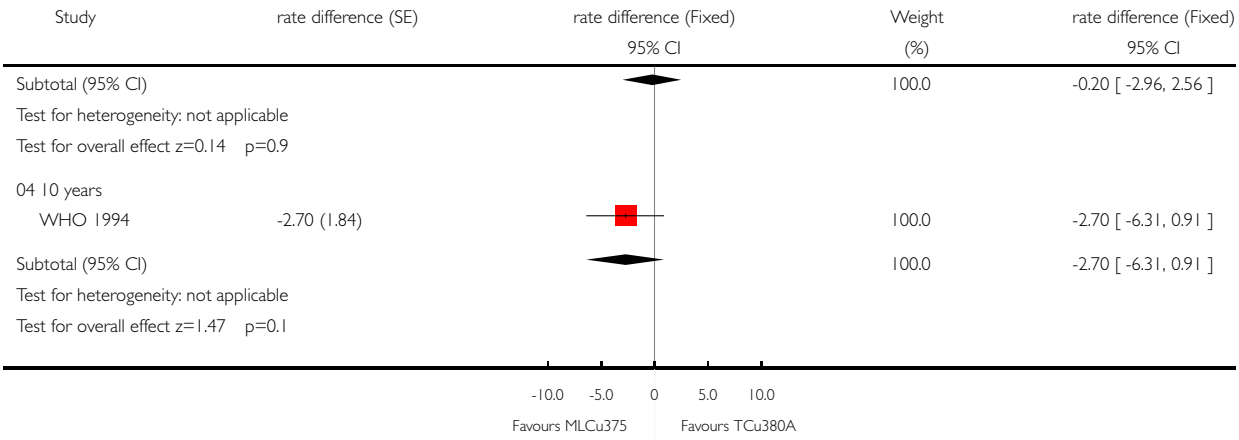
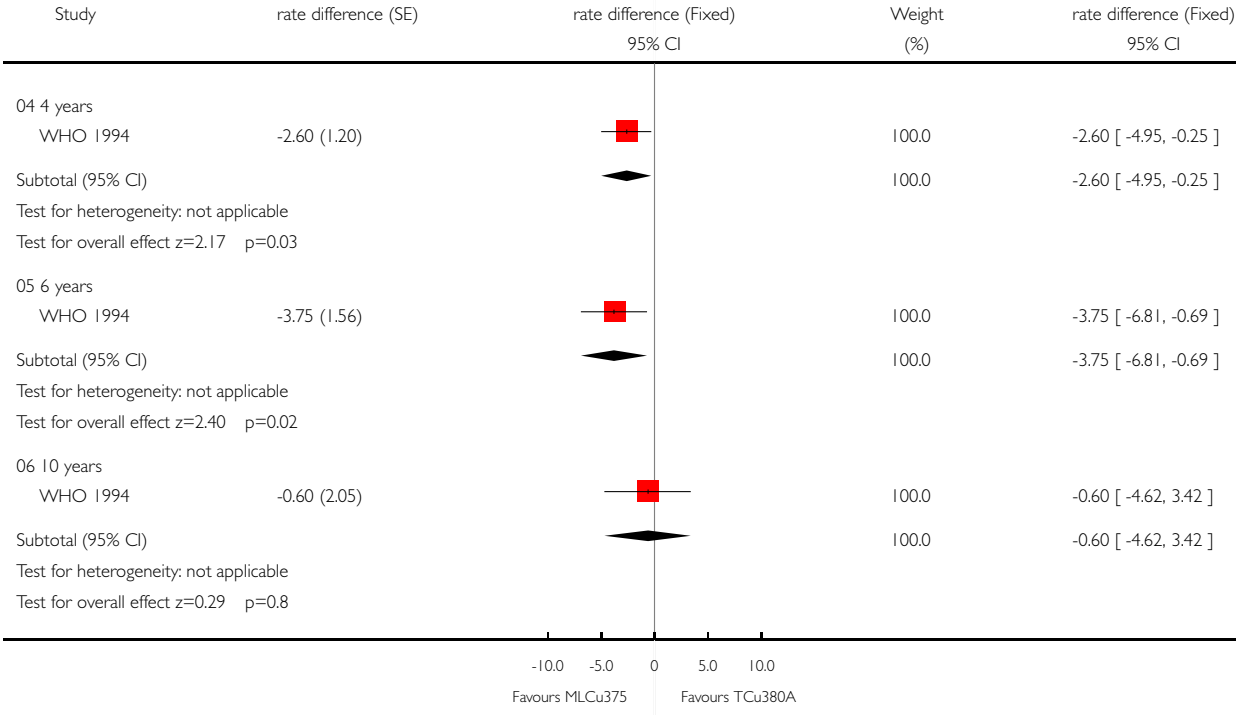


Analysis 01.09. Comparison 01 MLCu375 vs TCu380A, Outcome 09 Discontinuation: total medical

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 09 Discontinuation: total medical

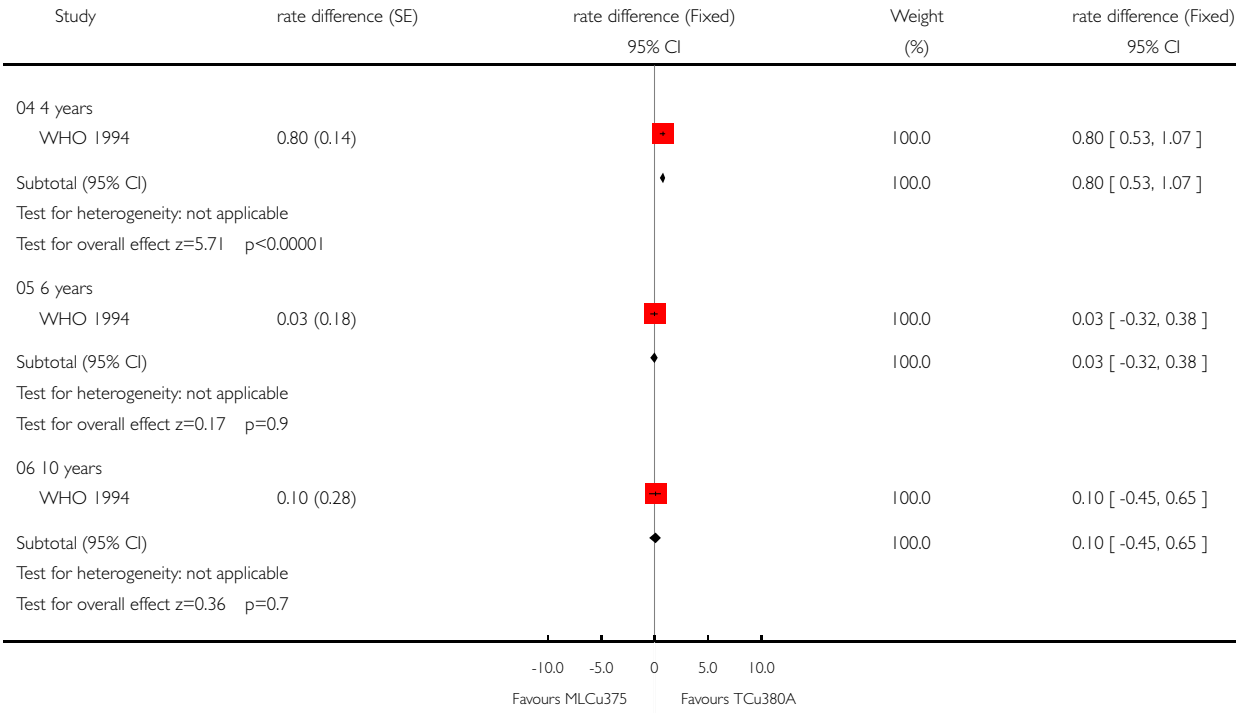


Analysis 01.10. Comparison 01 MLCu375 vs TCu380A, Outcome 10 Discontinuation: infection/PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 01 MLCu375 vs TCu380A

Outcome: 10 Discontinuation: infection/PID

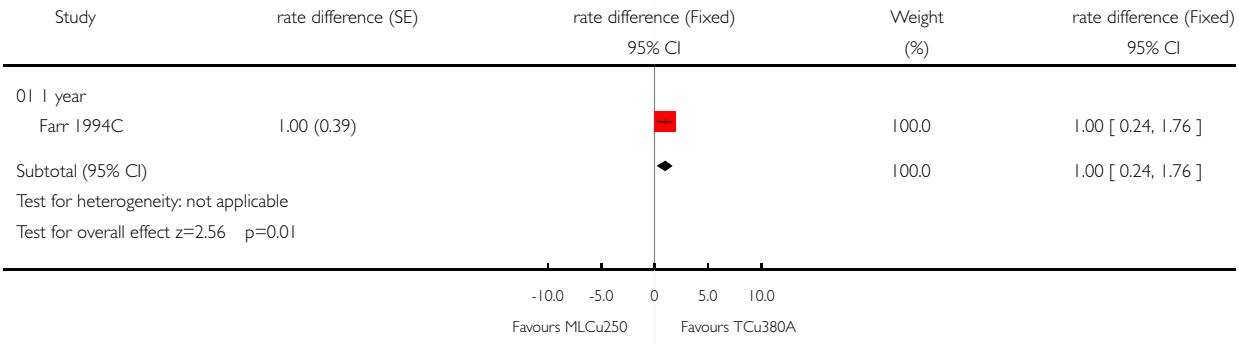


Analysis 02.01. Comparison 02 MLCu250 vsTCu380A, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 02 MLCu250 vsTCu380A

Outcome: 01 Pregnancy

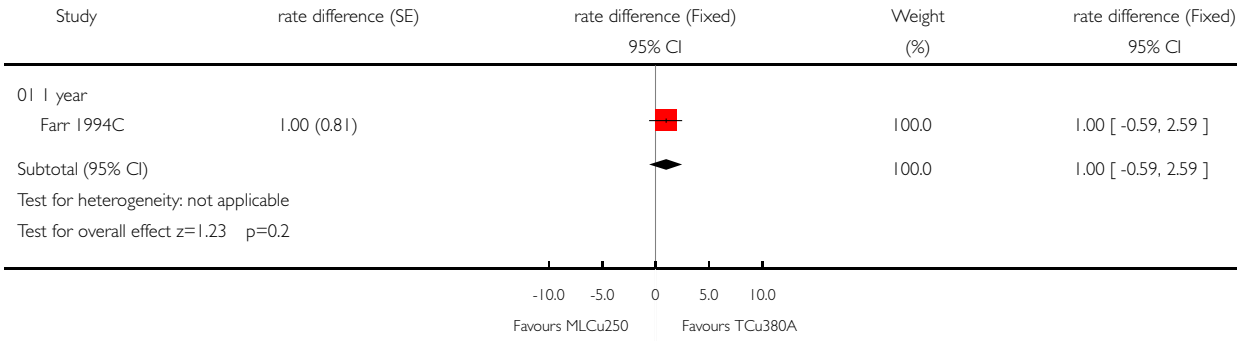


Analysis 02.02. Comparison 02 MLCu250 vsTCu380A, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 02 MLCu250 vsTCu380A

Outcome: 02 Expulsion

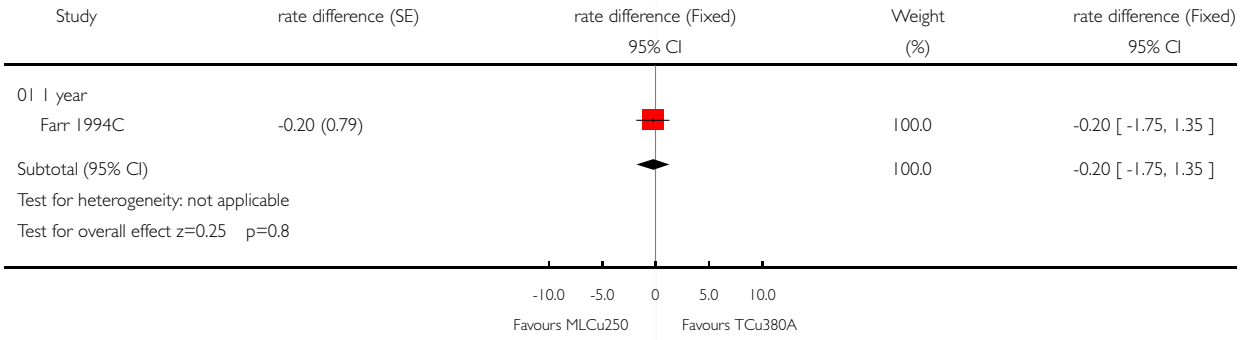


Analysis 02.03. Comparison 02 MLCu250 vsTCu380A, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 02 MLCu250 vsTCu380A

Outcome: 03 Discontinuation: bleeding and pain

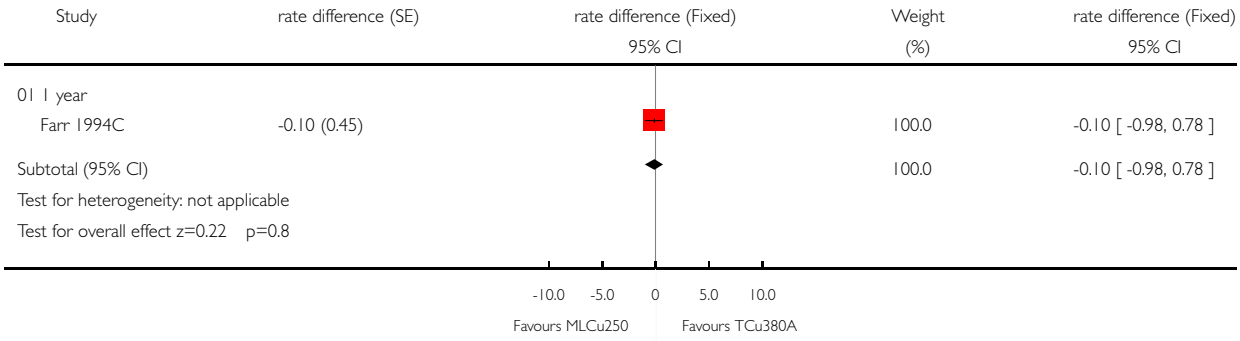


Analysis 02.04. Comparison 02 MLCu250 vsTCu380A, Outcome 04 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 02 MLCu250 vsTCu380A

Outcome: 04 Discontinuation: other medical reasons

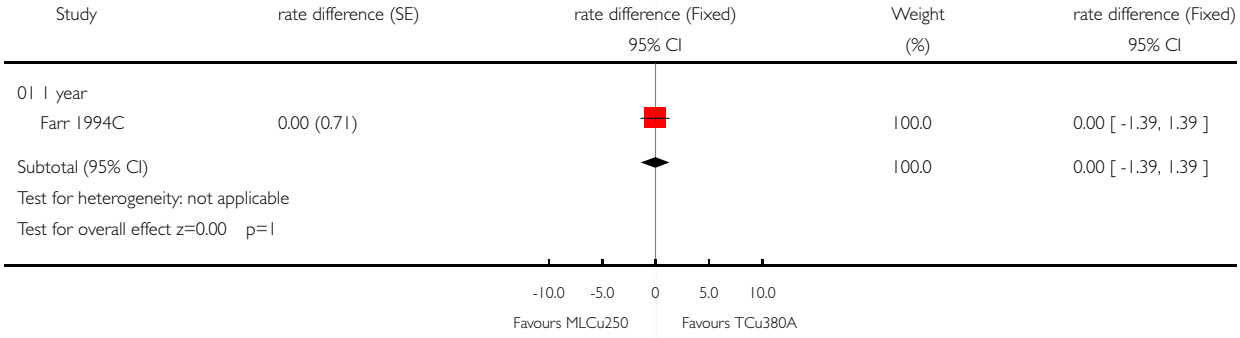


Analysis 02.05. Comparison 02 MLCu250 vsTCu380A, Outcome 05 Discontinuation: non-medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 02 MLCu250 vsTCu380A

Outcome: 05 Discontinuation: non-medical reasons

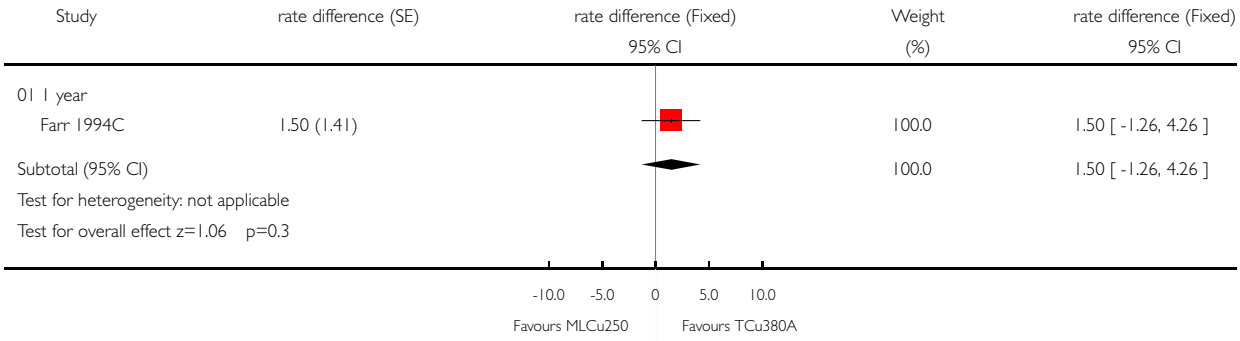


Analysis 02.06. Comparison 02 MLCu250 vsTCu380A, Outcome 06 Discontinuation: all

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 02 MLCu250 vsTCu380A

Outcome: 06 Discontinuation: all

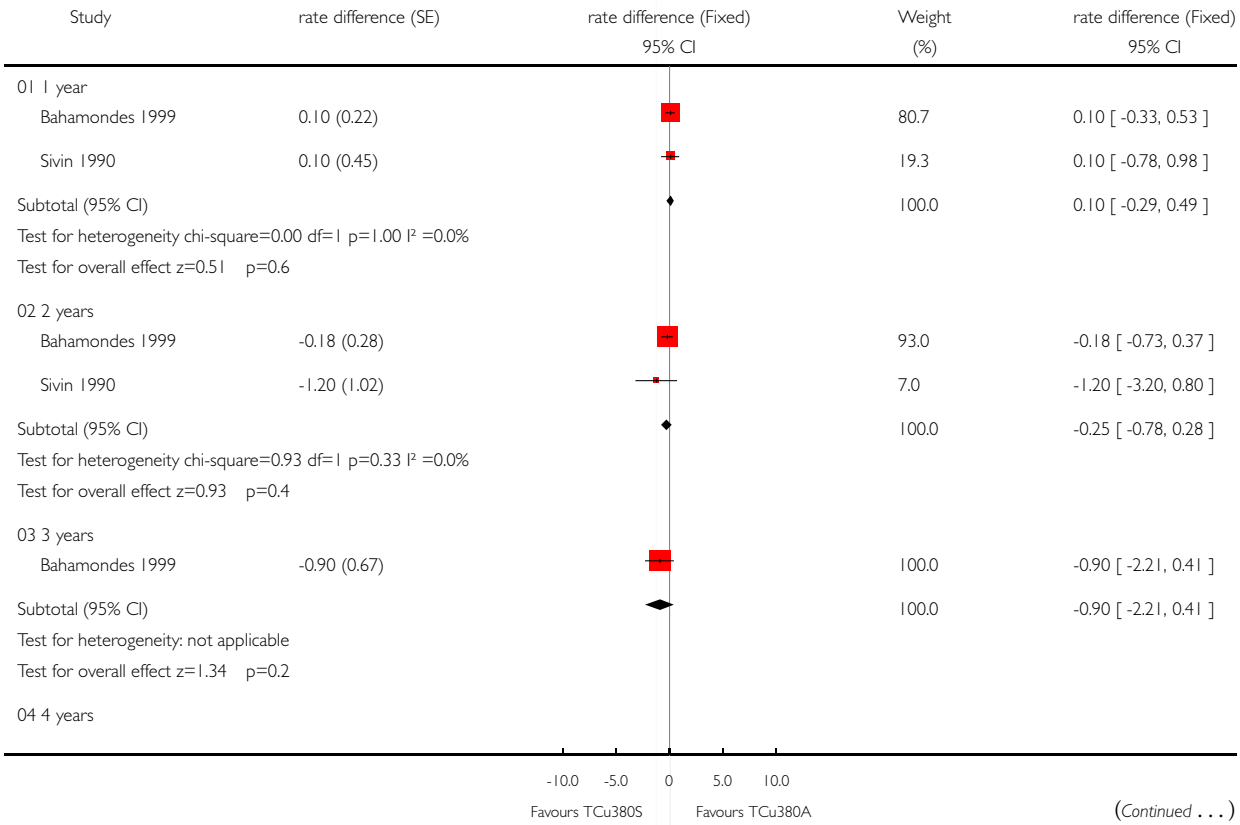


Analysis 03.01. Comparison 03 TCu380S vs TCu380A, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 03 TCu380S vs TCu380A

Outcome: 01 Pregnancy



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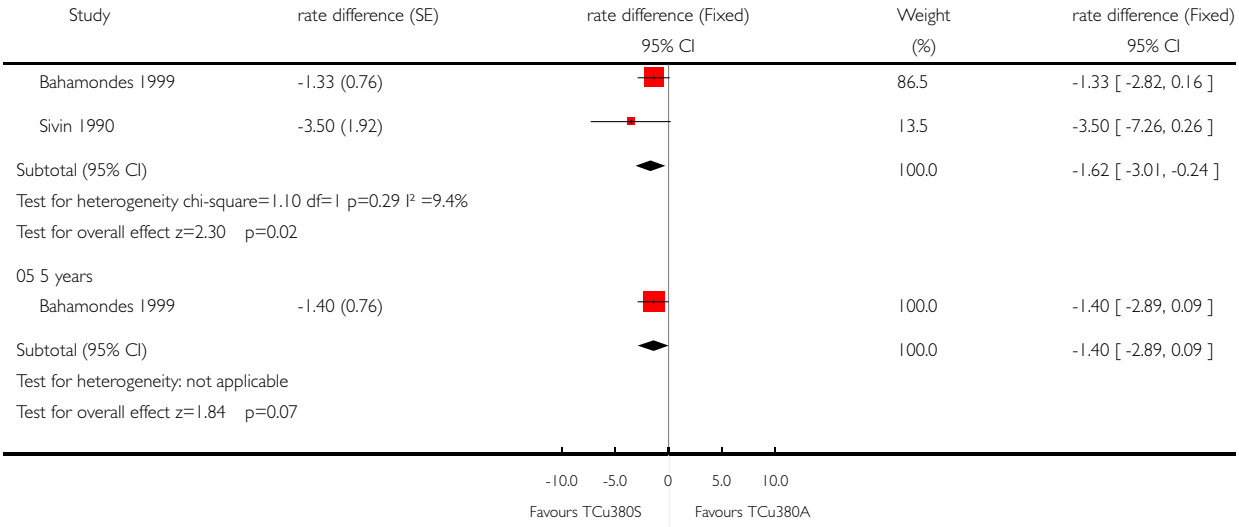
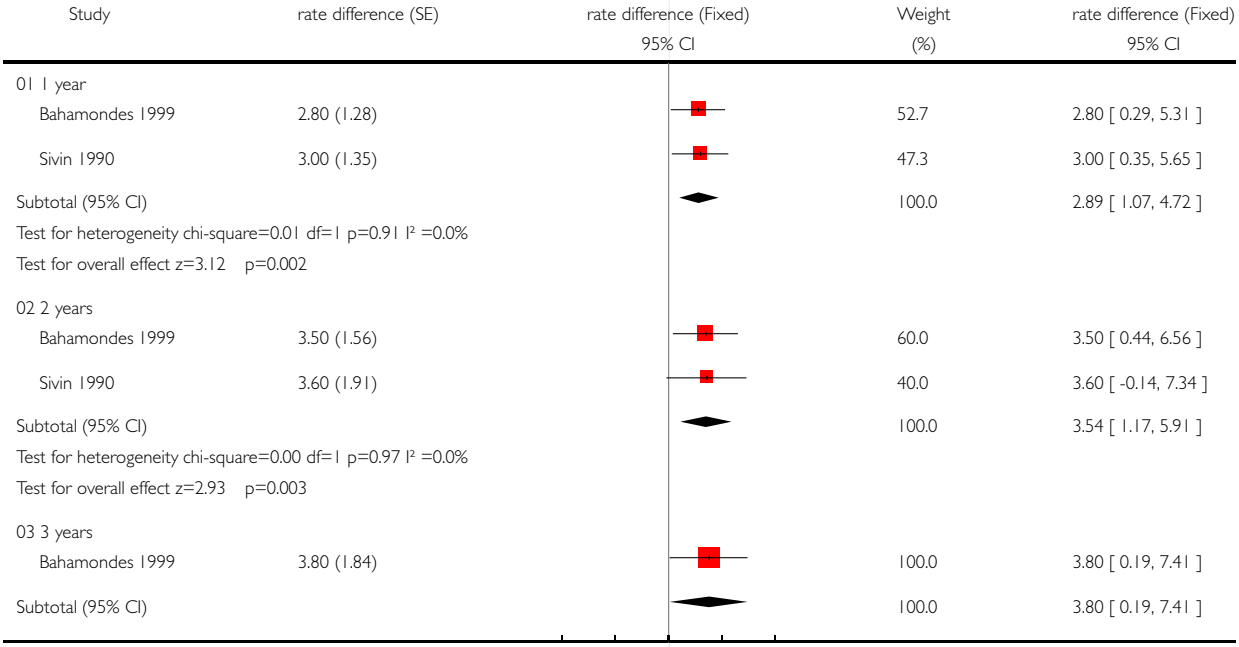


Analysis 03.02. Comparison 03 TCu380S vs TCu380A, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 03 TCu380S vs TCu380A

Outcome: 02 Expulsion



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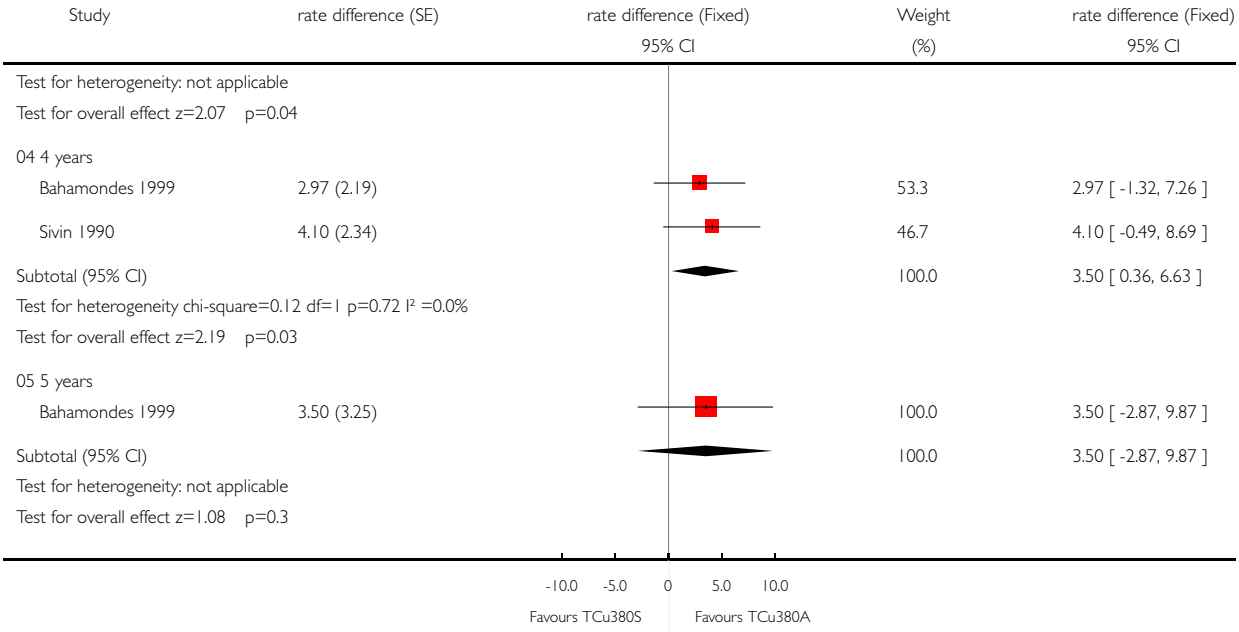
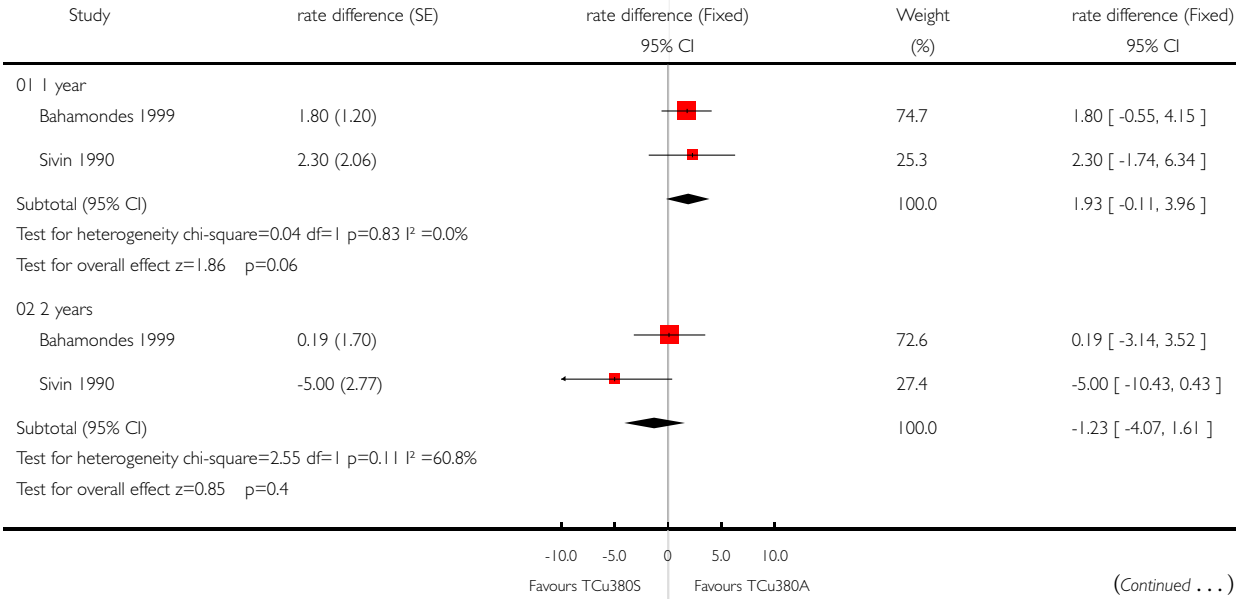


Analysis 03.03. Comparison 03 TCu380S vs TCu380A, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 03 TCu380S vs TCu380A

Outcome: 03 Discontinuation: bleeding and pain



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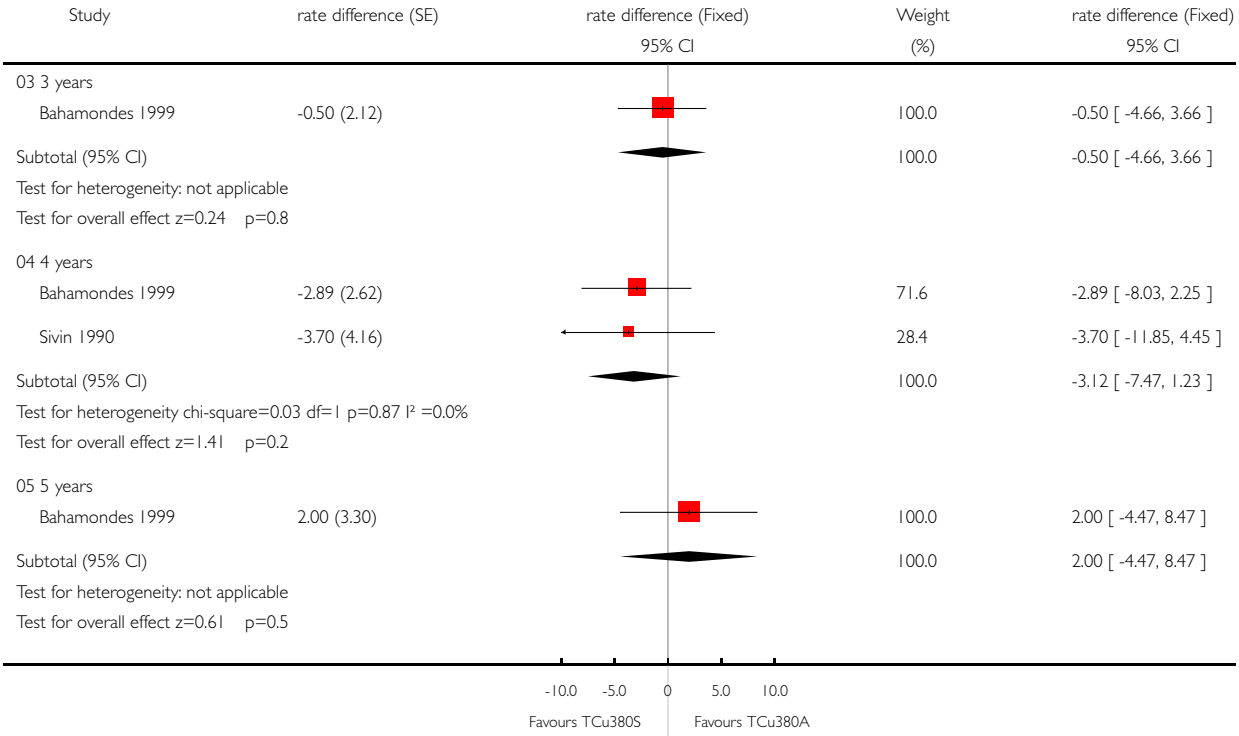
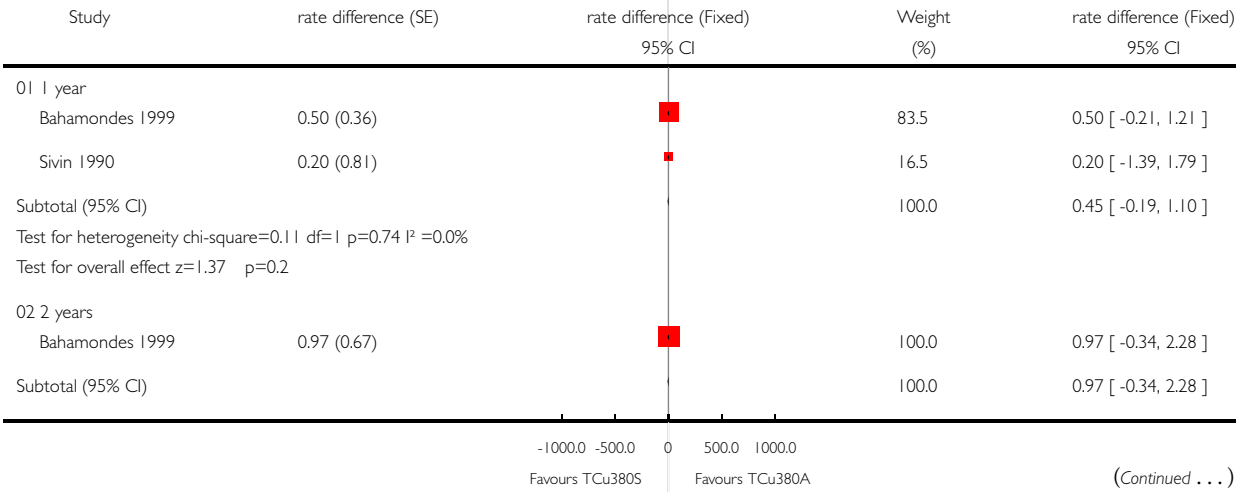


Analysis 03.04. Comparison 03 TCu380S vs TCu380A, Outcome 04 Discontinuation: PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 03 TCu380S vs TCu380A

Outcome: 04 Discontinuation: PID



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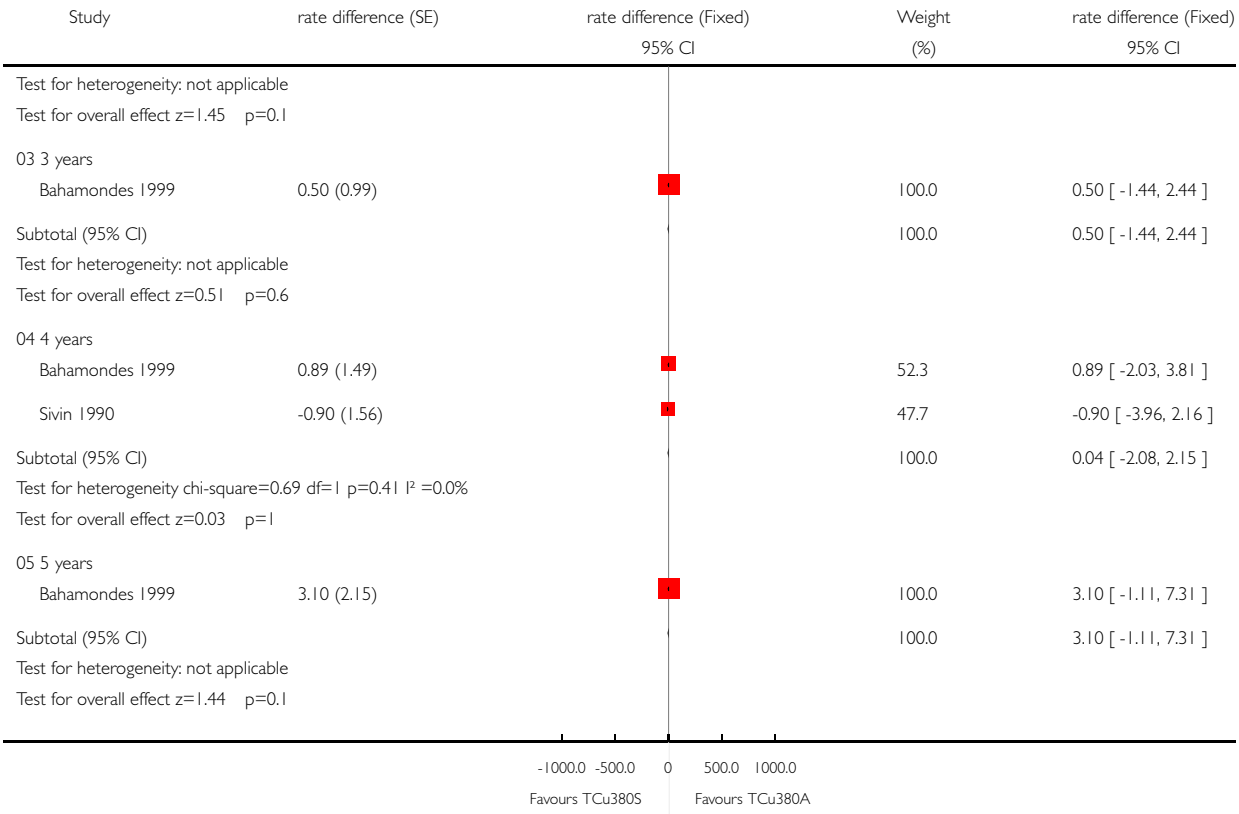
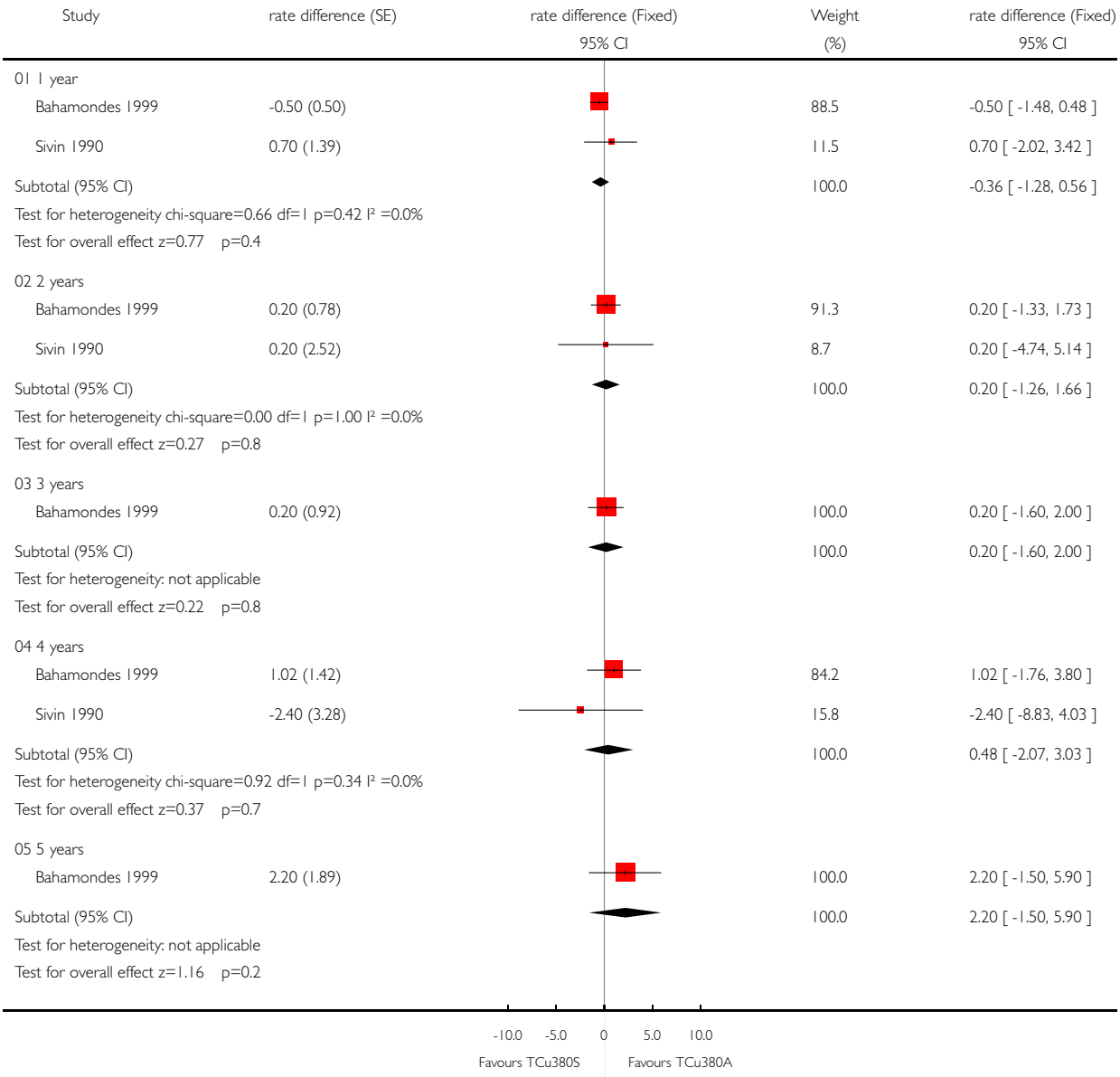


Analysis 03.05. Comparison 03 TCu380S vs TCu380A, Outcome 05 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 03 TCu380S vs TCu380A

Outcome: 05 Discontinuation: other medical reasons

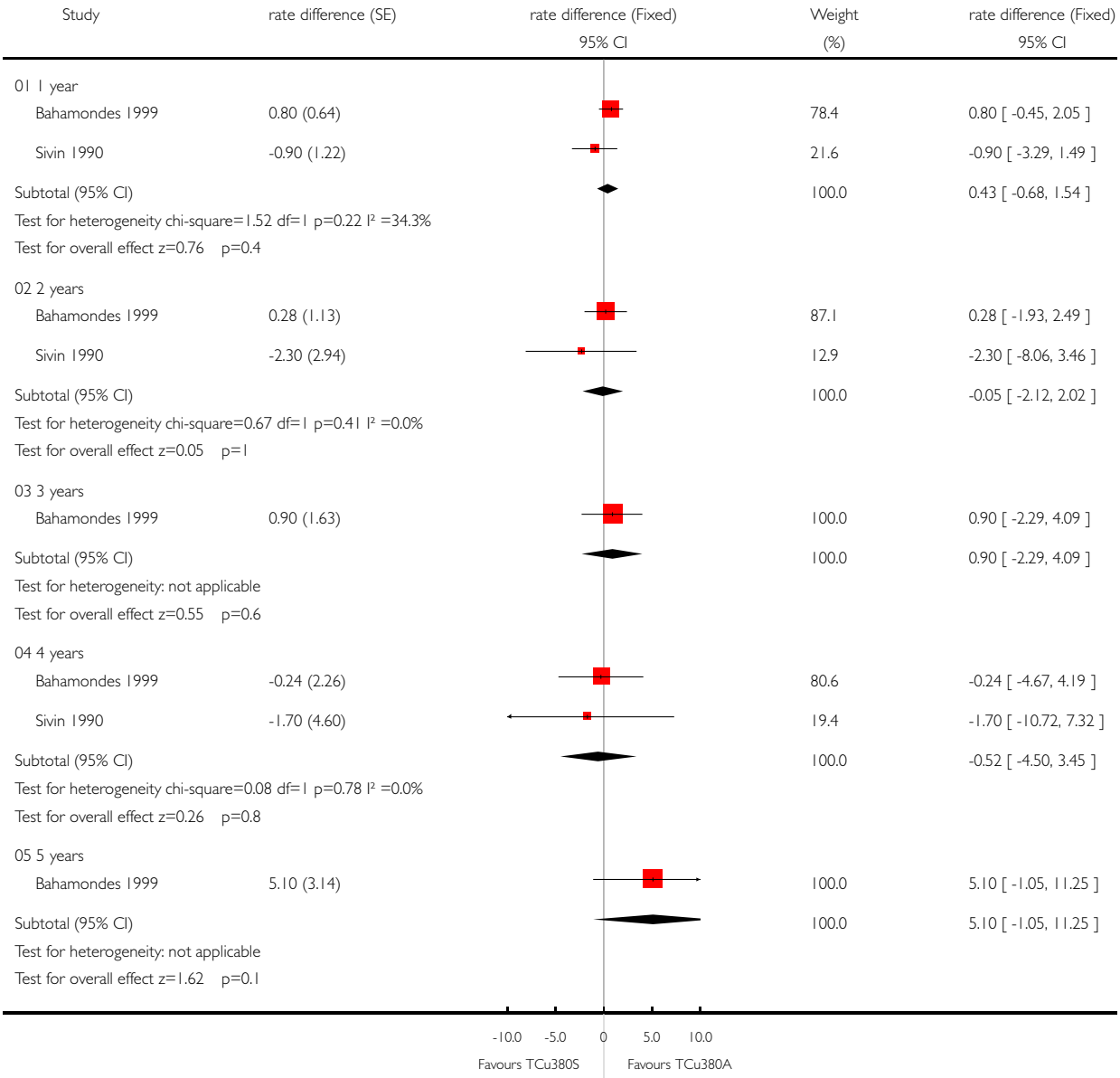


Analysis 03.06. Comparison 03 TCu380S vs TCu380A, Outcome 06 Discontinuation: planned pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 03 TCu380S vs TCu380A

Outcome: 06 Discontinuation: planned pregnancy

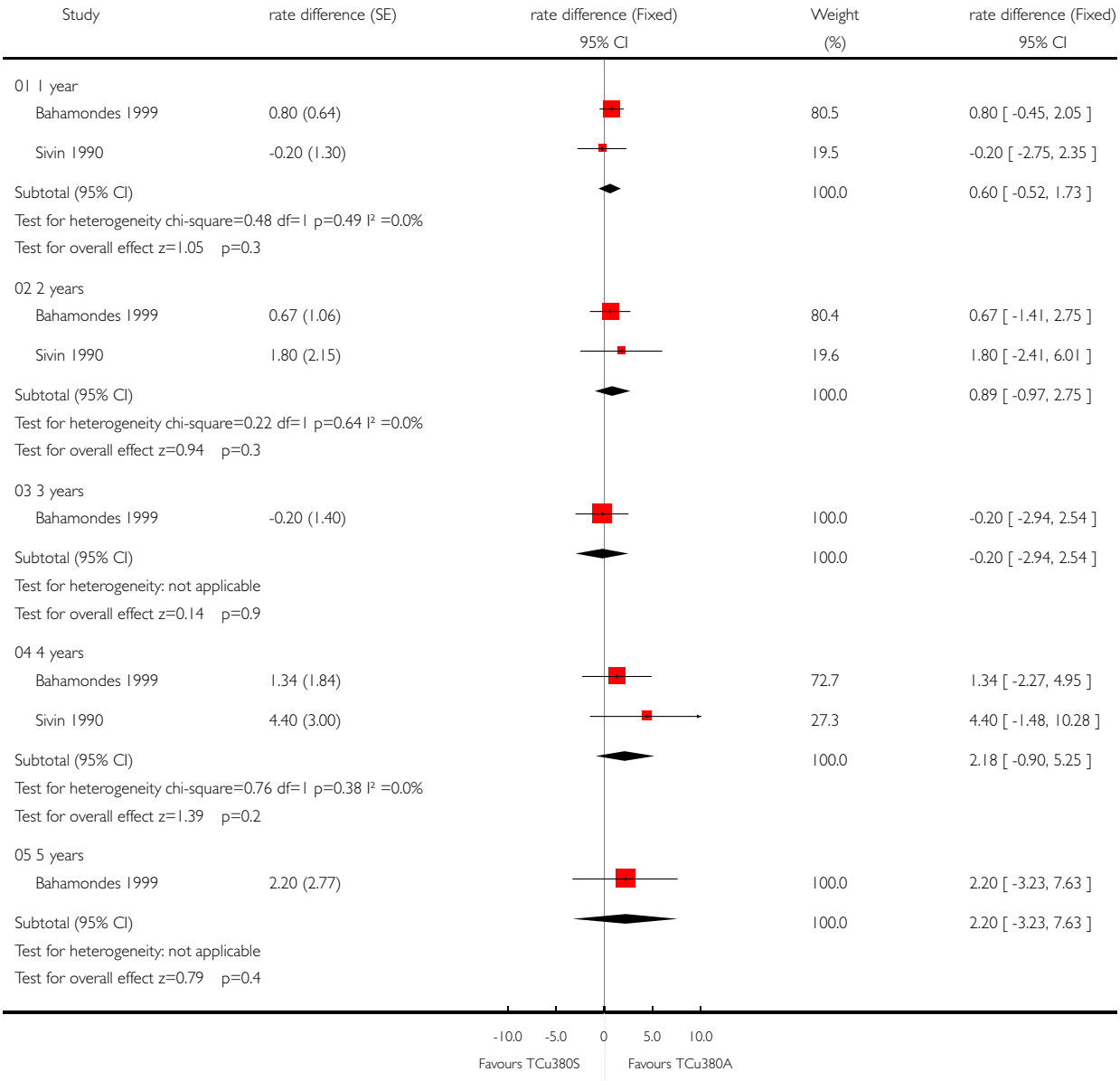


Analysis 03.07. Comparison 03 TCu380S vs TCu380A, Outcome 07 Discontinuation: other personal reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 03 TCu380S vs TCu380A

Outcome: 07 Discontinuation: other personal reasons

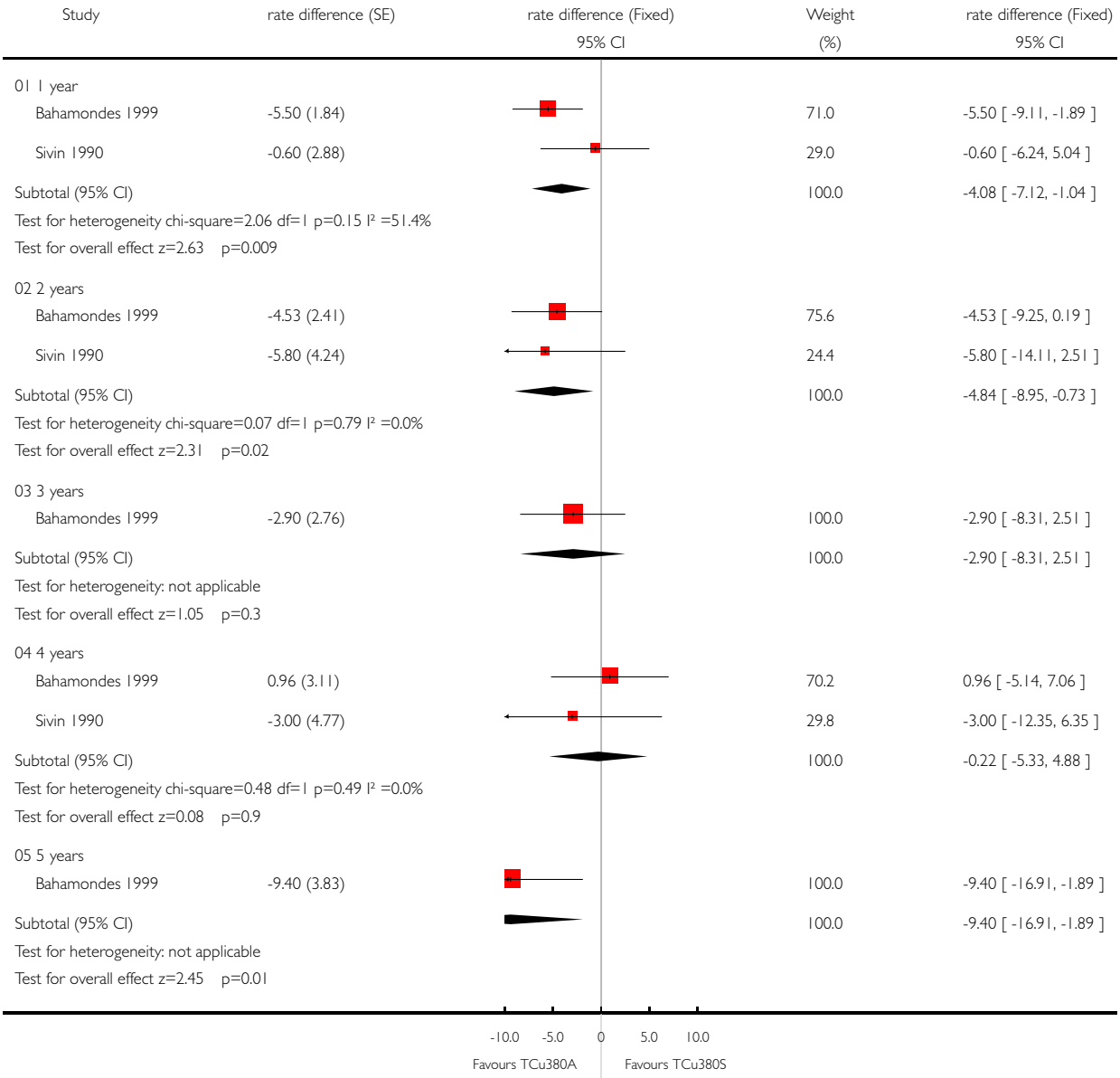


Analysis 03.08. Comparison 03 TCu380S vs TCu380A, Outcome 08 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 03 TCu380S vs TCu380A

Outcome: 08 Continuation

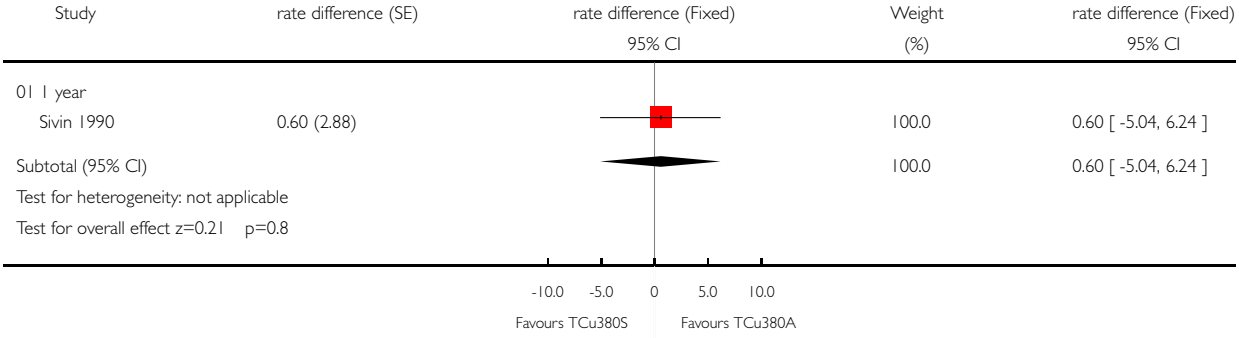


Analysis 03.09. Comparison 03 TCu380S vs TCu380A, Outcome 09 Discontinuation: all

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 03 TCu380S vs TCu380A

Outcome: 09 Discontinuation: all

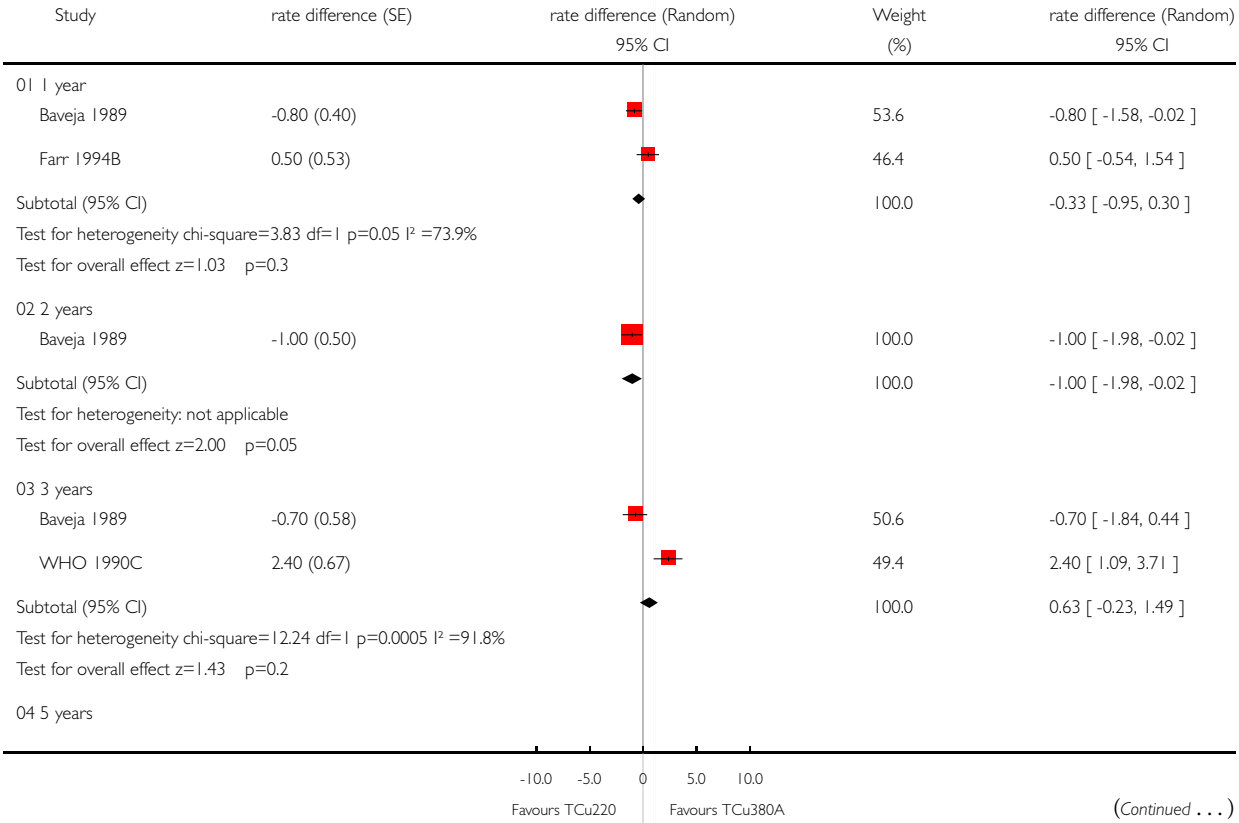


Analysis 04.01. Comparison 04 Cu220 vs TCu380A, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 04 Cu220 vs TCu380A

Outcome: 01 Pregnancy



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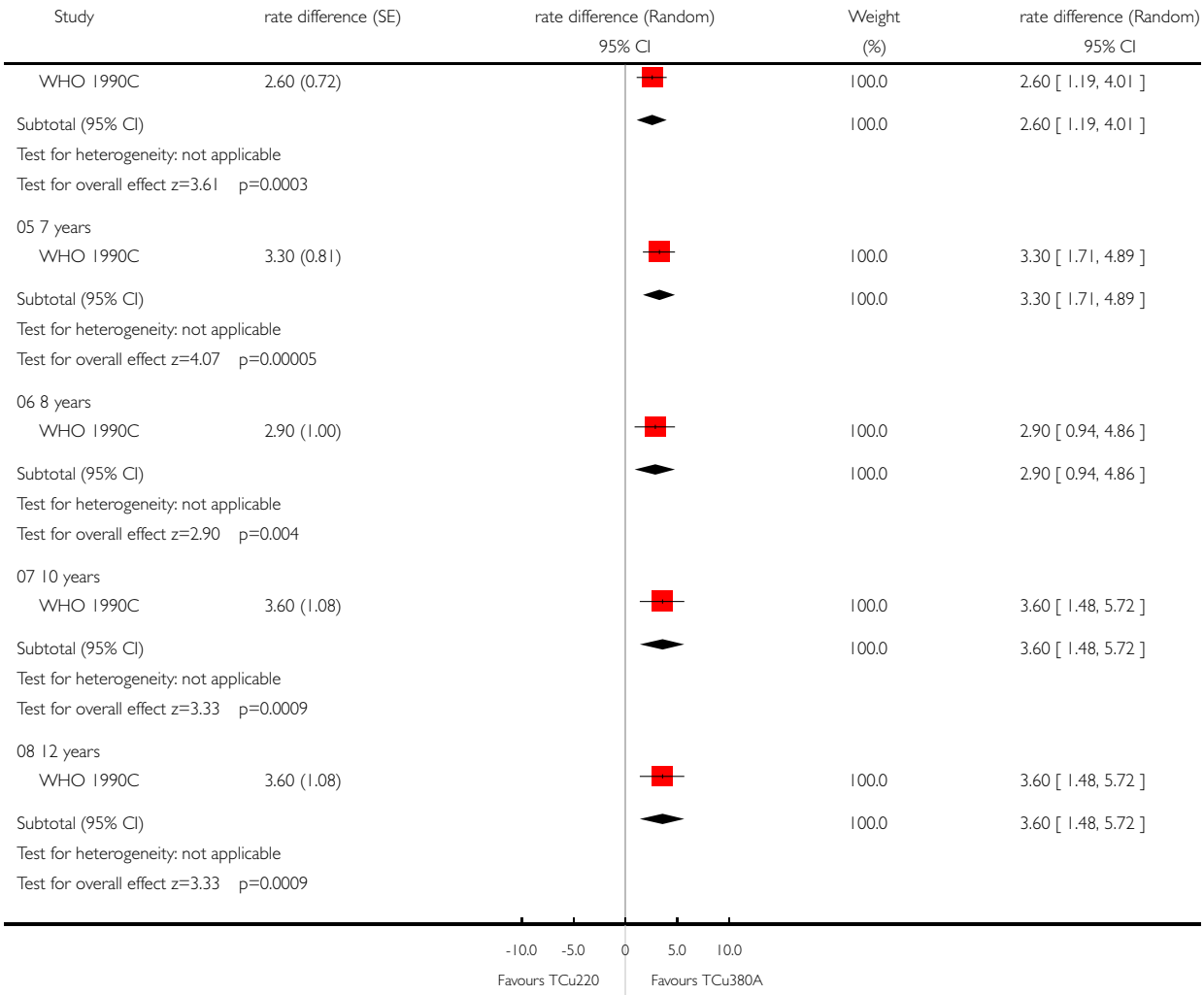
(... *Continued*)

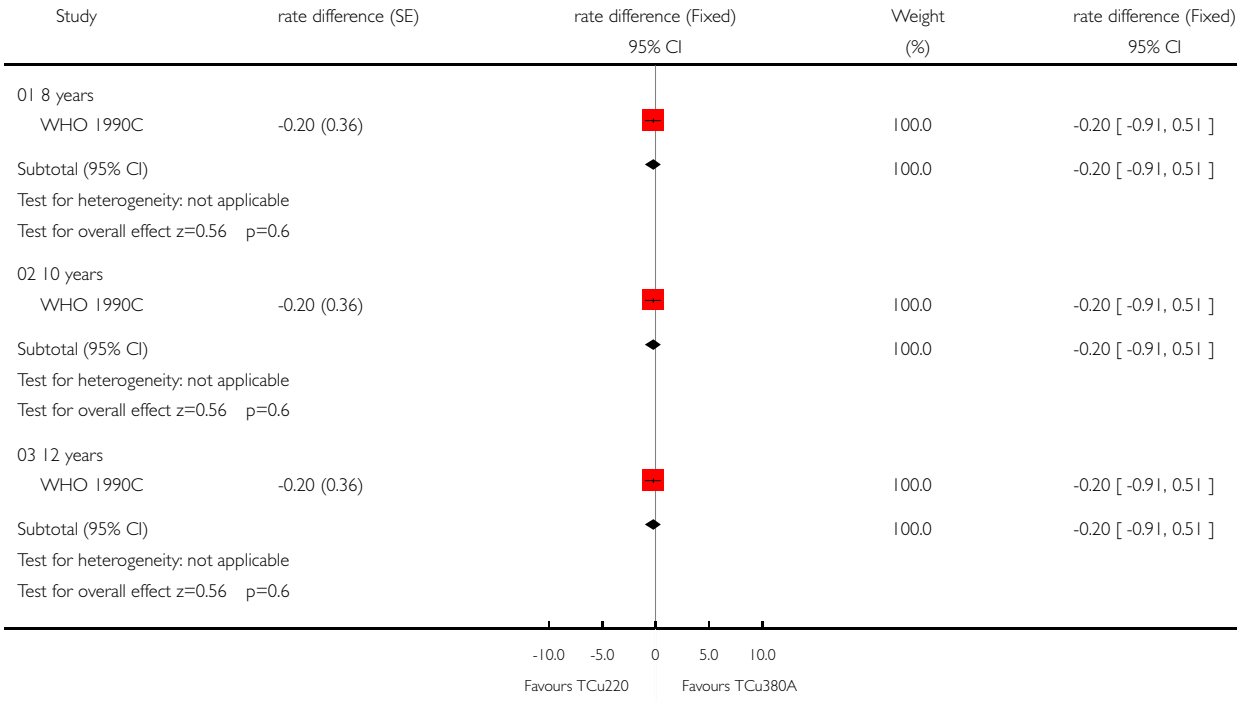


Analysis 04.02. Comparison 04 Cu220 vs TCu380A, Outcome 02 Ectopic pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 04 Cu220 vs TCu380A

Outcome: 02 Ectopic pregnancy

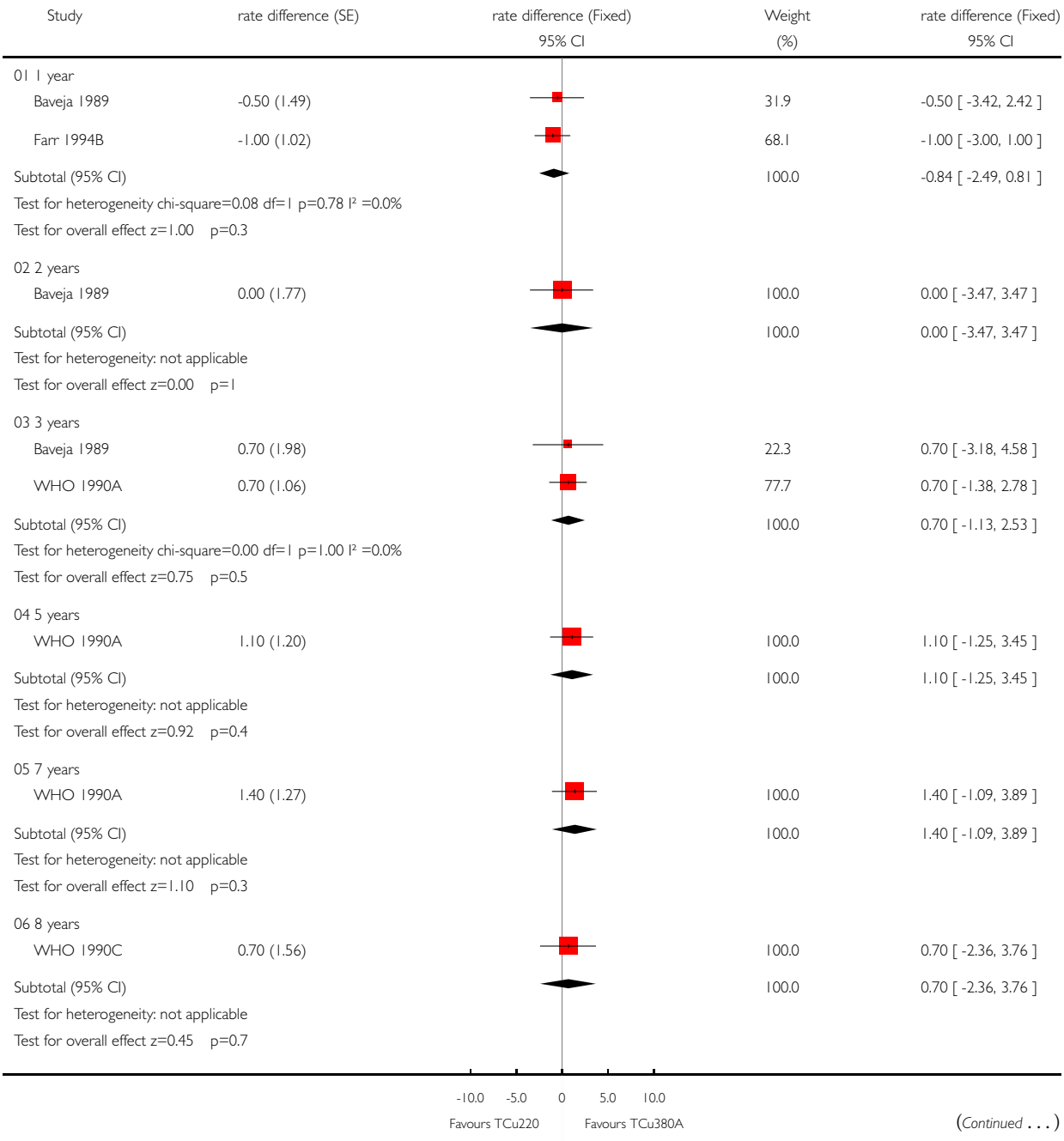


Analysis 04.03. Comparison 04 Cu220 vs TCu380A, Outcome 03 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

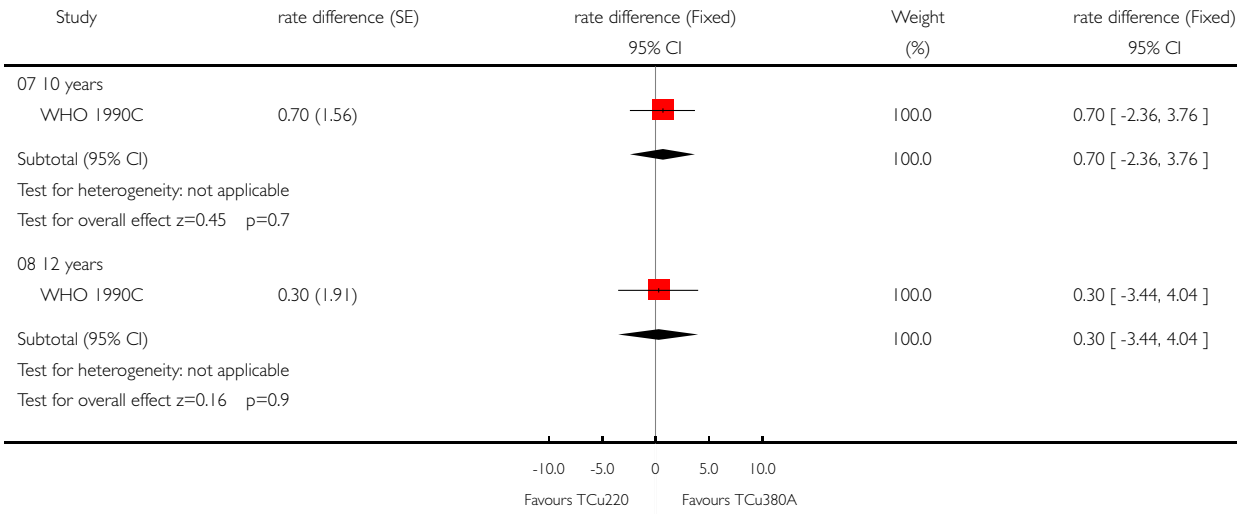
Comparison: 04 Cu220 vs TCu380A

Outcome: 03 Expulsion



(*Continued . . .*)

(. . . *Continued*)

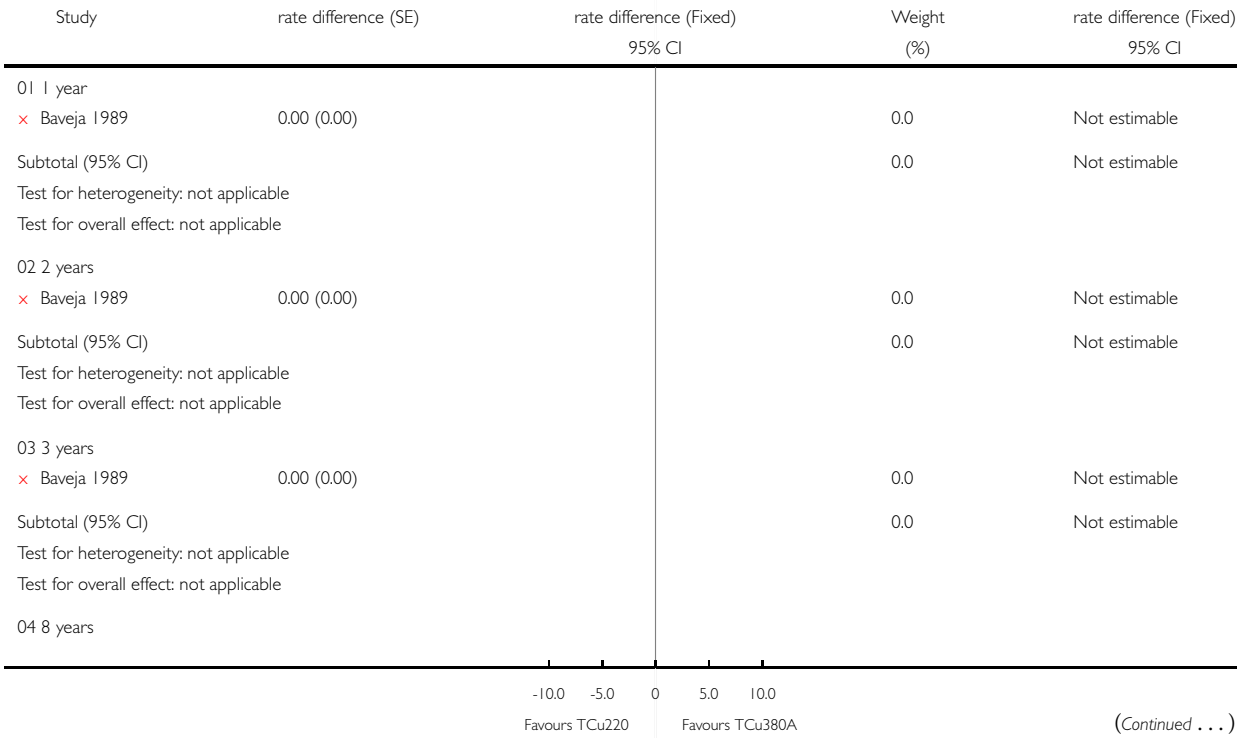


Analysis 04.04. Comparison 04 Cu220 vs TCu380A, Outcome 04 Perforation

Review: Copper containing, framed intra-uterine devices for contraception

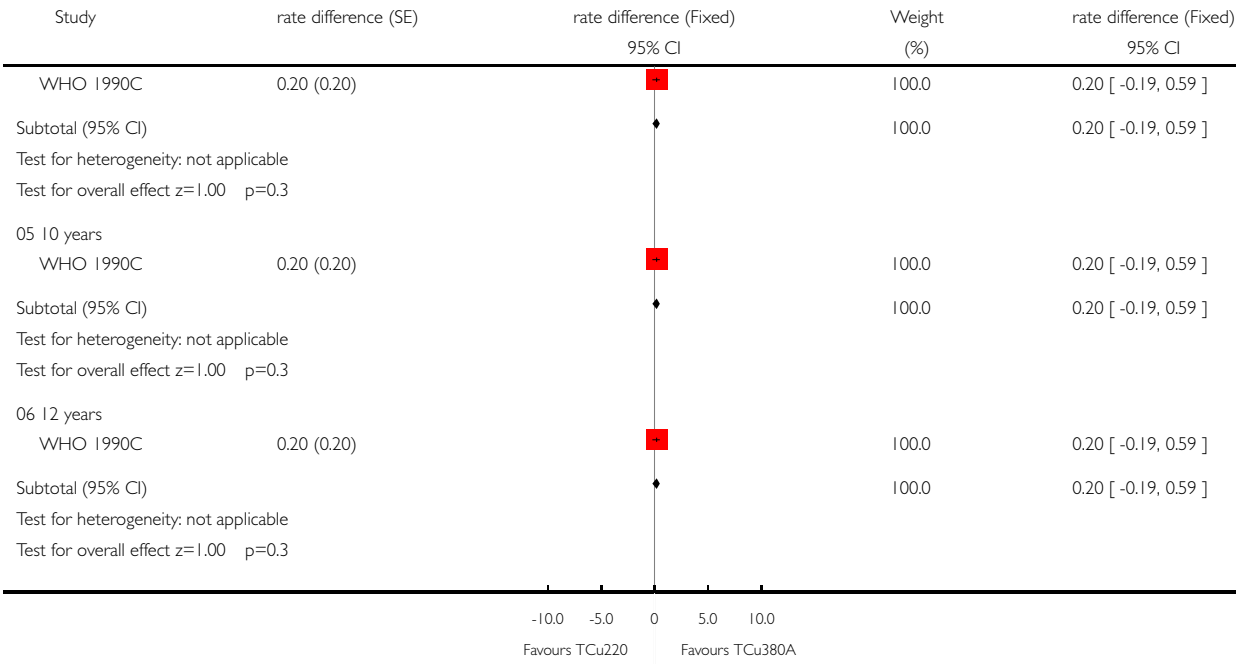
Comparison: 04 Cu220 vs TCu380A

Outcome: 04 Perforation



(*Continued* . . .)

(... *Continued*)

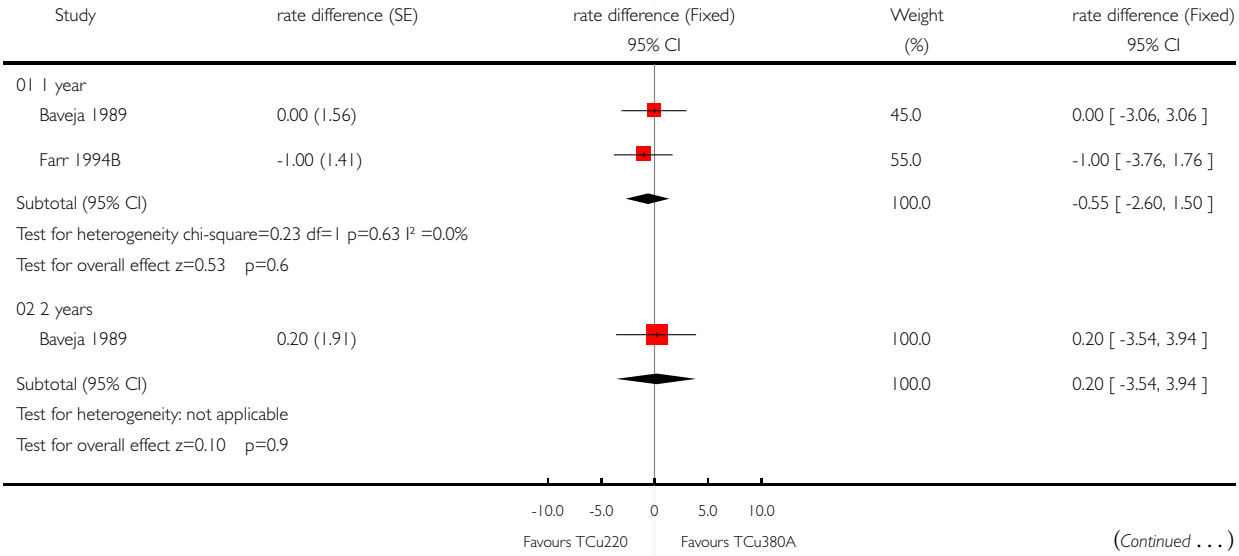


Analysis 04.05. Comparison 04 Cu220 vs TCu380A, Outcome 05 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

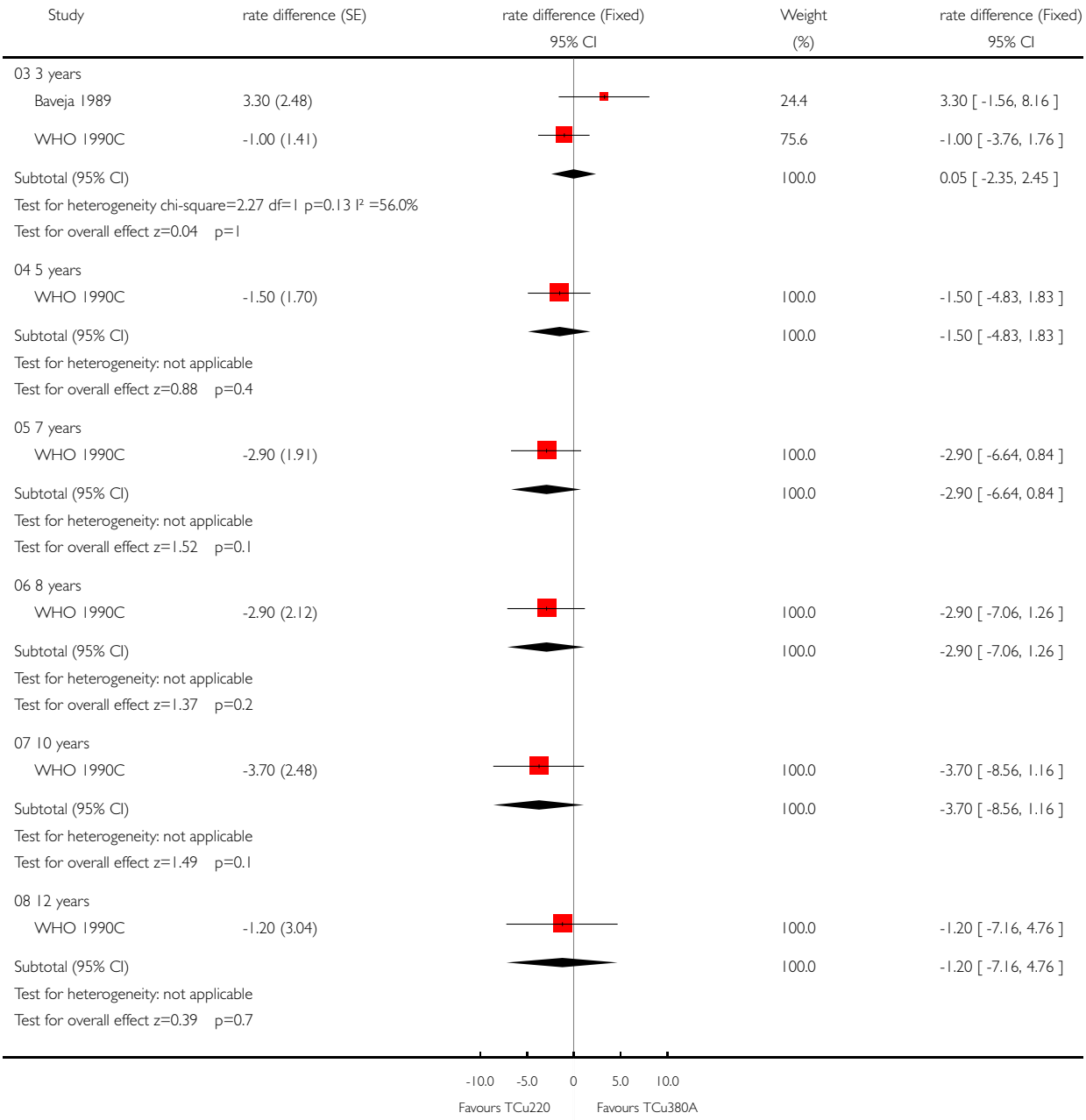
Comparison: 04 Cu220 vs TCu380A

Outcome: 05 Discontinuation: bleeding and pain



(*Continued* . . .)

(... *Continued*)

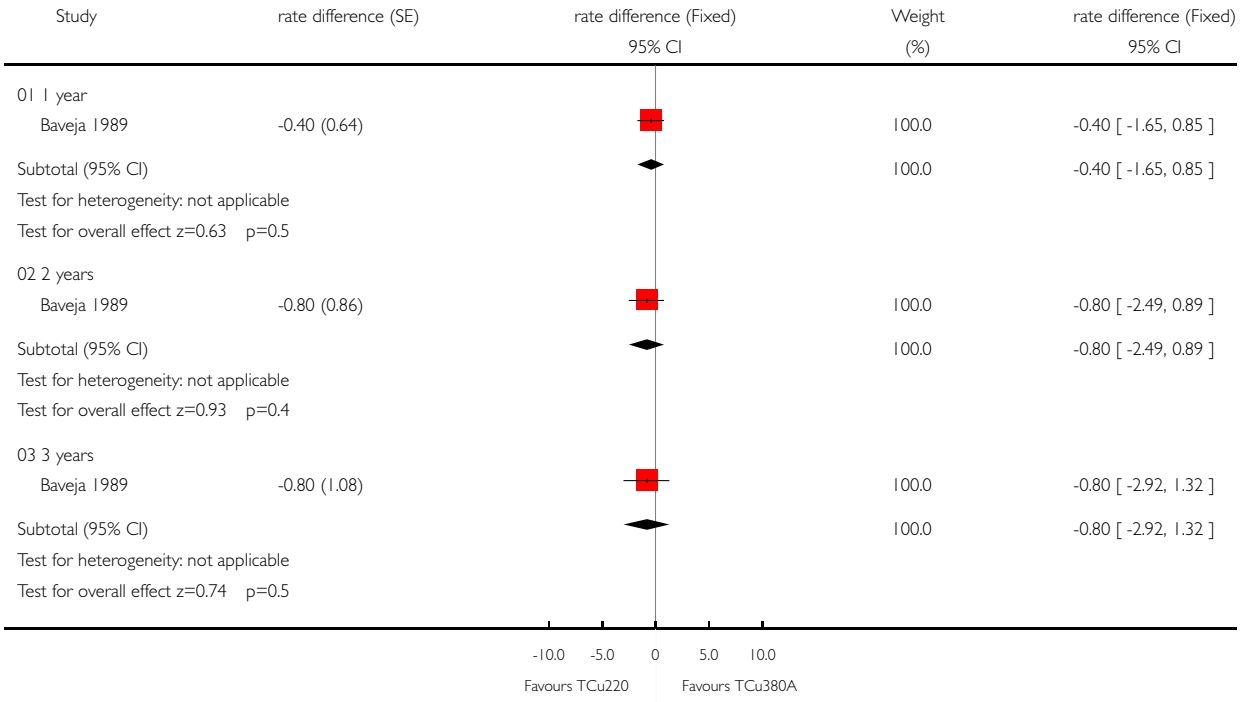


Analysis 04.06. Comparison 04 Cu220 vs TCu380A, Outcome 06 Discontinuation: intermenstrual bleeding

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 04 Cu220 vs TCu380A

Outcome: 06 Discontinuation: intermenstrual bleeding

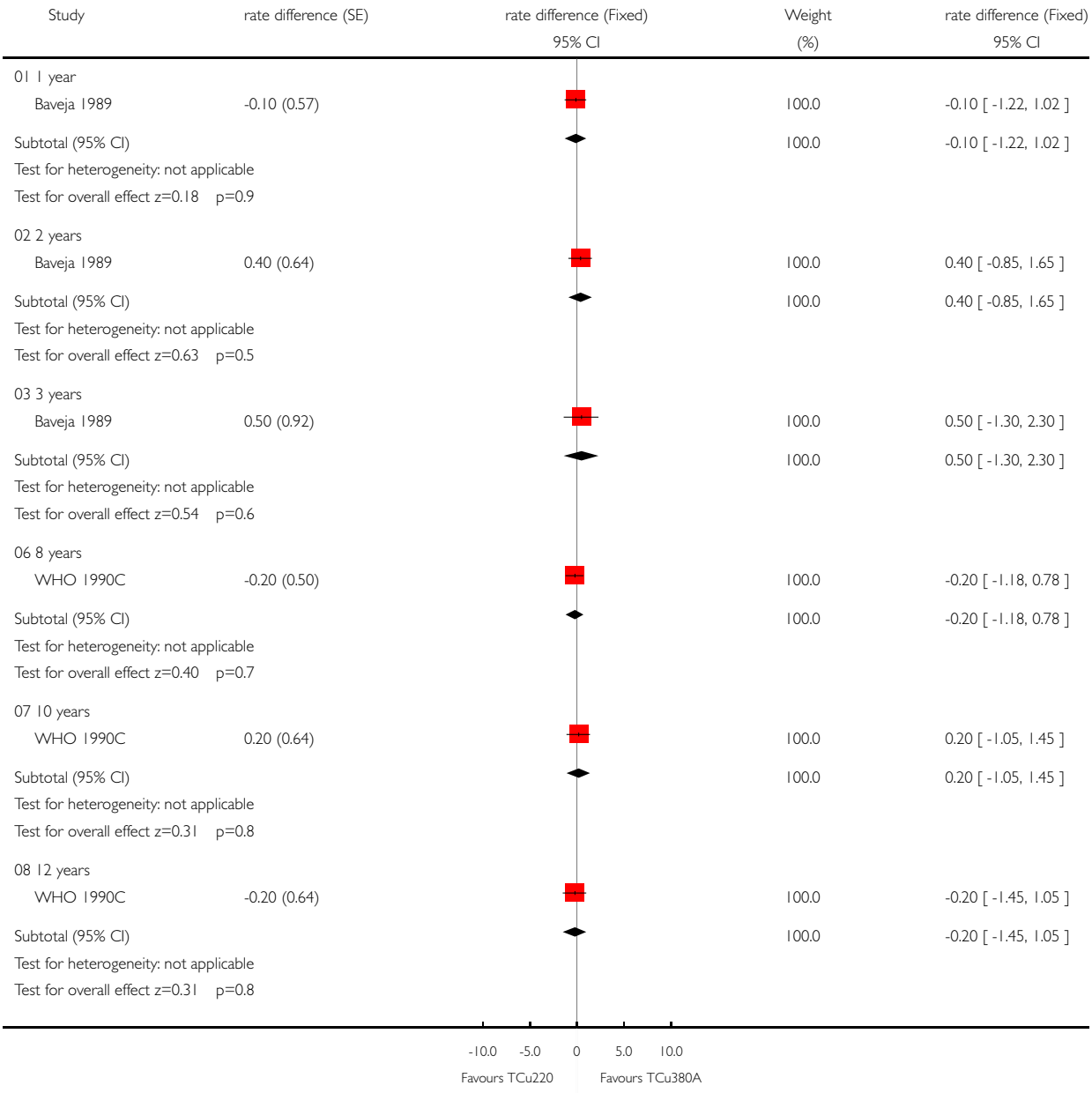


Analysis 04.07. Comparison 04 Cu220 vs TCu380A, Outcome 07 Discontinuation: infection/PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 04 Cu220 vs TCu380A

Outcome: 07 Discontinuation: infection/PID

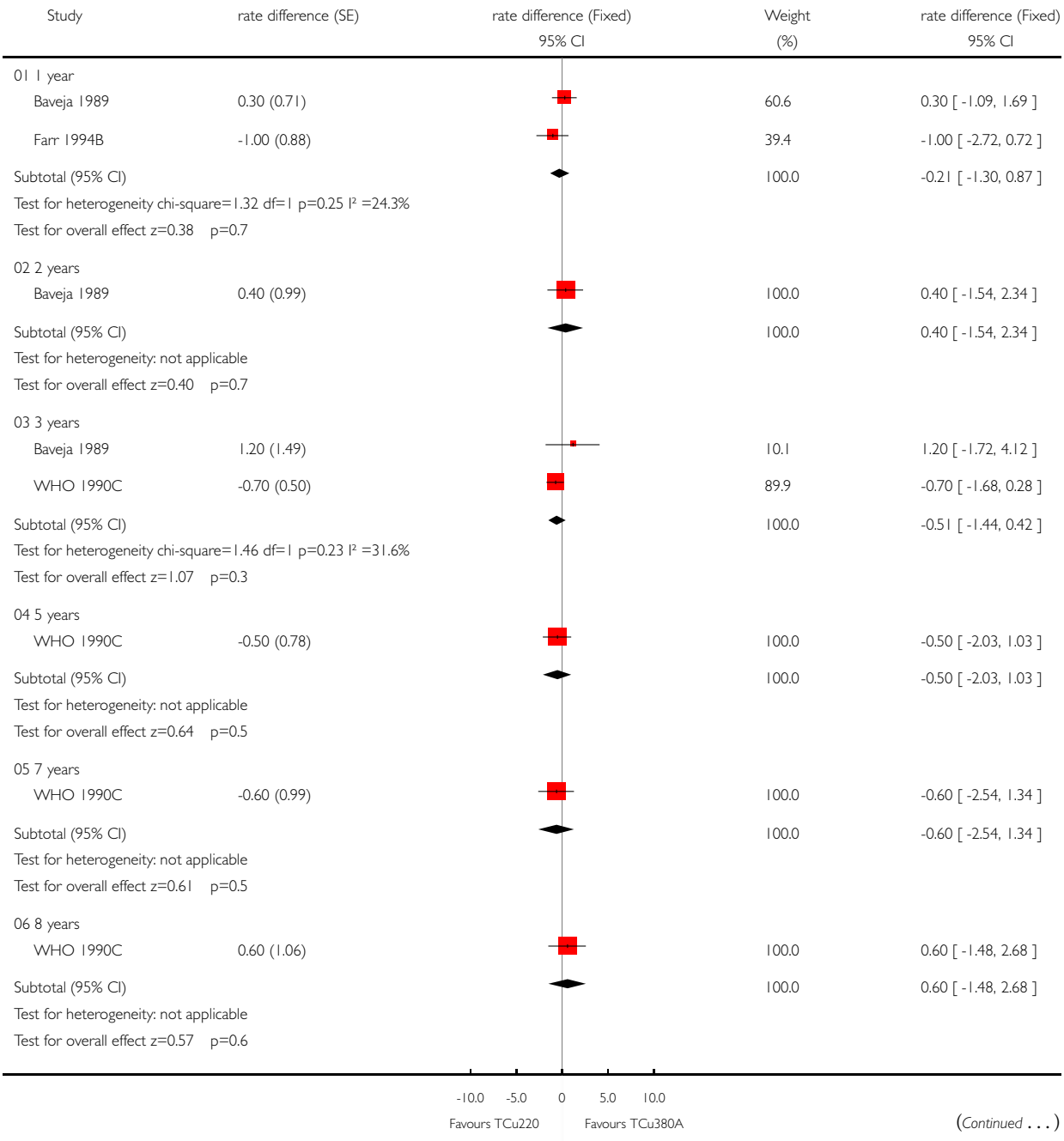


Analysis 04.08. Comparison 04 Cu220 vs TCu380A, Outcome 08 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

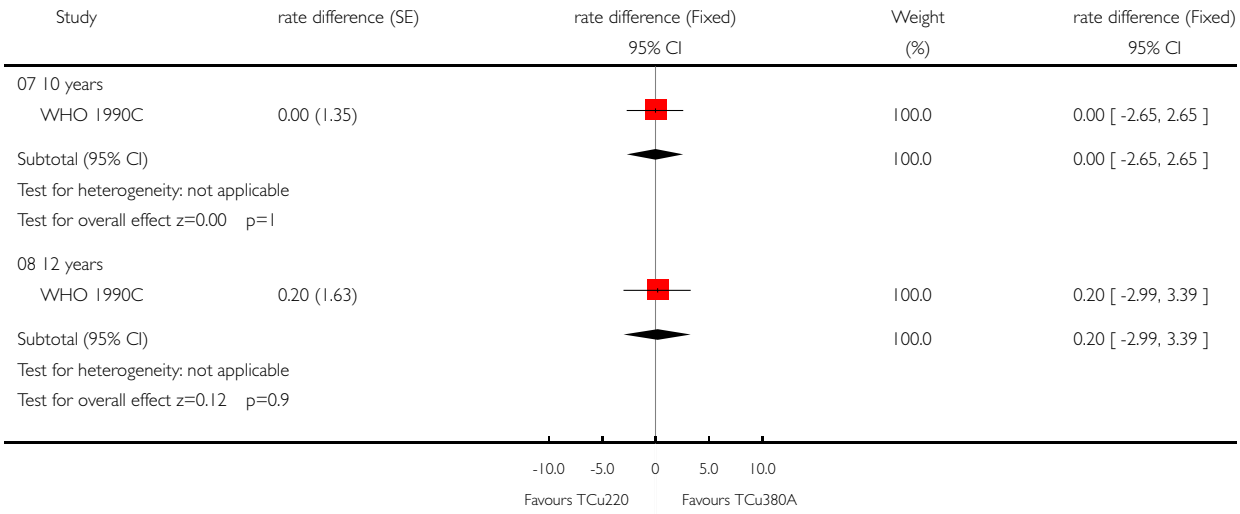
Comparison: 04 Cu220 vs TCu380A

Outcome: 08 Discontinuation: other medical reasons



(*Continued . . .*)

(. . . *Continued*)

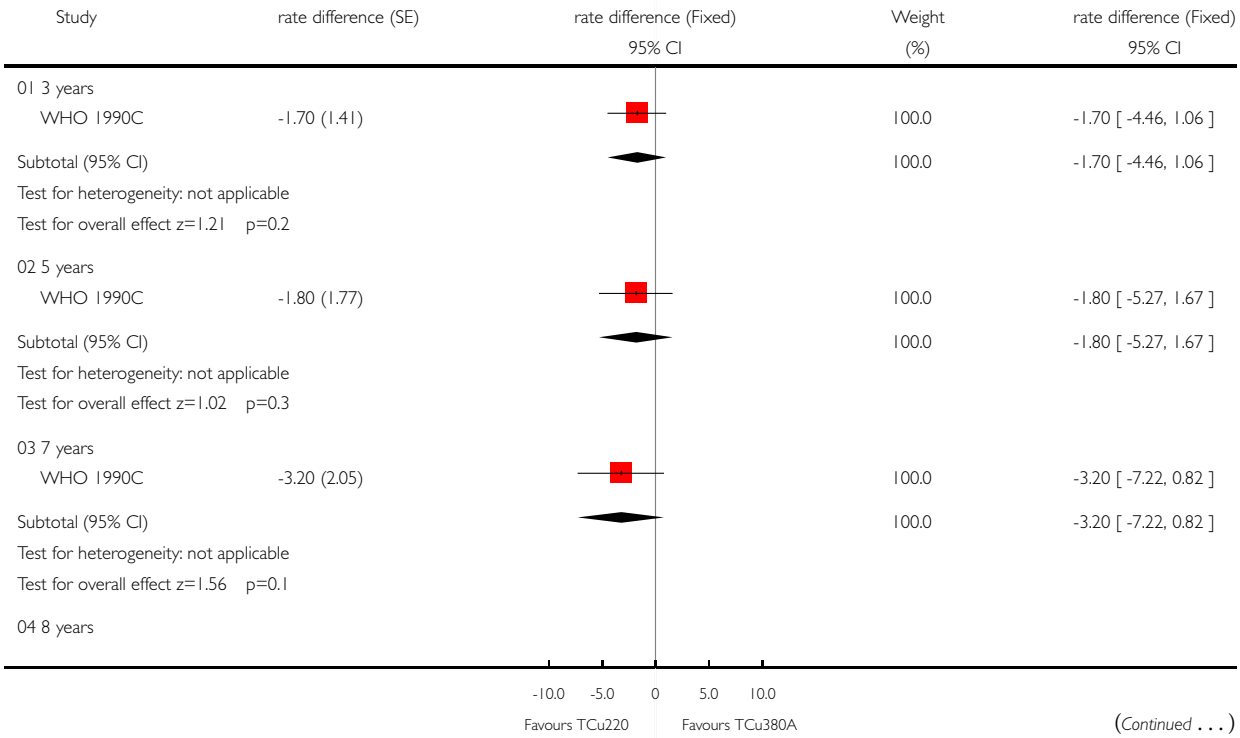


Analysis 04.09. Comparison 04 Cu220 vs TCu380A, Outcome 09 Discontinuation: total medical

Review: Copper containing, framed intra-uterine devices for contraception

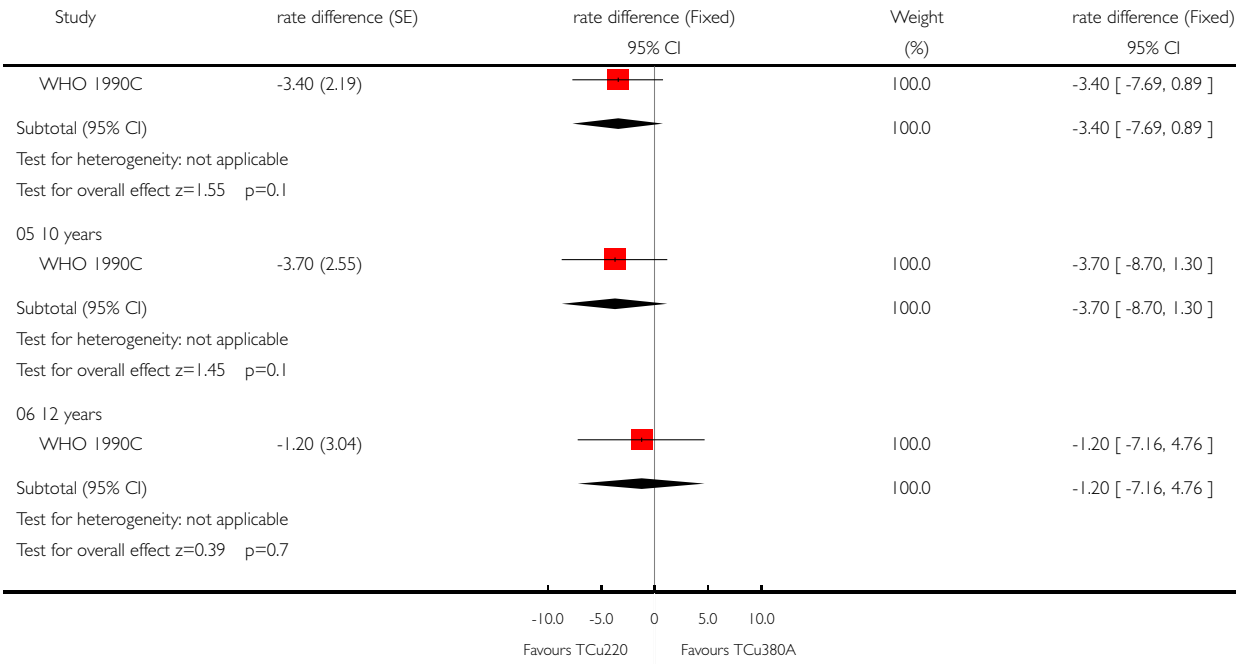
Comparison: 04 Cu220 vs TCu380A

Outcome: 09 Discontinuation: total medical



(*Continued* . . .)

(. . . *Continued*)

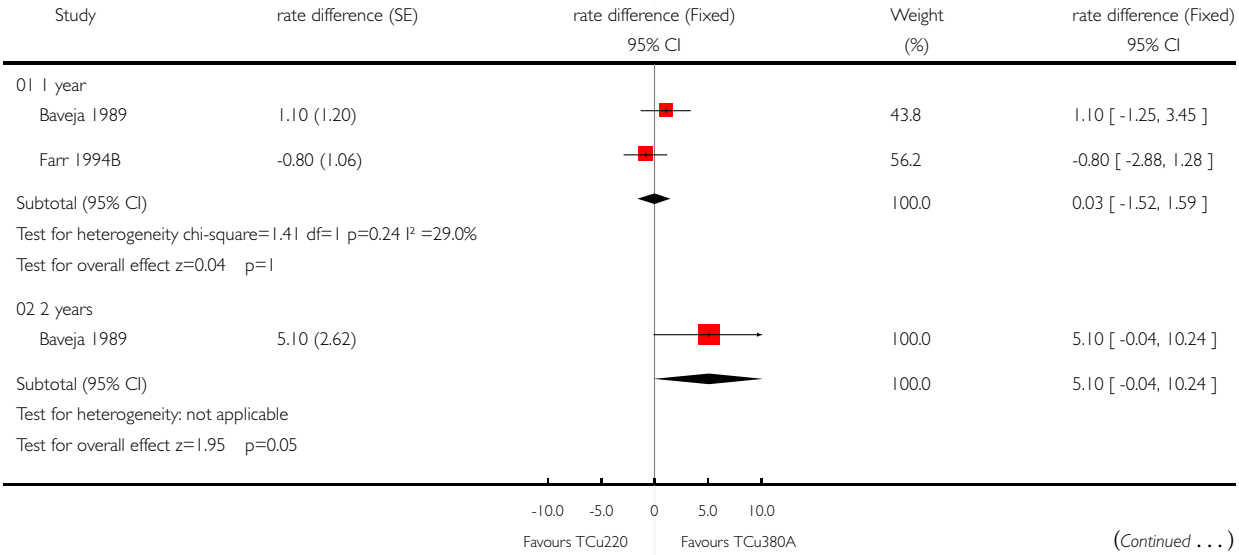


Analysis 04.10. Comparison 04 Cu220 vs TCu380A, Outcome 10 Discontinuation: non-medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

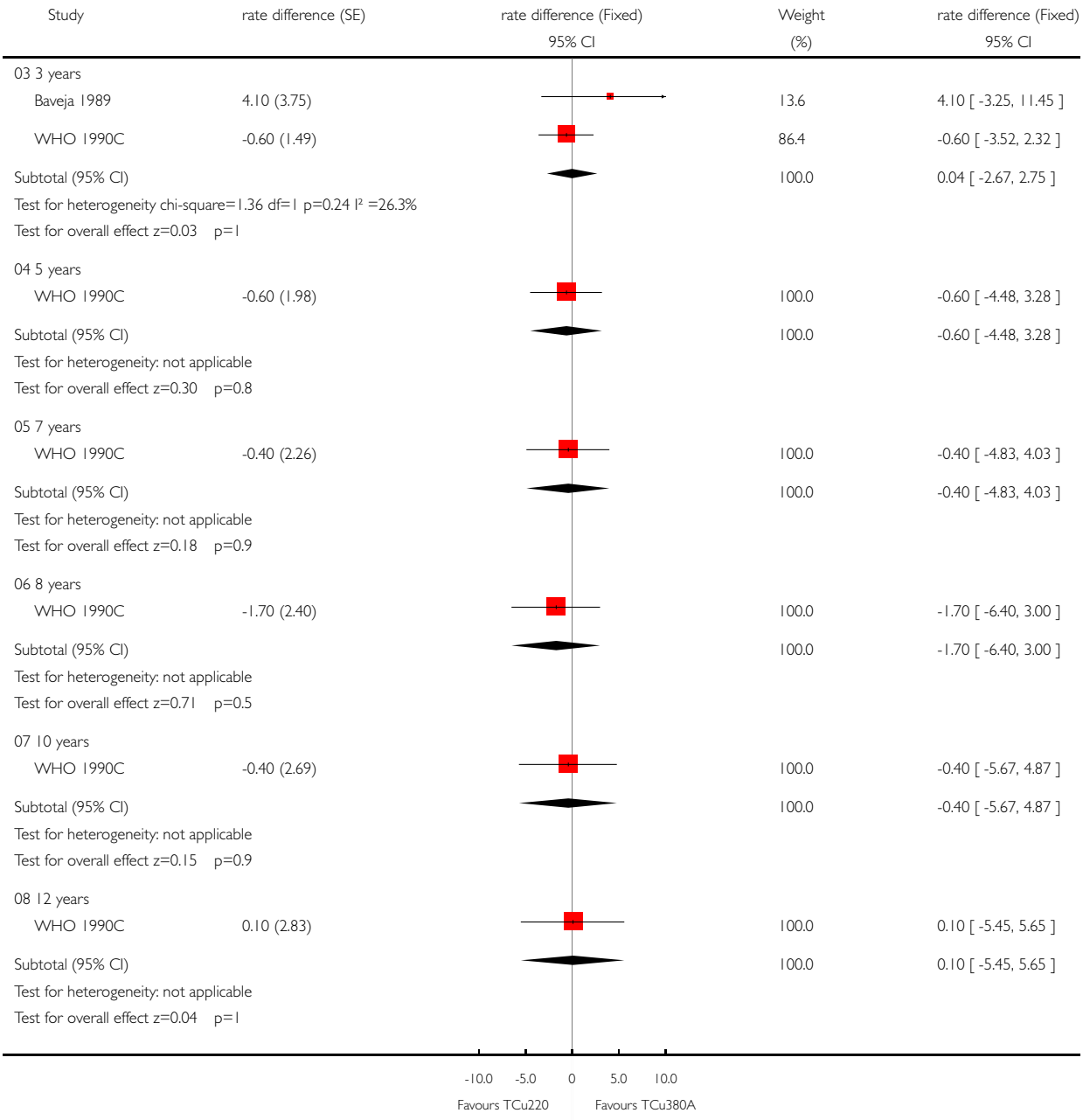
Comparison: 04 Cu220 vs TCu380A

Outcome: 10 Discontinuation: non-medical reasons



(*Continued* . . .)

(. . . *Continued*)

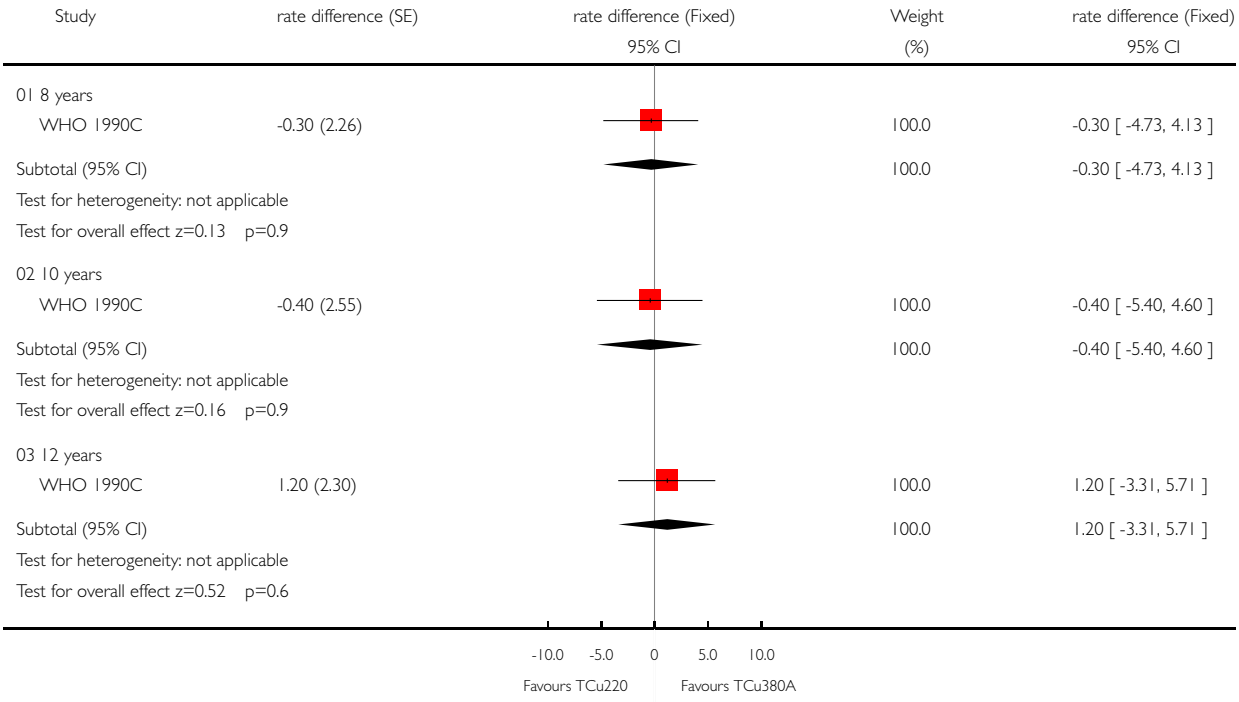


Analysis 04.11. Comparison 04 Cu220 vs TCu380A, Outcome 11 Discontinuation: total use related

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 04 Cu220 vs TCu380A

Outcome: 11 Discontinuation: total use related

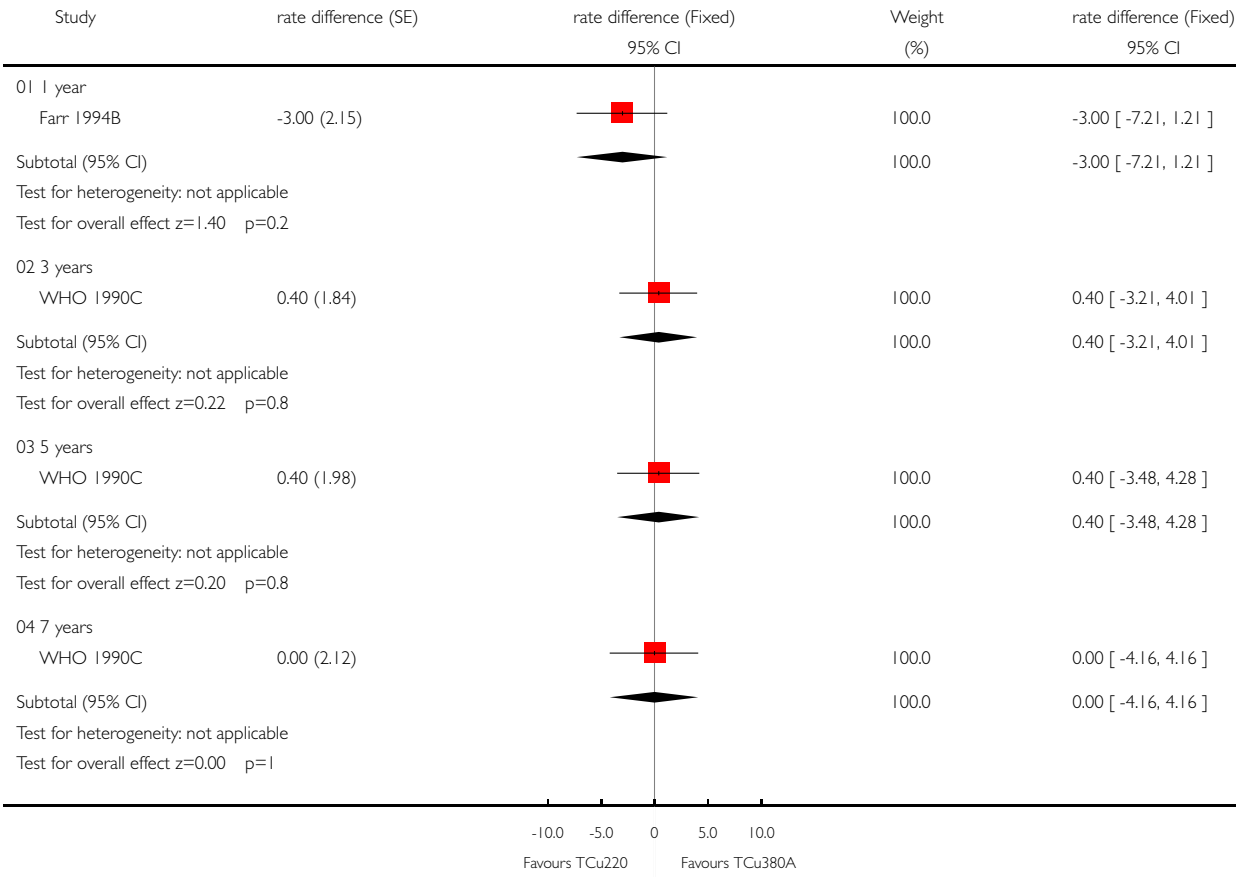


Analysis 04.12. Comparison 04 Cu220 vs TCu380A, Outcome 12 Discontinuation: all

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 04 Cu220 vs TCu380A

Outcome: 12 Discontinuation: all

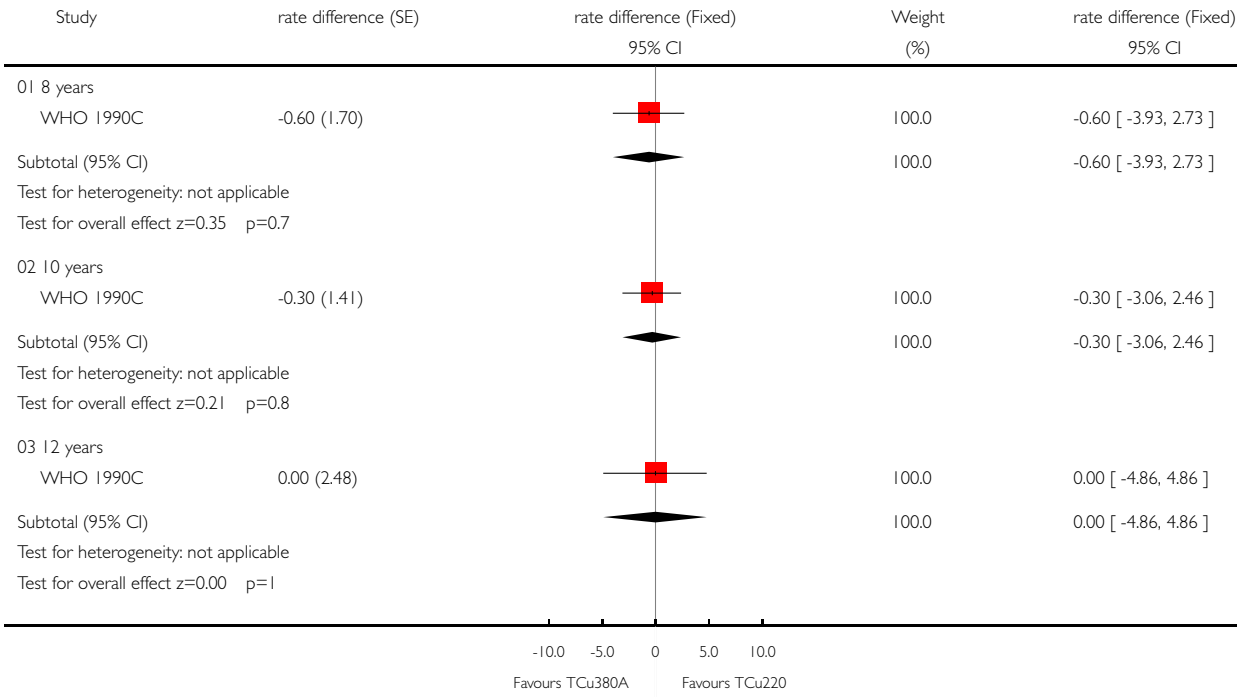


Analysis 04.13. Comparison 04 Cu220 vs TCu380A, Outcome 13 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 04 Cu220 vs TCu380A

Outcome: 13 Continuation

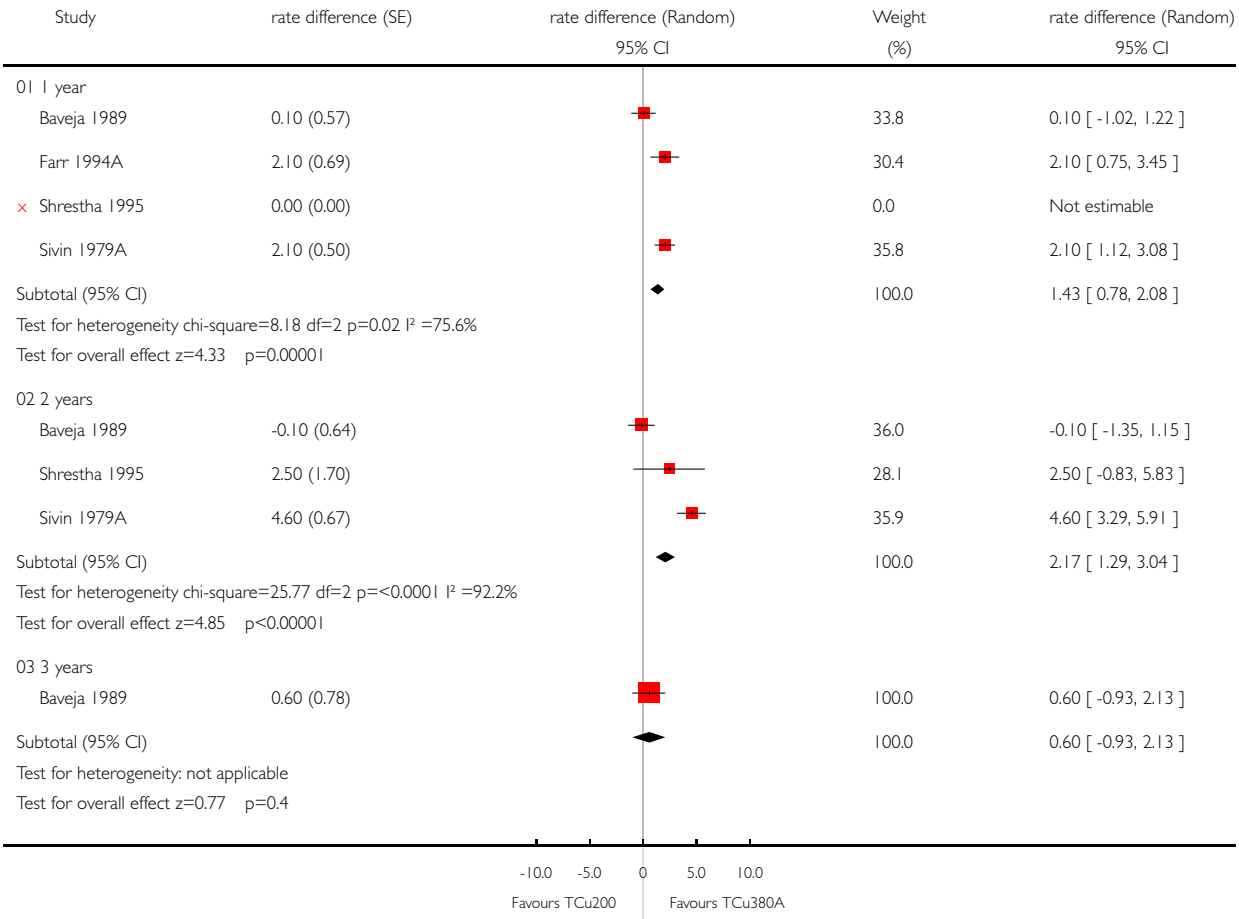


Analysis 05.01. Comparison 05 TCu200 vs TCu380A, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 01 Pregnancy

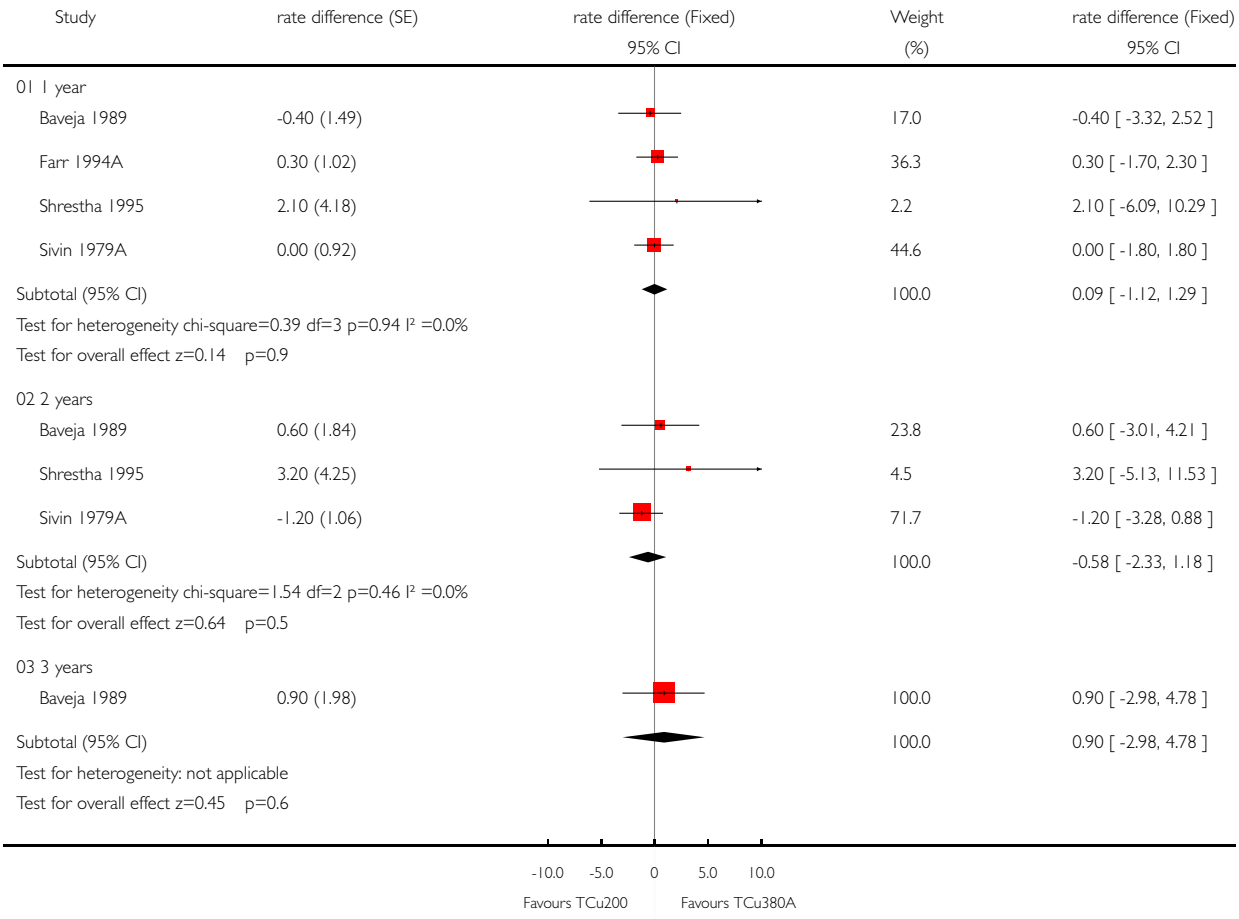


Analysis 05.02. Comparison 05 TCu200 vs TCu380A, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 02 Expulsion

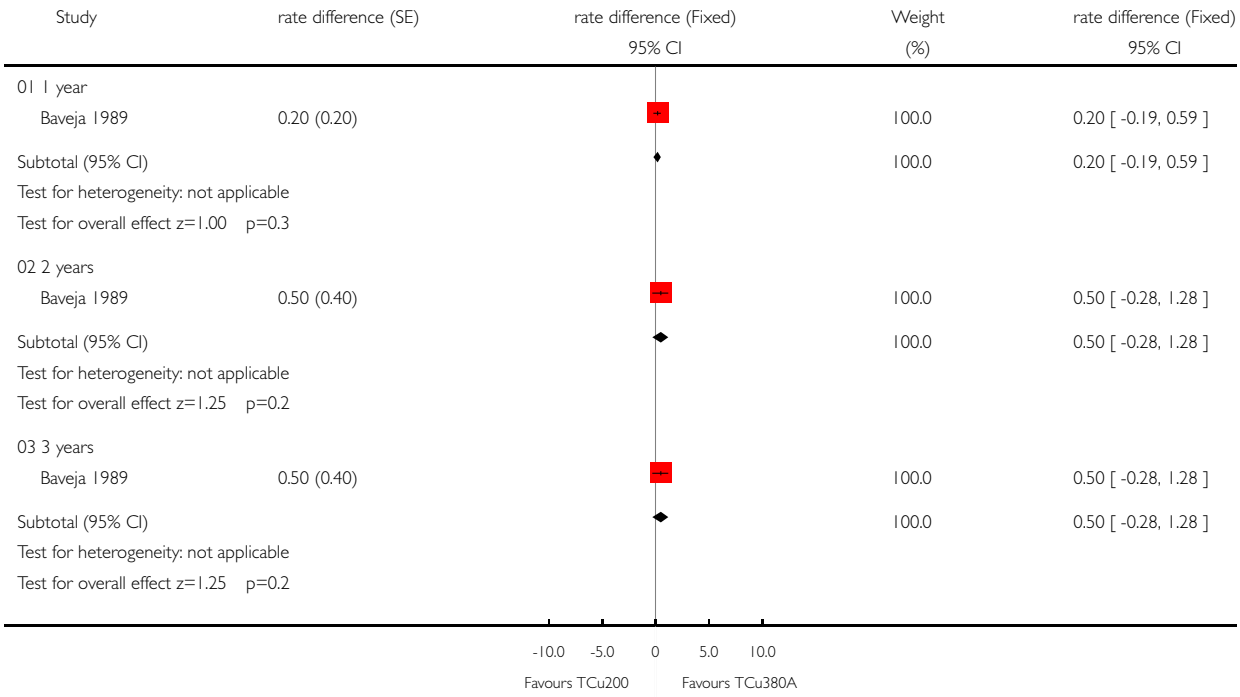


Analysis 05.03. Comparison 05 TCu200 vs TCu380A, Outcome 03 Perforation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 03 Perforation

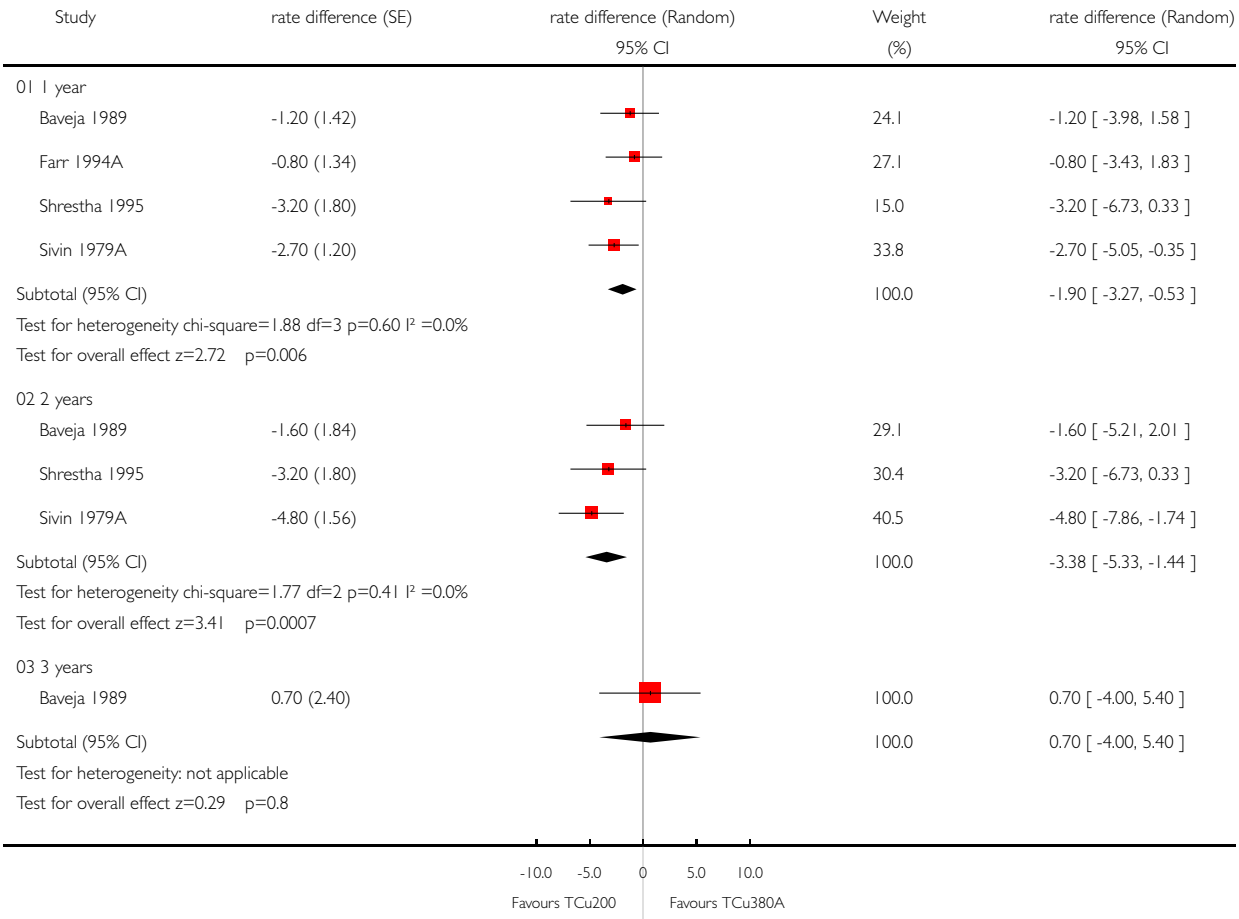


Analysis 05.04. Comparison 05 TCu200 vs TCu380A, Outcome 04 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 04 Discontinuation: bleeding and pain

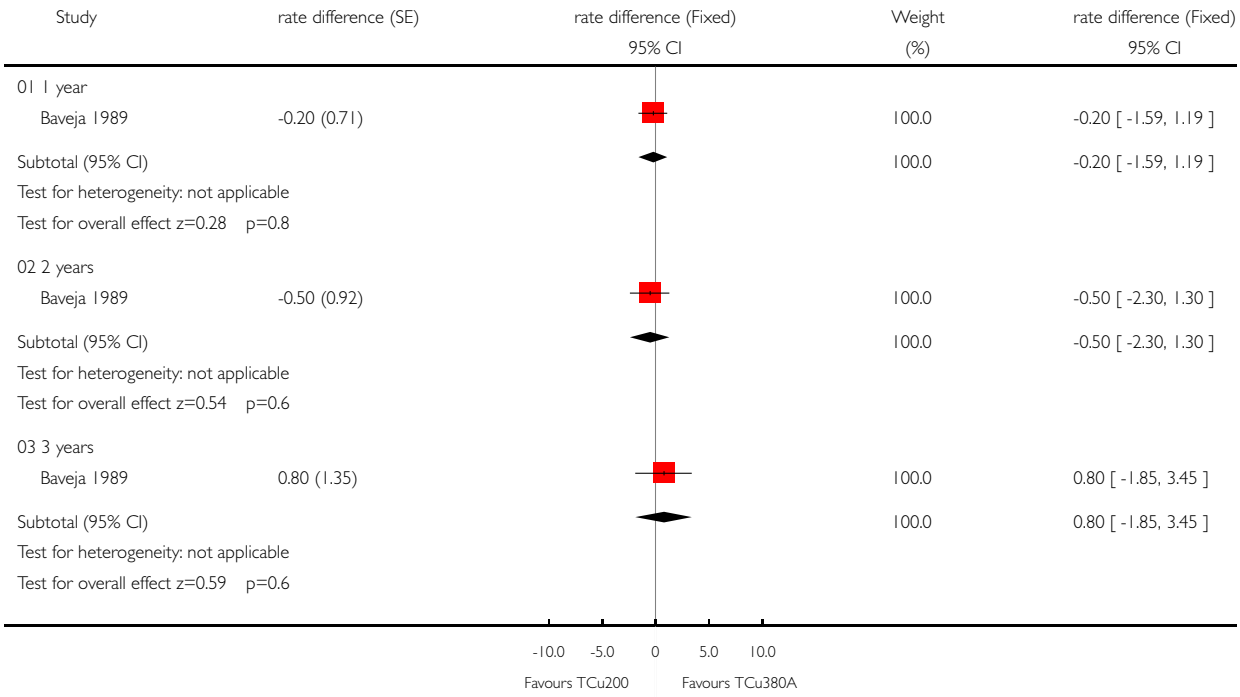


Analysis 05.05. Comparison 05 TCu200 vs TCu380A, Outcome 05 Discontinuation: intermenstrual bleeding

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 05 Discontinuation: intermenstrual bleeding

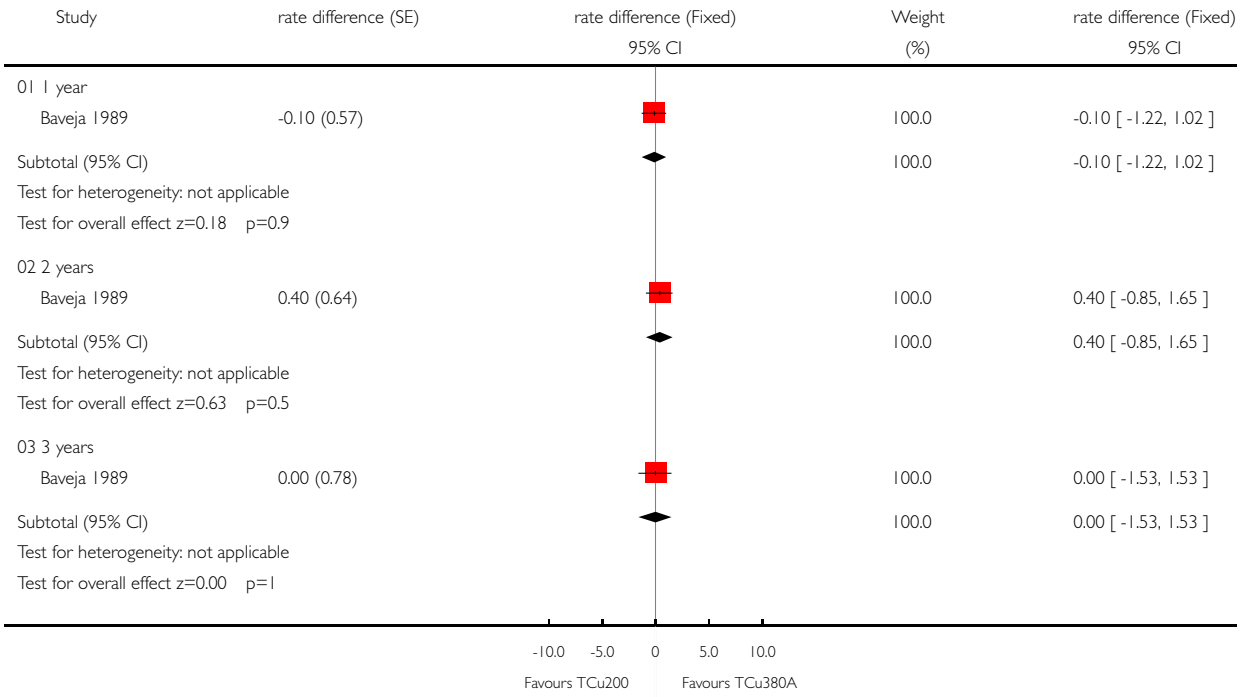


Analysis 05.06. Comparison 05 TCu200 vs TCu380A, Outcome 06 Discontinuation: infection/PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 06 Discontinuation: infection/PID

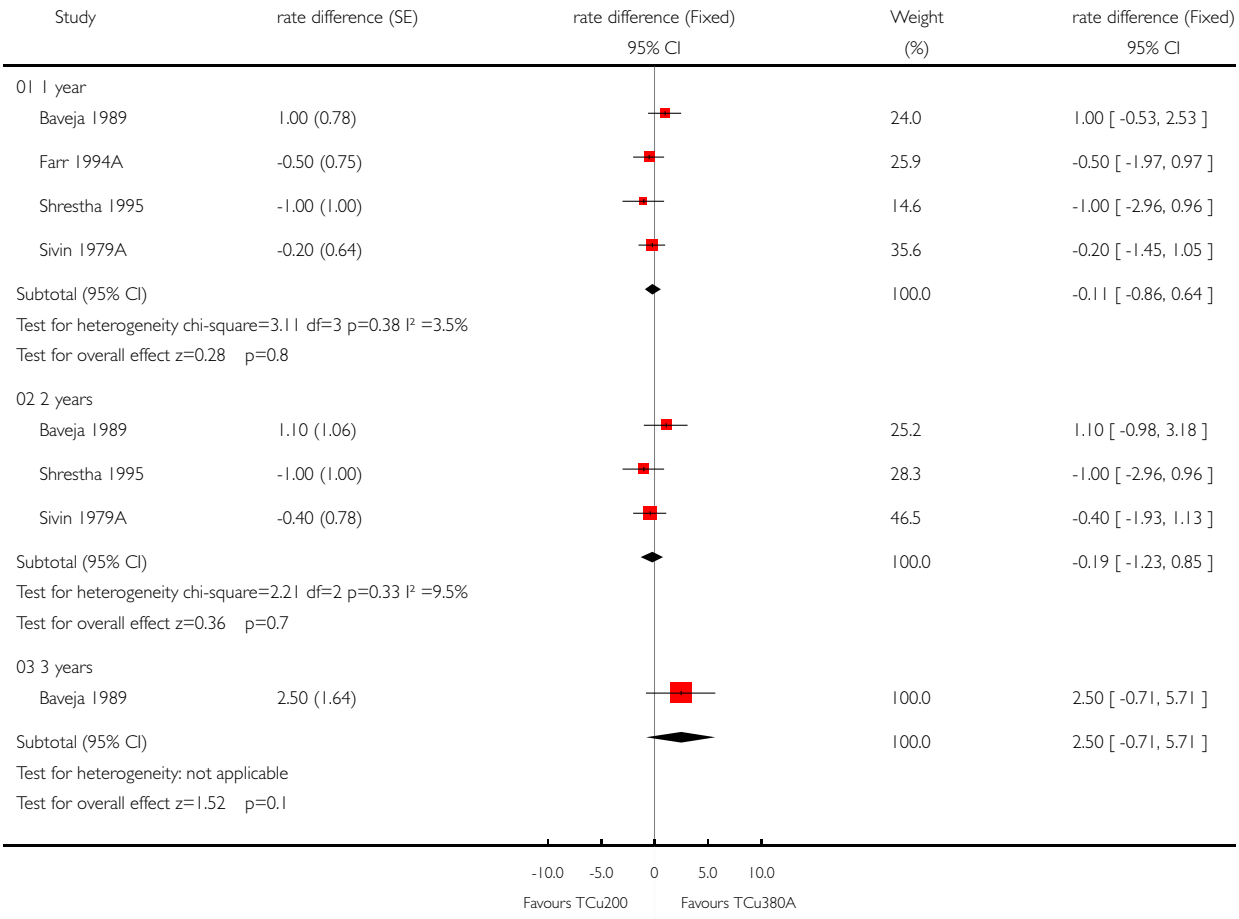


Analysis 05.07. Comparison 05 TCu200 vs TCu380A, Outcome 07 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 07 Discontinuation: other medical reasons

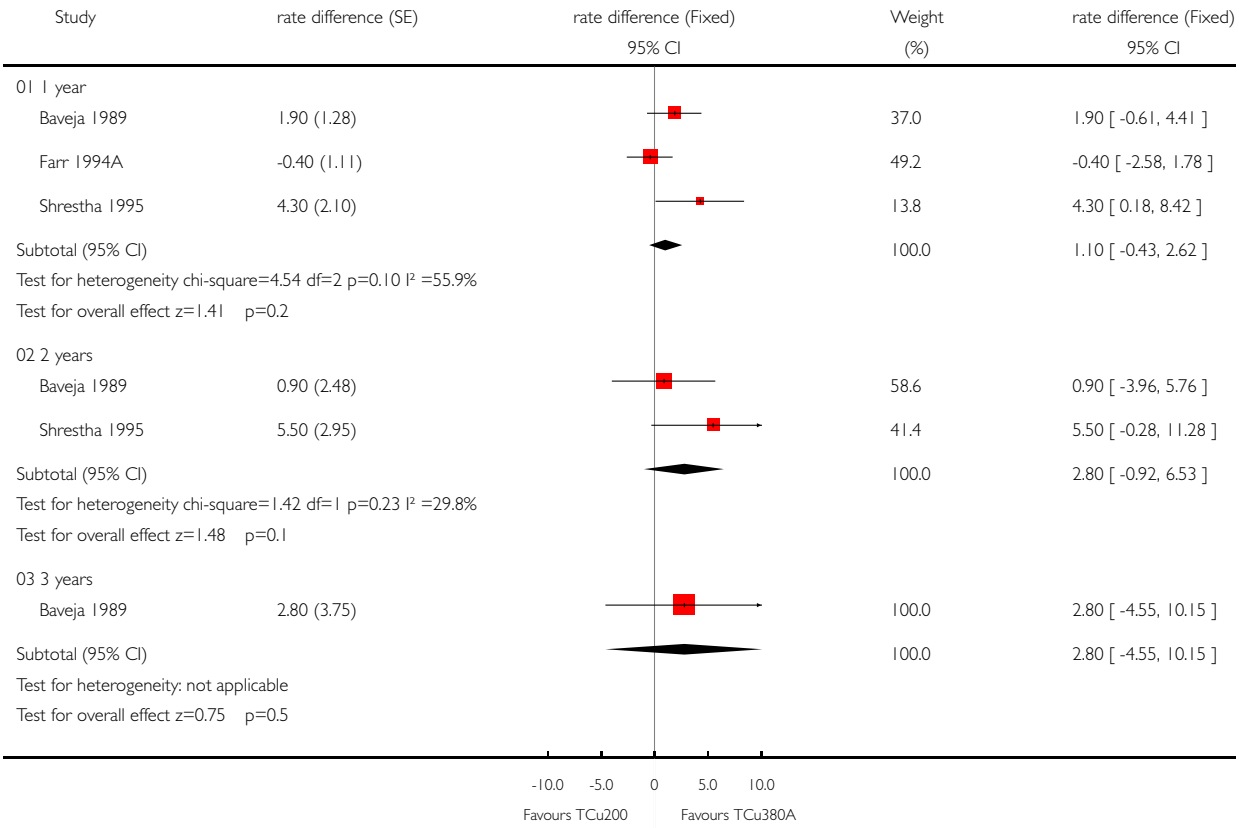


Analysis 05.08. Comparison 05 TCu200 vs TCu380A, Outcome 08 Discontinuation: non-medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 08 Discontinuation: non-medical reasons

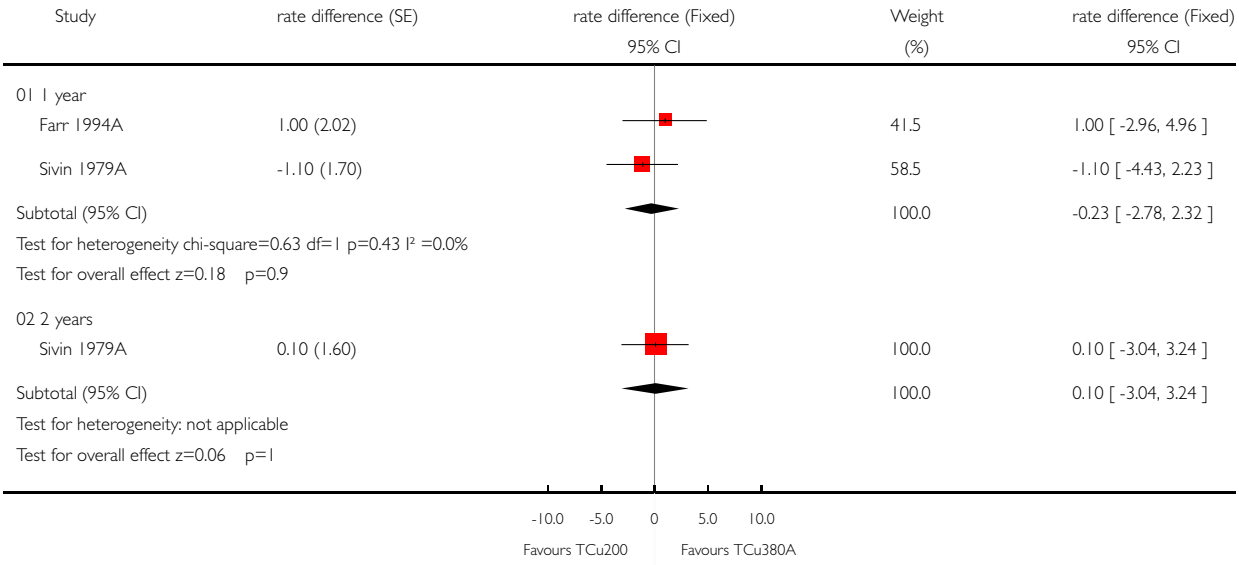


Analysis 05.09. Comparison 05 TCu200 vs TCu380A, Outcome 09 Discontinuation: all

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 09 Discontinuation: all

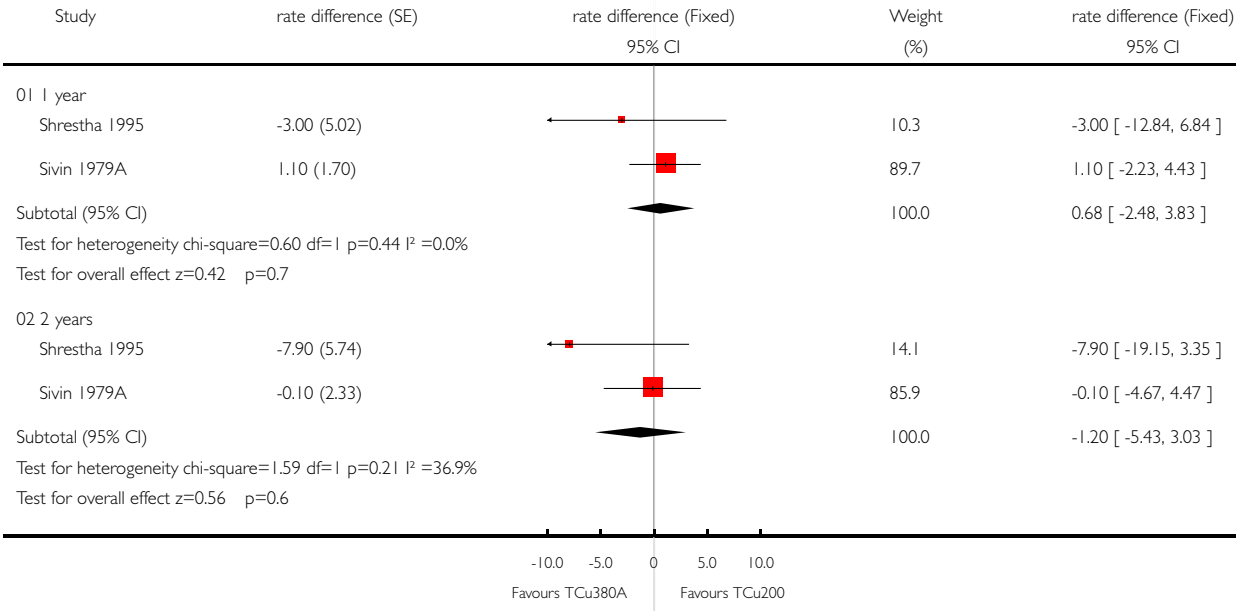


Analysis 05.10. Comparison 05 TCu200 vs TCu380A, Outcome 10 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 10 Continuation

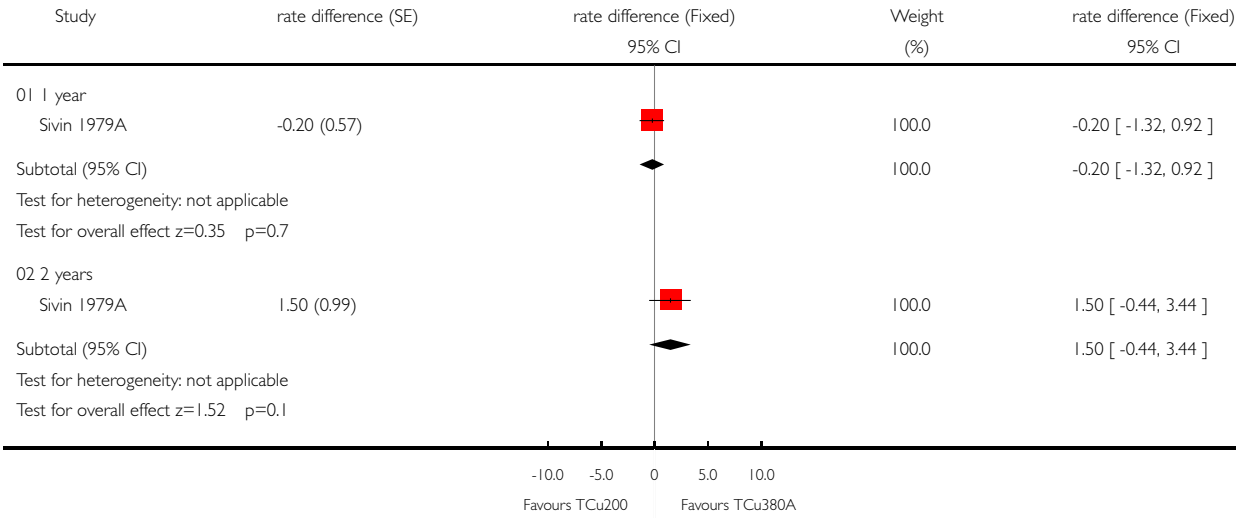


Analysis 05.11. Comparison 05 TCu200 vs TCu380A, Outcome 11 Discontinuation: planned pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 11 Discontinuation: planned pregnancy

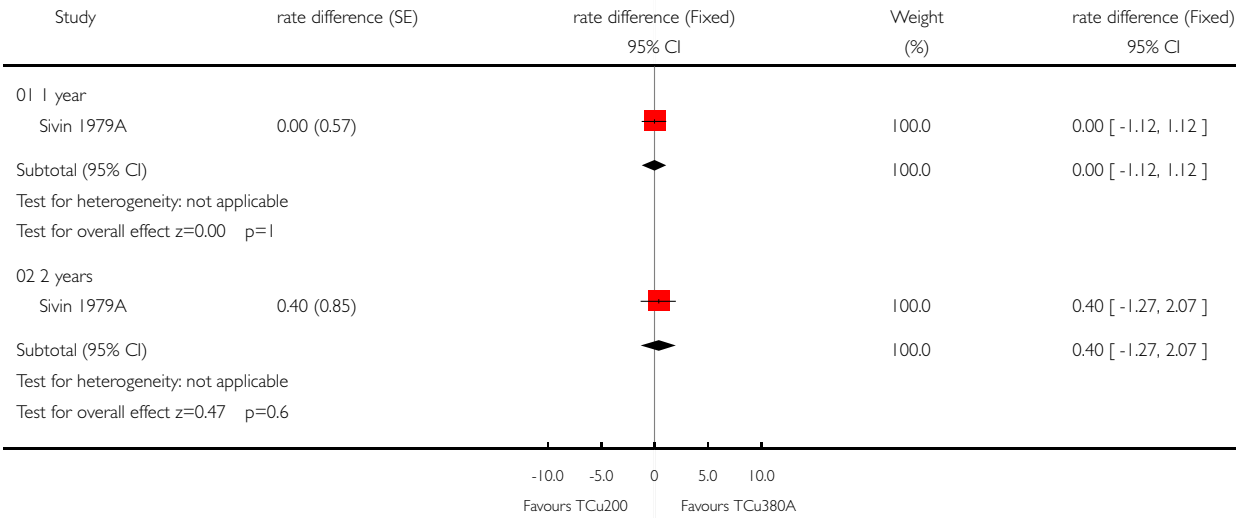


Analysis 05.12. Comparison 05 TCu200 vs TCu380A, Outcome 12 Discontinuation: other personal reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 05 TCu200 vs TCu380A

Outcome: 12 Discontinuation: other personal reasons

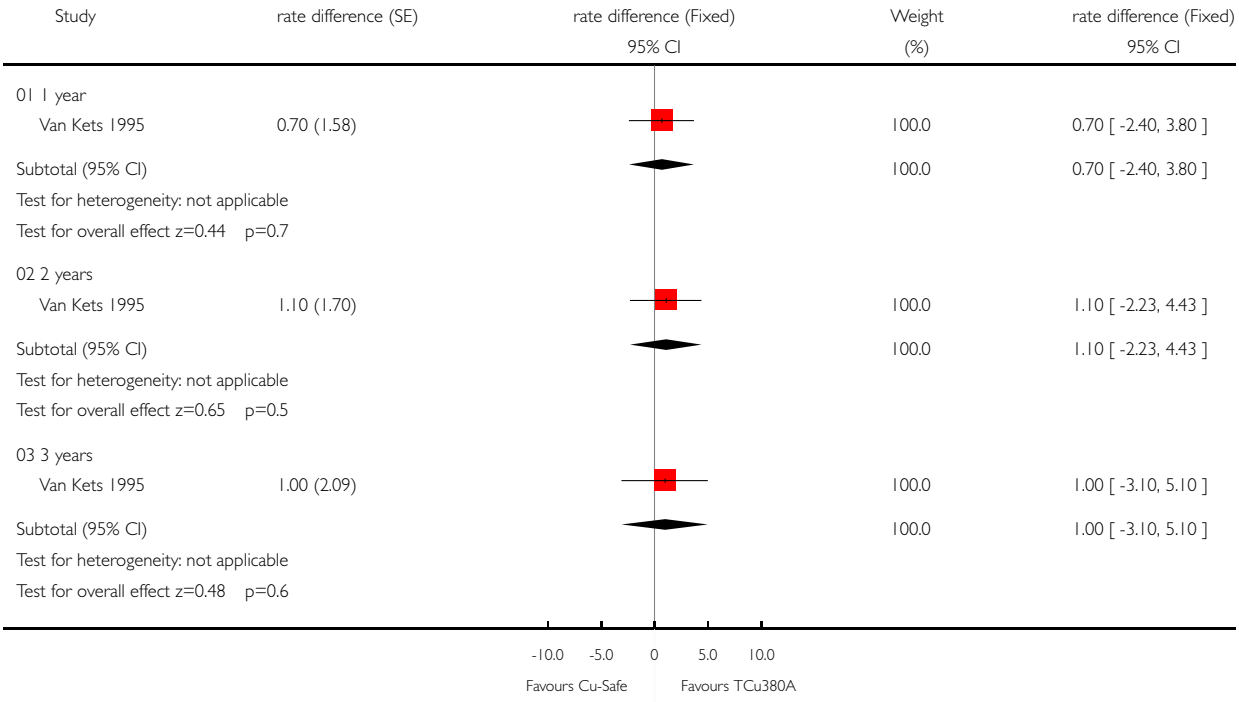


Analysis 06.01. Comparison 06 Cu-Safe 300 vs TCu380A, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 06 Cu-Safe 300 vs TCu380A

Outcome: 01 Pregnancy

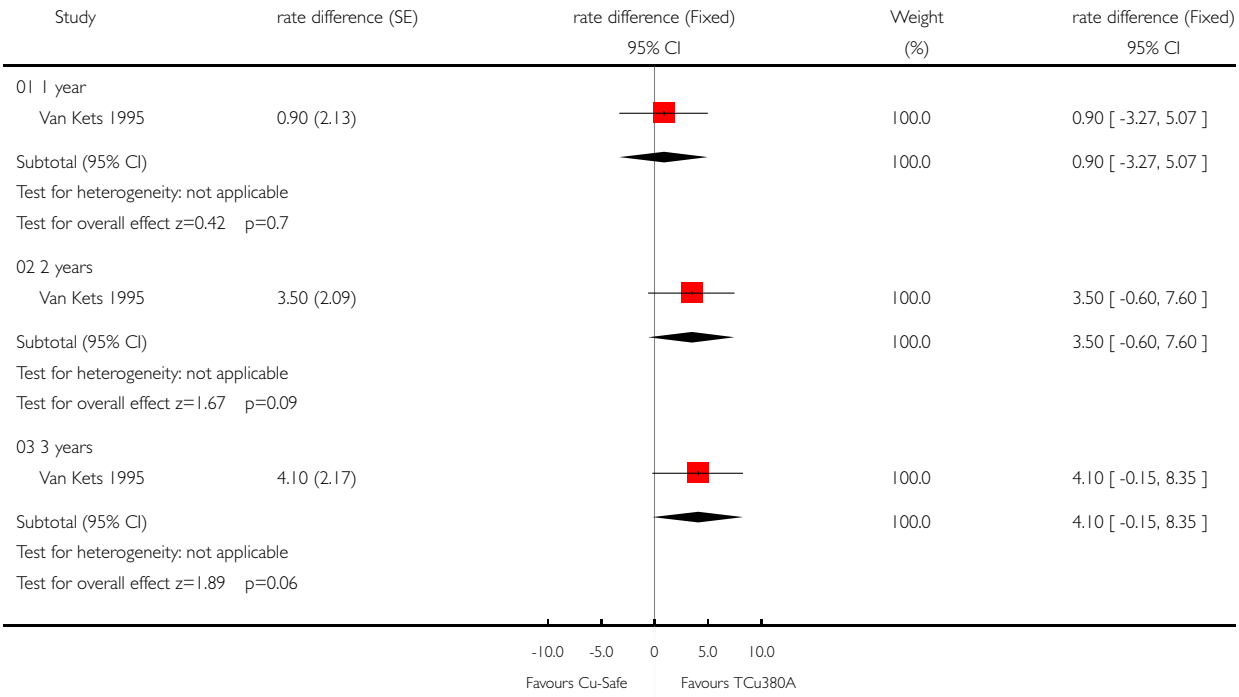


Analysis 06.02. Comparison 06 Cu-Safe 300 vs TCu380A, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 06 Cu-Safe 300 vs TCu380A

Outcome: 02 Expulsion

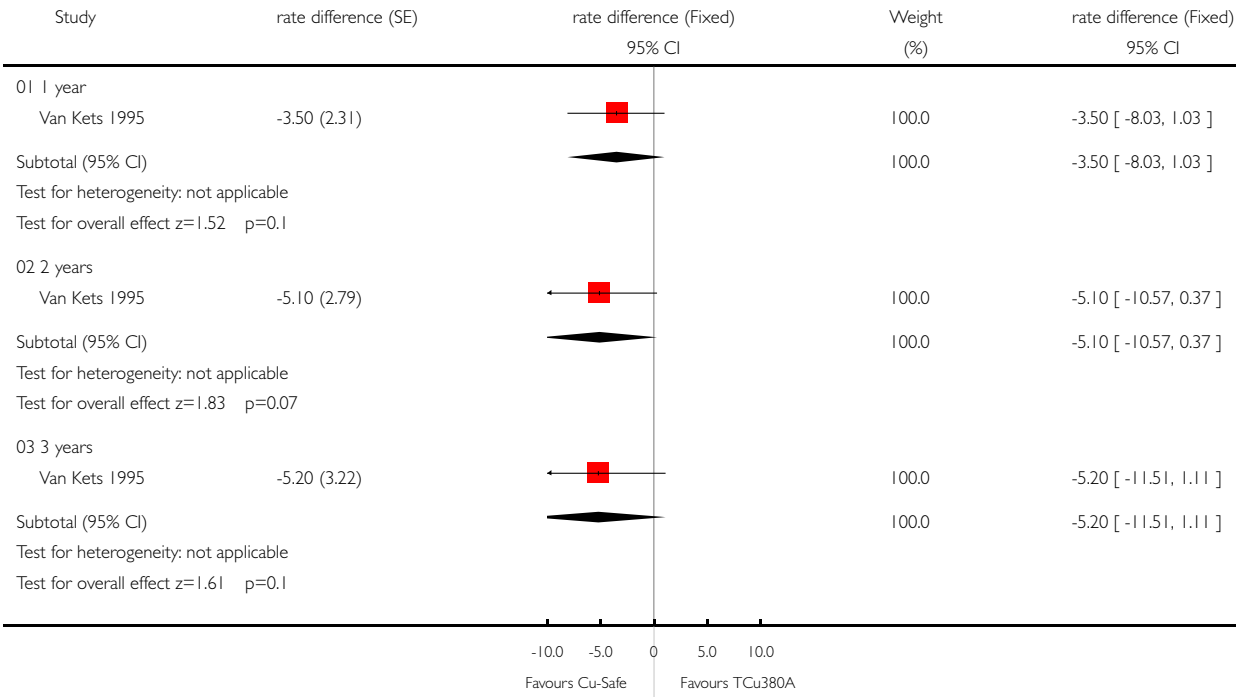


Analysis 06.03. Comparison 06 Cu-Safe 300 vs TCu380A, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 06 Cu-Safe 300 vs TCu380A

Outcome: 03 Discontinuation: bleeding and pain

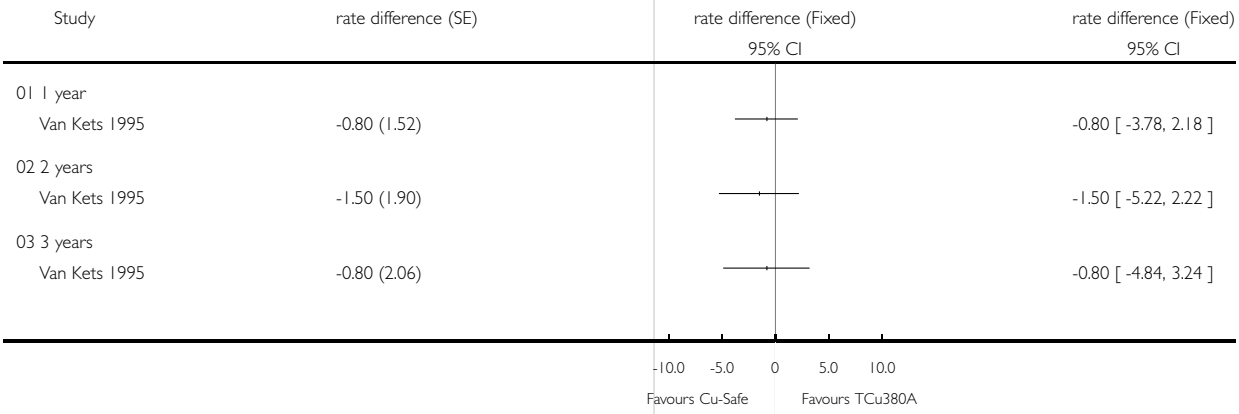


Analysis 06.04. Comparison 06 Cu-Safe 300 vs TCu380A, Outcome 04 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 06 Cu-Safe 300 vs TCu380A

Outcome: 04 Discontinuation: other medical reasons

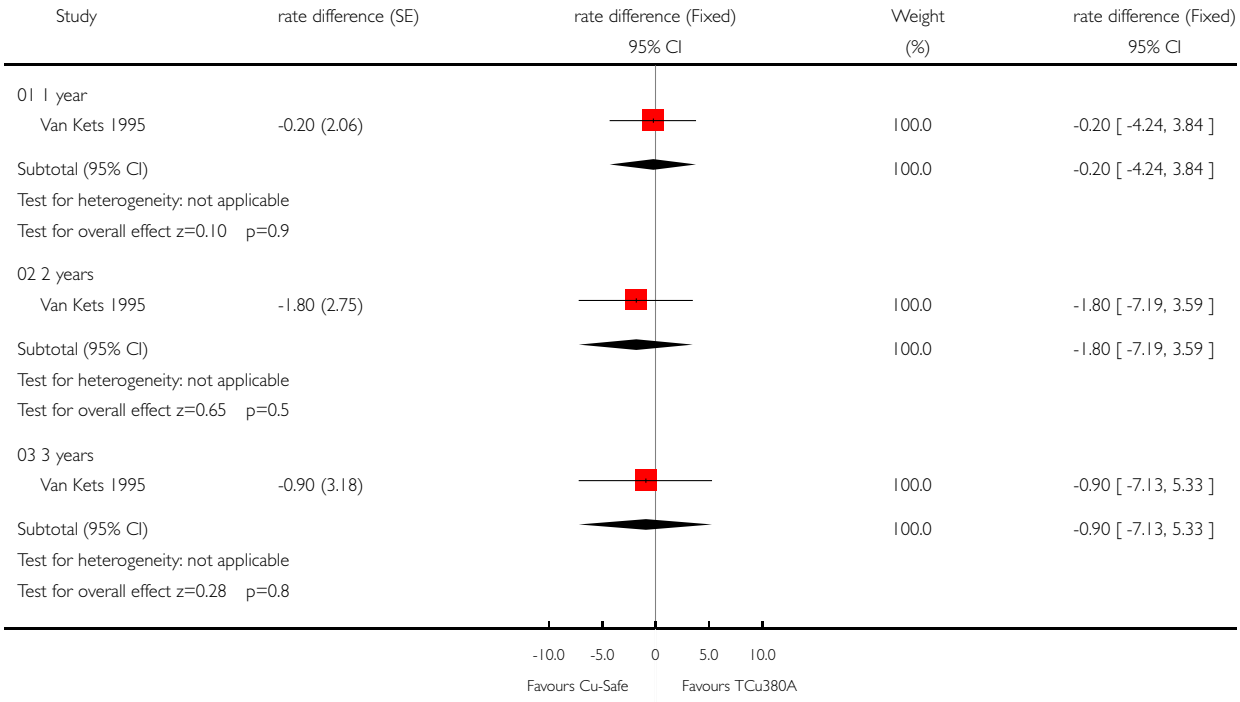


Analysis 06.05. Comparison 06 Cu-Safe 300 vs TCu380A, Outcome 05 Discontinuation: planned pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 06 Cu-Safe 300 vs TCu380A

Outcome: 05 Discontinuation: planned pregnancy

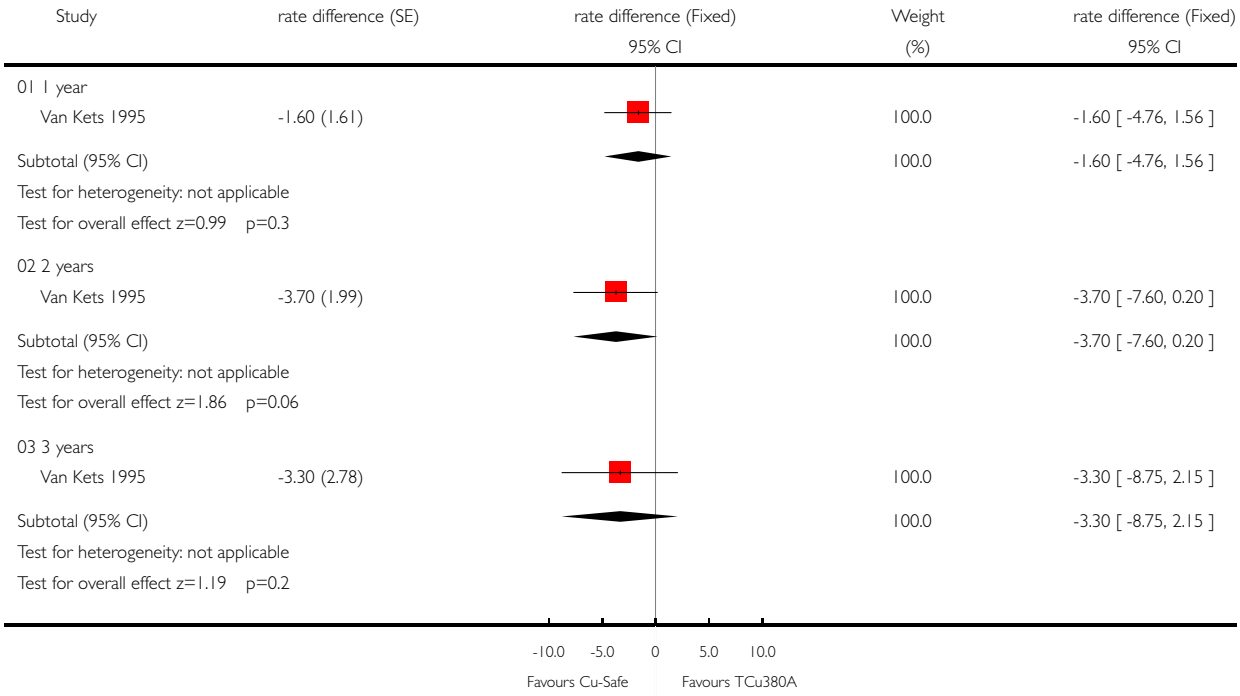


Analysis 06.06. Comparison 06 Cu-Safe 300 vs TCu380A, Outcome 06 Discontinuation: other personal reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 06 Cu-Safe 300 vs TCu380A

Outcome: 06 Discontinuation: other personal reasons

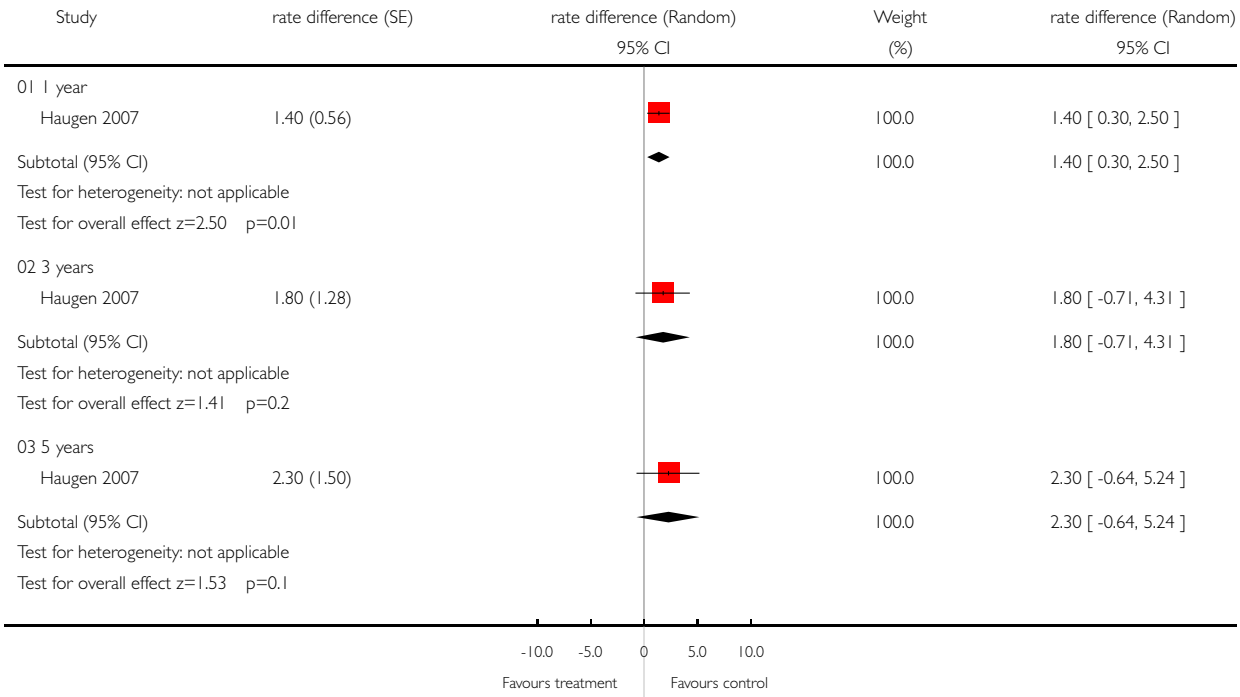


Analysis 08.01. Comparison 08 NovaT380 vs TCu380S, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 08 NovaT380 vs TCu380S

Outcome: 01 Pregnancy

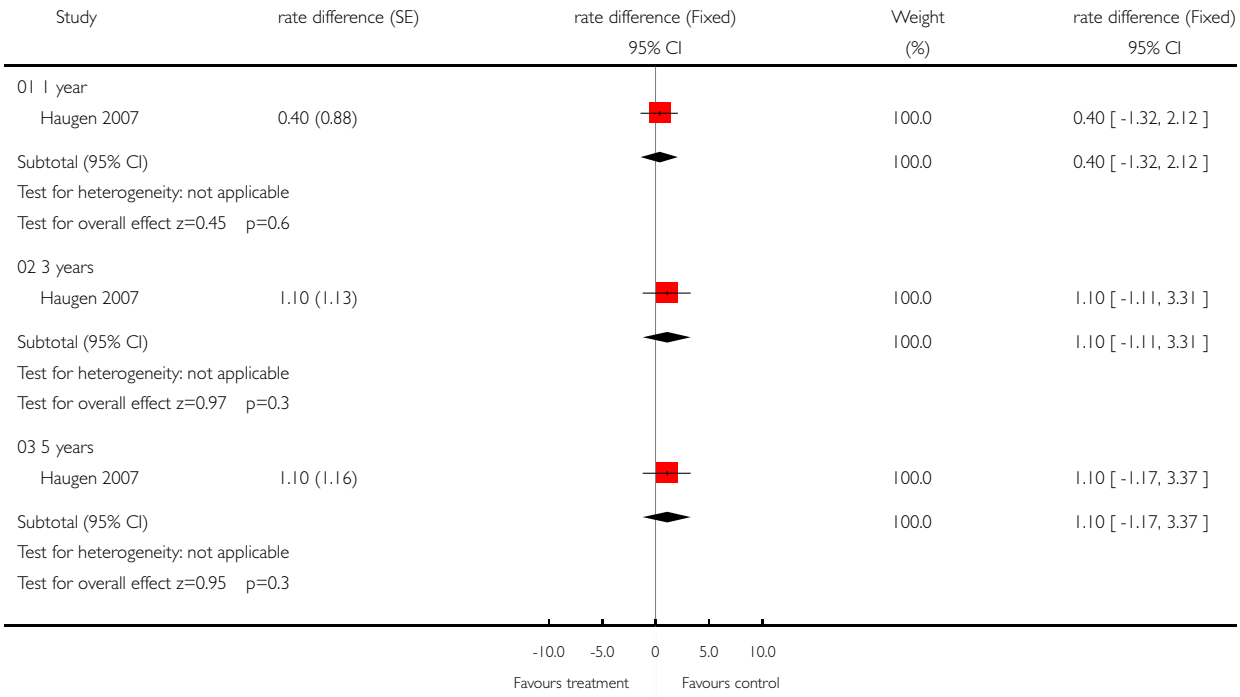


Analysis 08.02. Comparison 08 NovaT380 vs TCu380S, Outcome 02 Expulsion (full)

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 08 NovaT380 vs TCu380S

Outcome: 02 Expulsion (full)



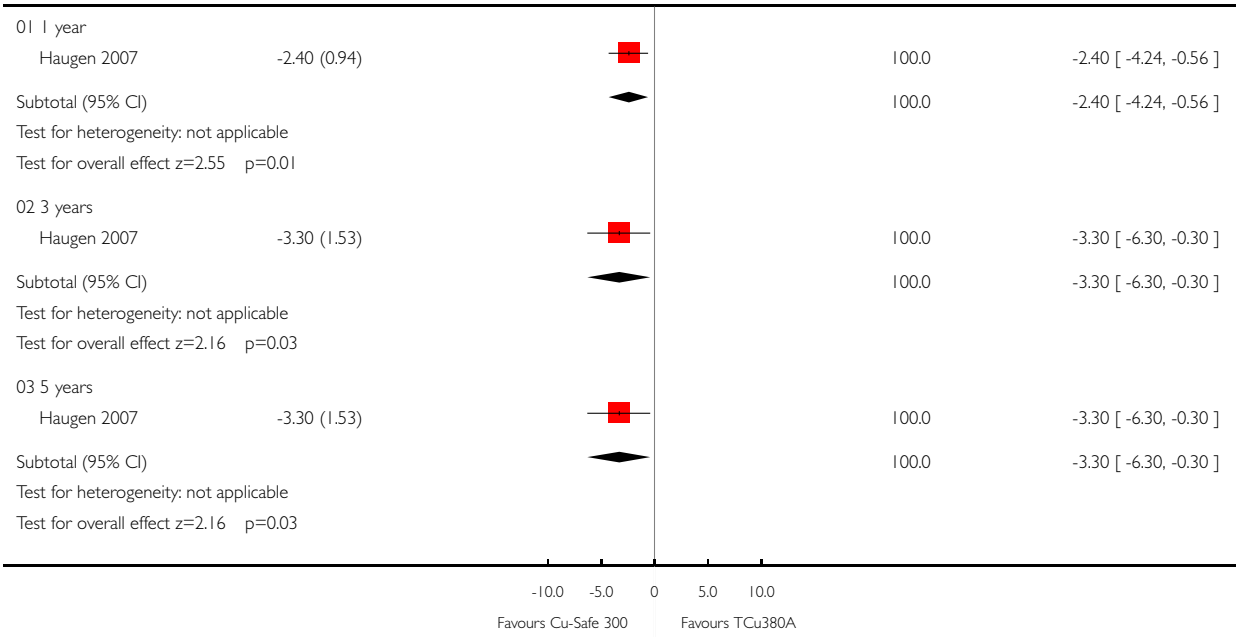
Analysis 08.03. Comparison 08 NovaT380 vs TCu380S, Outcome 03 Expulsion (partial)

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 08 NovaT380 vs TCu380S

Outcome: 03 Expulsion (partial)

Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
Haugen 2007	-2.40 (0.94)		100.0	-2.40 [-4.24, -0.56]
Subtotal (95% CI)			100.0	-2.40 [-4.24, -0.56]
Test for heterogeneity: not applicable				
Test for overall effect z=2.55 p=0.01				
02 3 years				
Haugen 2007	-3.30 (1.53)		100.0	-3.30 [-6.30, -0.30]
Subtotal (95% CI)			100.0	-3.30 [-6.30, -0.30]
Test for heterogeneity: not applicable				
Test for overall effect z=2.16 p=0.03				
03 5 years				
Haugen 2007	-3.30 (1.53)		100.0	-3.30 [-6.30, -0.30]
Subtotal (95% CI)			100.0	-3.30 [-6.30, -0.30]
Test for heterogeneity: not applicable				
Test for overall effect z=2.16 p=0.03				

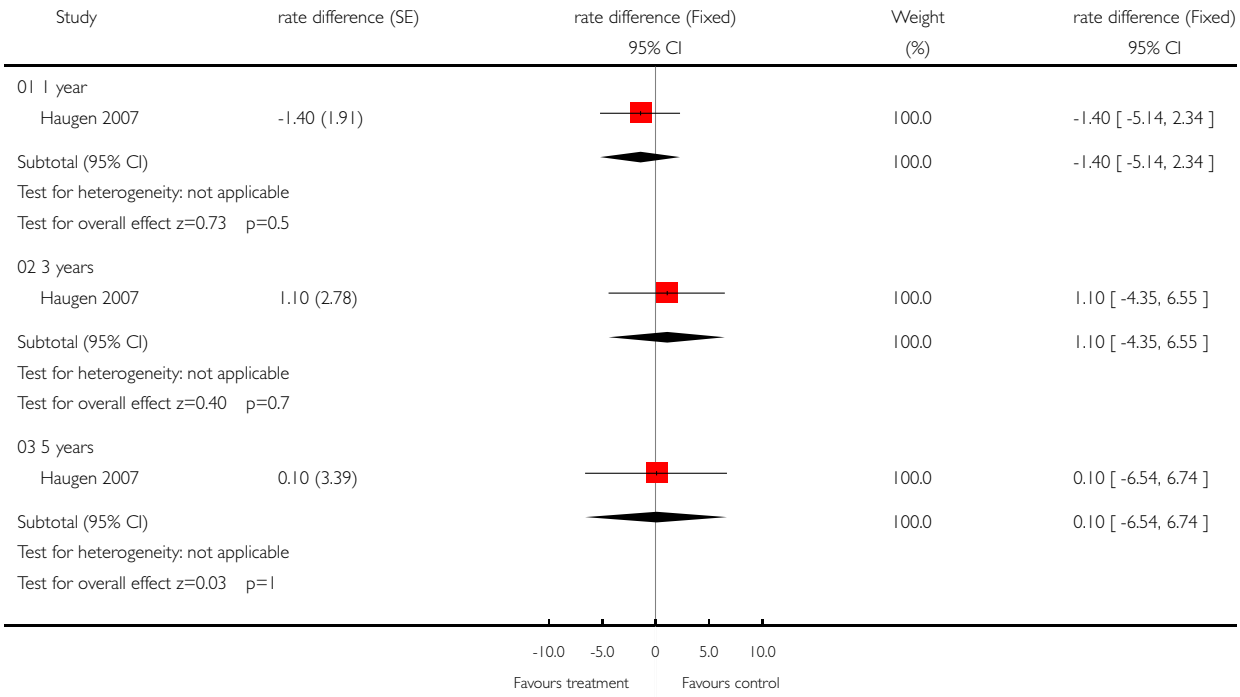


Analysis 08.04. Comparison 08 NovaT380 vs TCu380S, Outcome 04 Discontinuation: bleeding

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 08 NovaT380 vs TCu380S

Outcome: 04 Discontinuation: bleeding

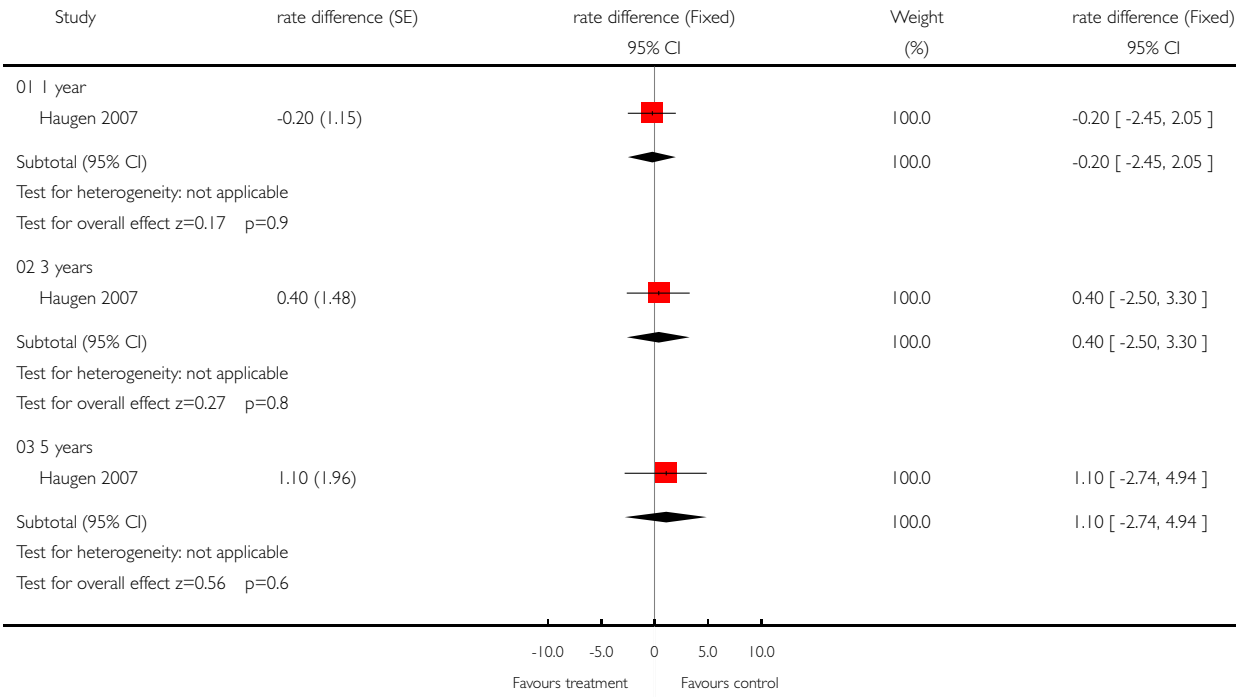


Analysis 08.05. Comparison 08 NovaT380 vs TCu380S, Outcome 05 Discontinuation: pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 08 NovaT380 vs TCu380S

Outcome: 05 Discontinuation: pain

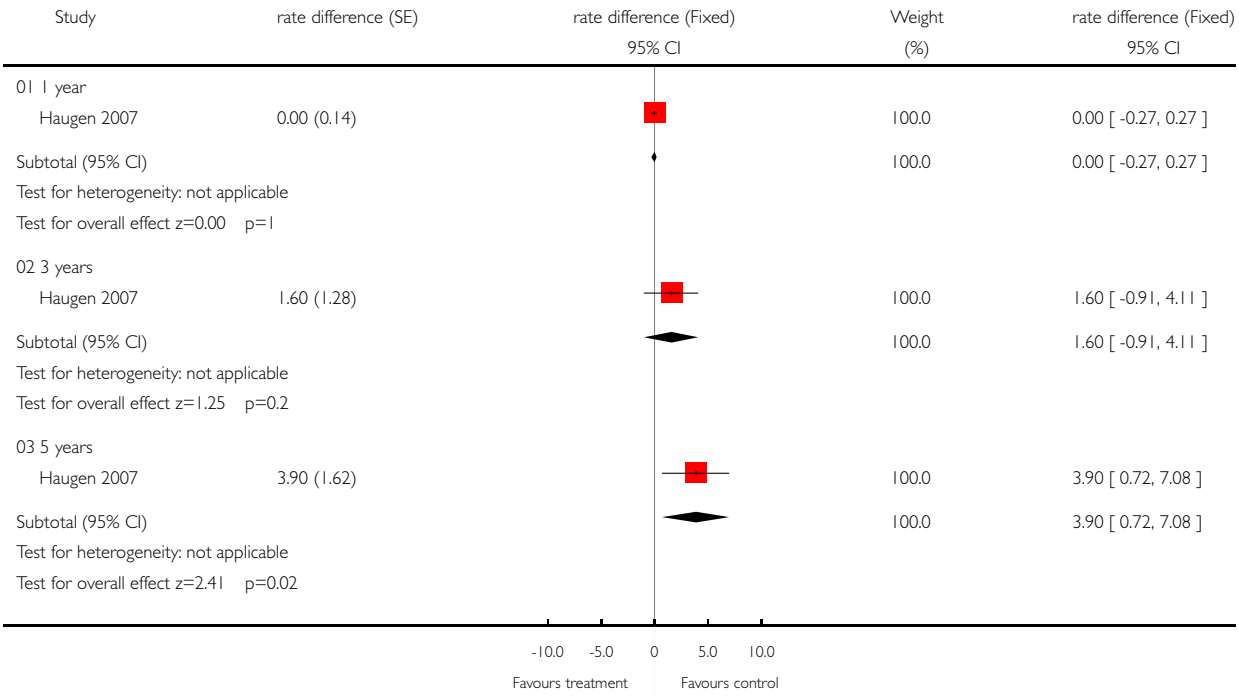


Analysis 08.06. Comparison 08 NovaT380 vs TCu380S, Outcome 06 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 08 NovaT380 vs TCu380S

Outcome: 06 Discontinuation: other medical reasons

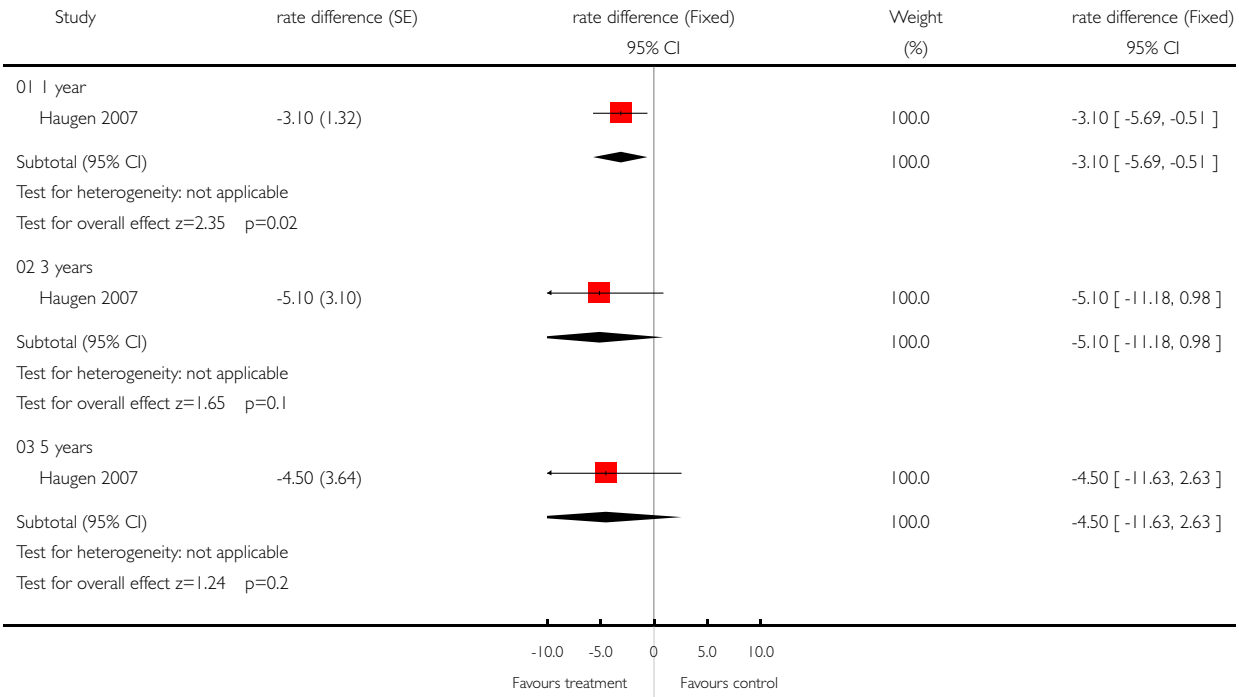


Analysis 08.07. Comparison 08 NovaT380 vs TCu380S, Outcome 07 Discontinuation: other personal reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 08 NovaT380 vs TCu380S

Outcome: 07 Discontinuation: other personal reasons

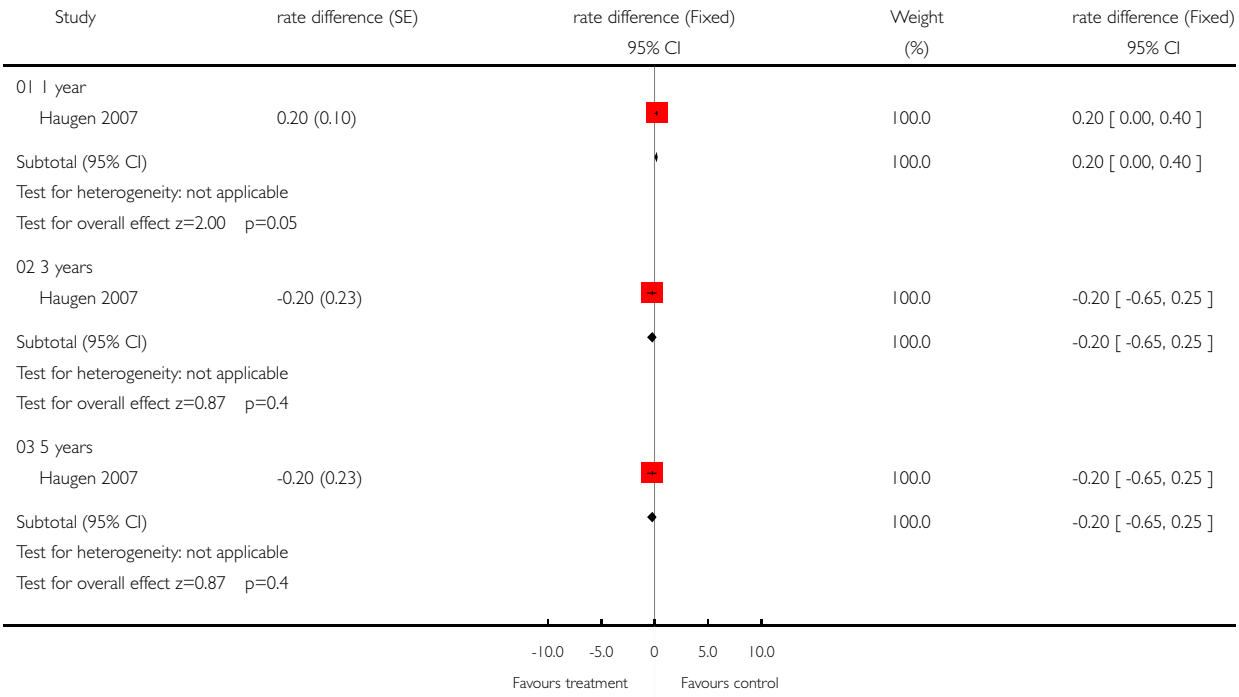


Analysis 08.08. Comparison 08 NovaT380 vs TCu380S, Outcome 08 Discontinuation: Infection/PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 08 NovaT380 vs TCu380S

Outcome: 08 Discontinuation: Infection/PID

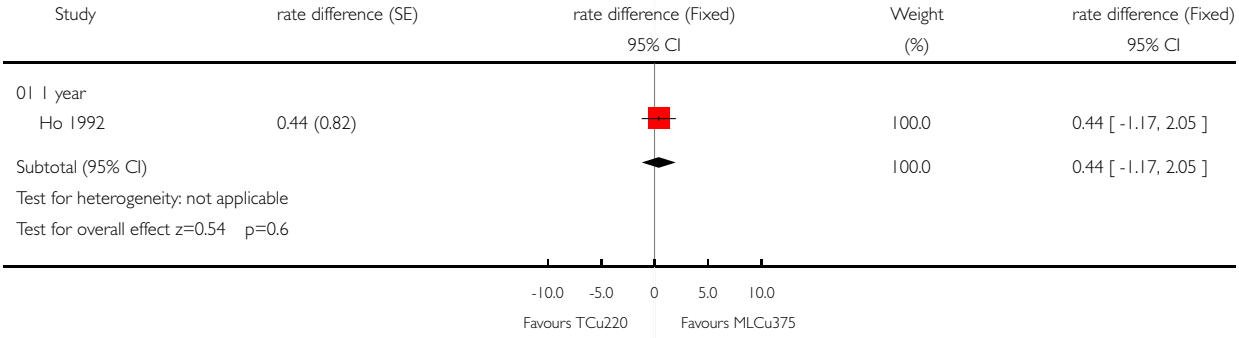


Analysis 09.01. Comparison 09 TCu220 vs MLCu375, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 09 TCu220 vs MLCu375

Outcome: 01 Pregnancy

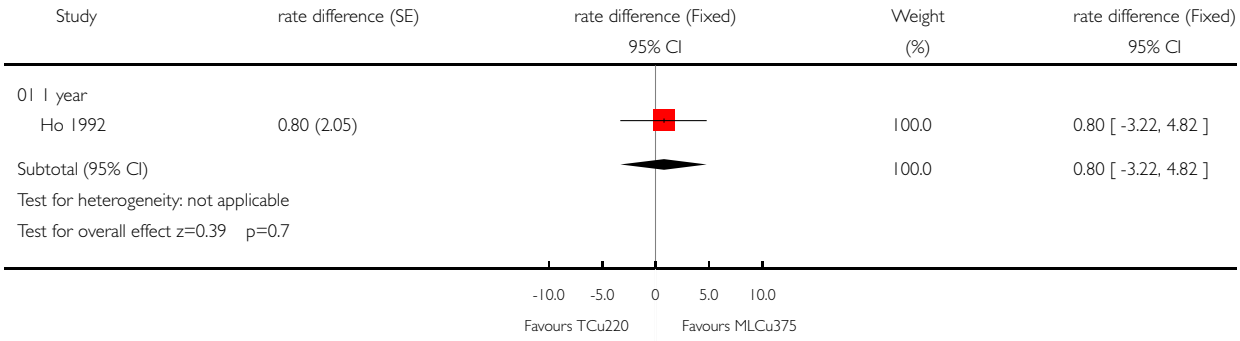


Analysis 09.02. Comparison 09 TCu220 vs MLCu375, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 09 TCu220 vs MLCu375

Outcome: 02 Expulsion

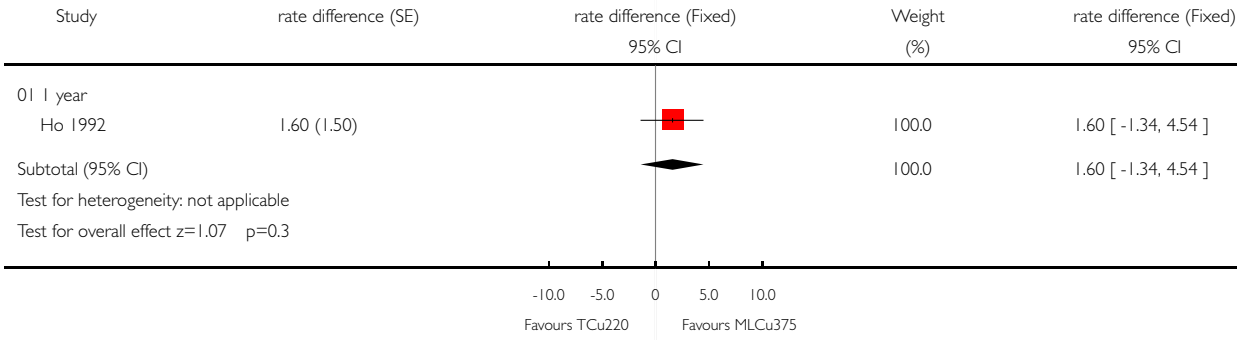


Analysis 09.03. Comparison 09 TCu220 vs MLCu375, Outcome 03 Discontinuation: total medical

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 09 TCu220 vs MLCu375

Outcome: 03 Discontinuation: total medical

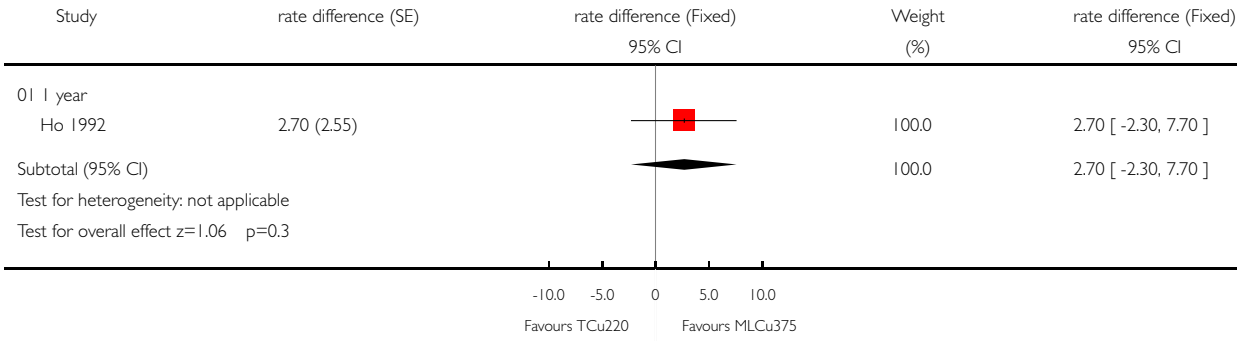


Analysis 09.04. Comparison 09 TCu220 vs MLCu375, Outcome 04 Discontinuation: total use related

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 09 TCu220 vs MLCu375

Outcome: 04 Discontinuation: total use related

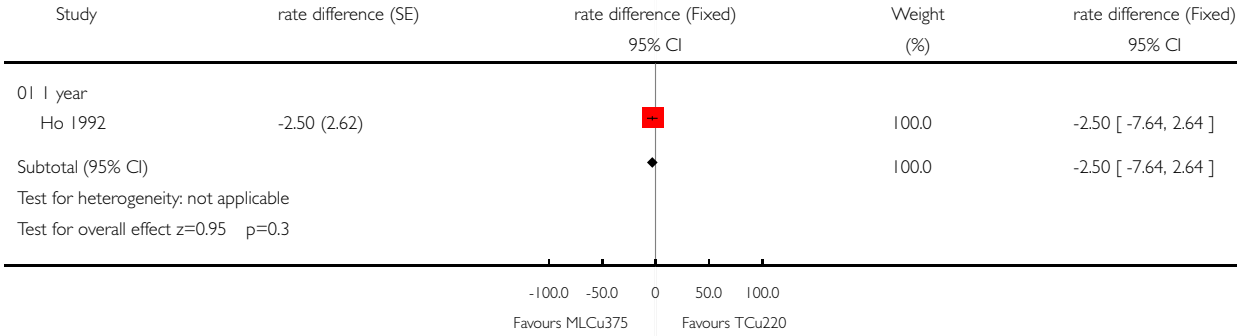


Analysis 09.05. Comparison 09 TCu220 vs MLCu375, Outcome 05 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 09 TCu220 vs MLCu375

Outcome: 05 Continuation

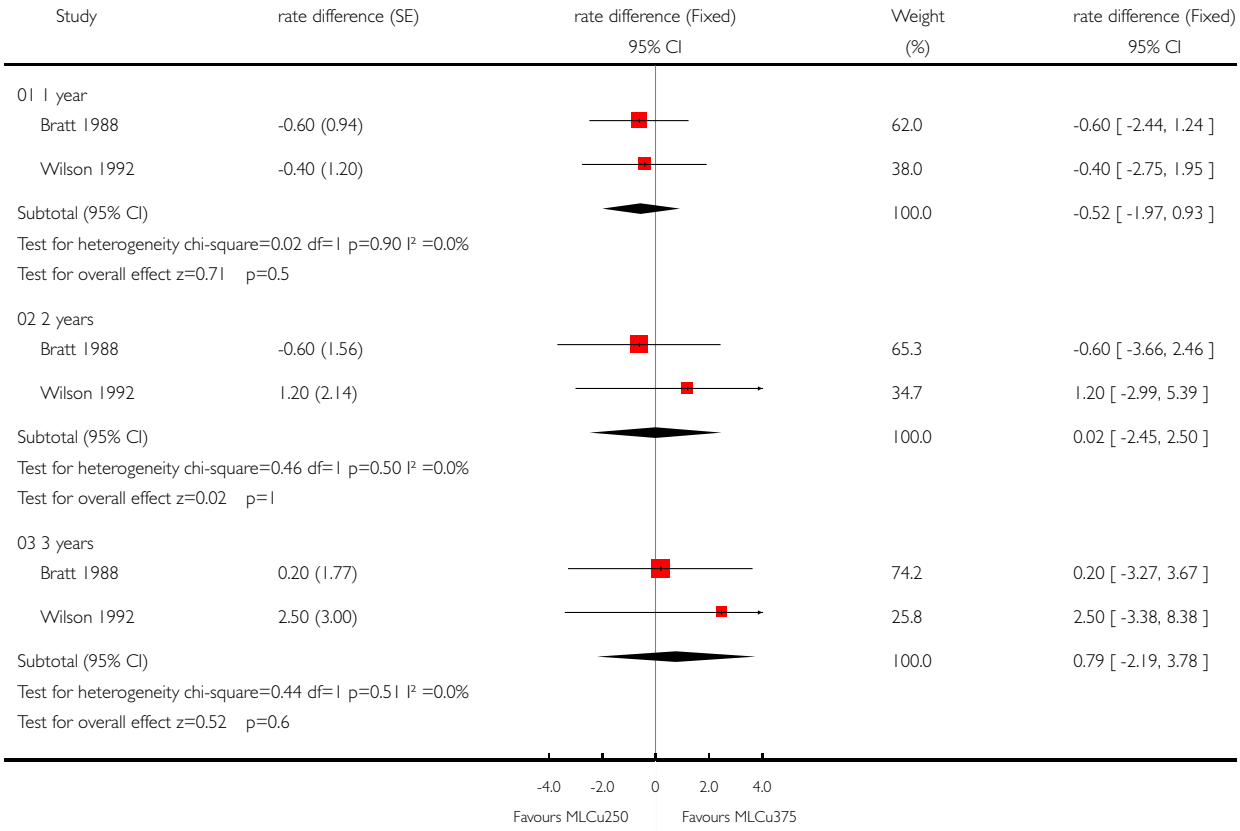


Analysis 10.01. Comparison 10 MLCu250 vs MLCu375, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 10 MLCu250 vs MLCu375

Outcome: 01 Pregnancy

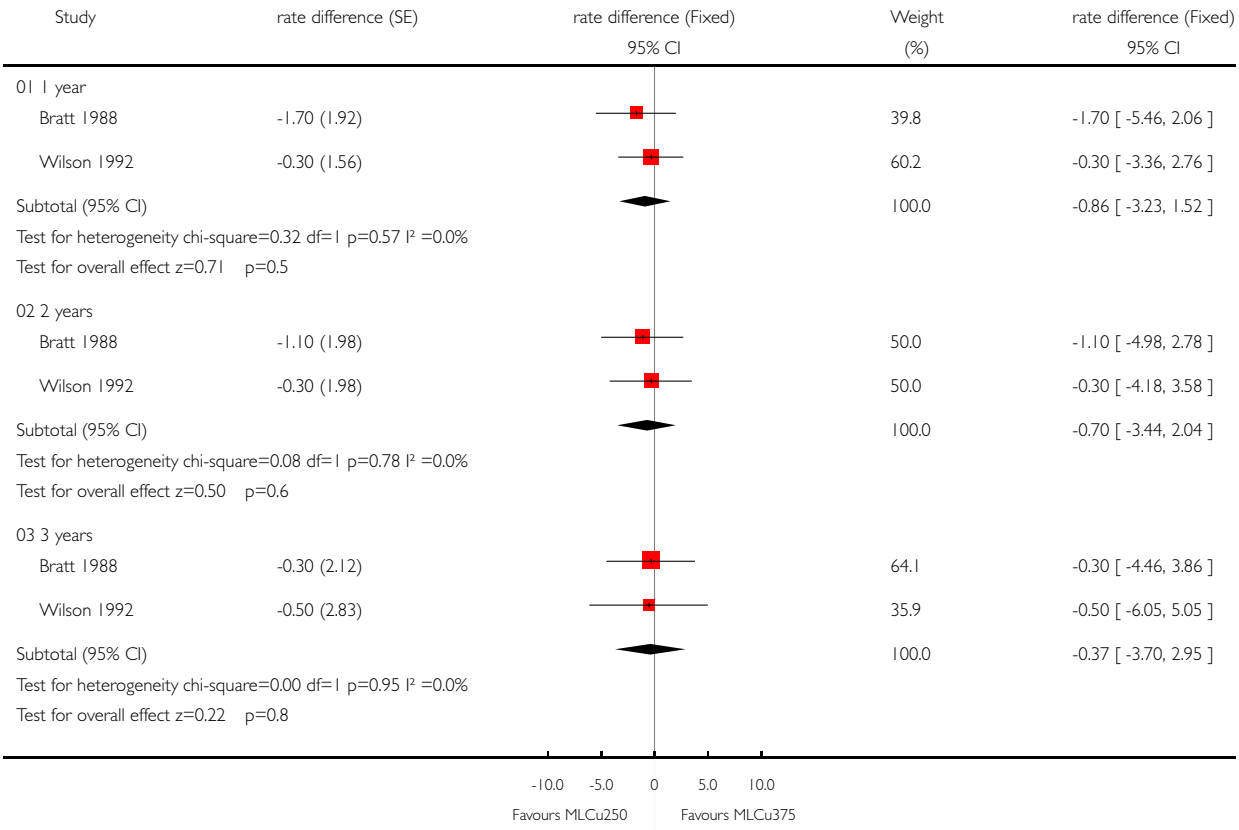


Analysis 10.02. Comparison 10 MLCu250 vs MLCu375, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 10 MLCu250 vs MLCu375

Outcome: 02 Expulsion

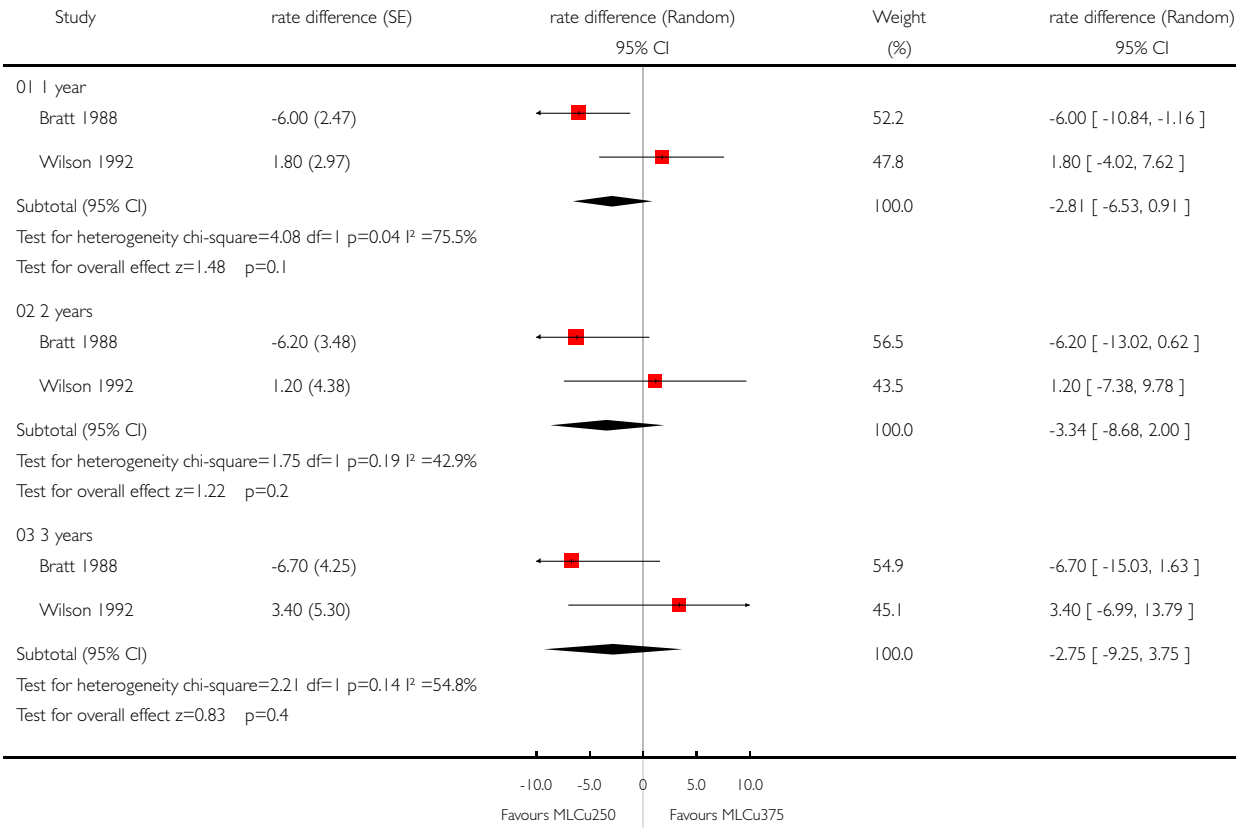


Analysis 10.03. Comparison 10 MLCu250 vs MLCu375, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 10 MLCu250 vs MLCu375

Outcome: 03 Discontinuation: bleeding and pain



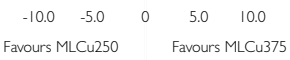
Analysis 10.04. Comparison 10 MLCu250 vs MLCu375, Outcome 04 Discontinuation: PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 10 MLCu250 vs MLCu375

Outcome: 04 Discontinuation: PID

Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
Bratt 1988	-1.10 (1.03)		52.4	-1.10 [-3.12, 0.92]
Wilson 1992	-0.60 (1.08)		47.6	-0.60 [-2.72, 1.52]
Subtotal (95% CI)			100.0	-0.86 [-2.32, 0.60]
Test for heterogeneity chi-square=0.11 df=1 p=0.74 I^2 =0.0%				
Test for overall effect z=1.16 p=0.2				
02 2 years				
Bratt 1988	-1.10 (1.36)		57.4	-1.10 [-3.77, 1.57]
Wilson 1992	-0.70 (1.58)		42.6	-0.70 [-3.80, 2.40]
Subtotal (95% CI)			100.0	-0.93 [-2.95, 1.09]
Test for heterogeneity chi-square=0.04 df=1 p=0.85 I^2 =0.0%				
Test for overall effect z=0.90 p=0.4				
03 3 years				
Bratt 1988	-1.10 (1.70)		52.0	-1.10 [-4.43, 2.23]
Wilson 1992	-0.10 (1.77)		48.0	-0.10 [-3.57, 3.37]
Subtotal (95% CI)			100.0	-0.62 [-3.02, 1.78]
Test for heterogeneity chi-square=0.17 df=1 p=0.68 I^2 =0.0%				
Test for overall effect z=0.51 p=0.6				

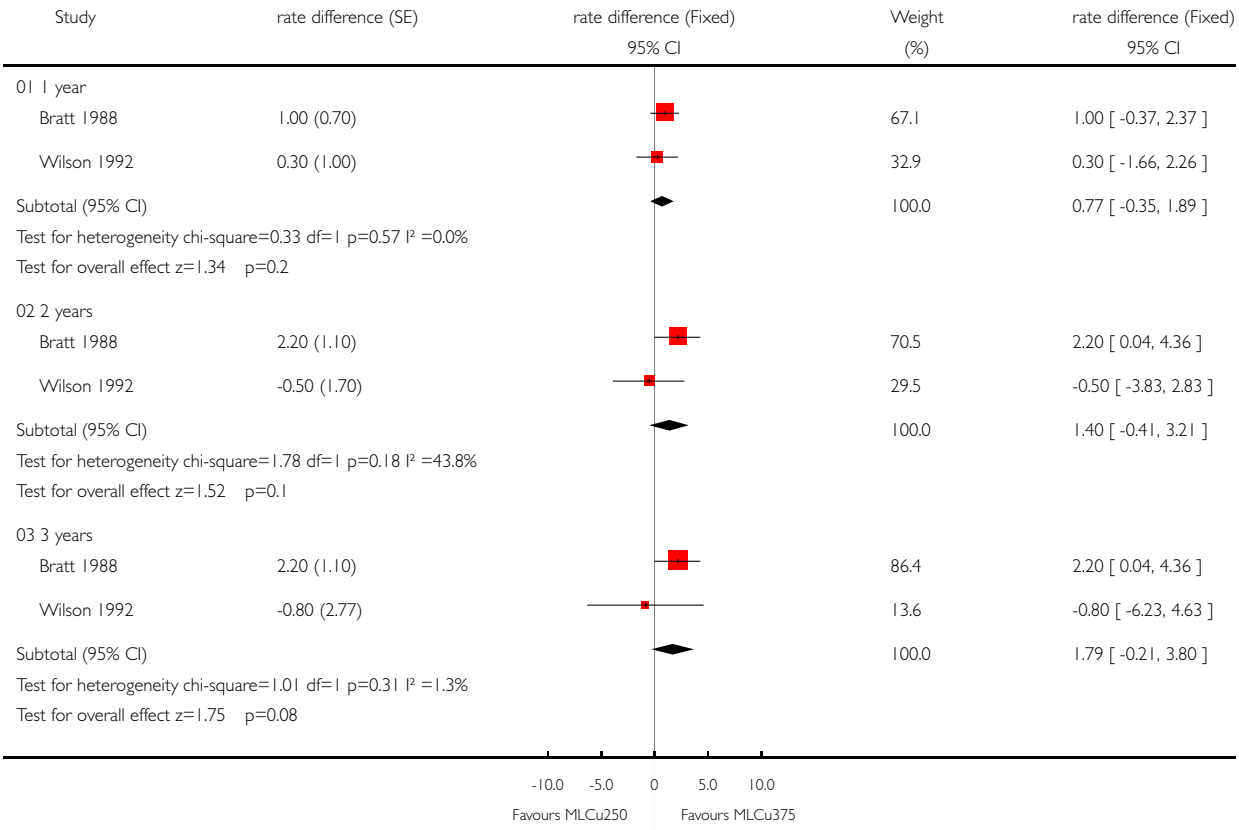


Analysis 10.05. Comparison 10 MLCu250 vs MLCu375, Outcome 05 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 10 MLCu250 vs MLCu375

Outcome: 05 Discontinuation: other medical reasons

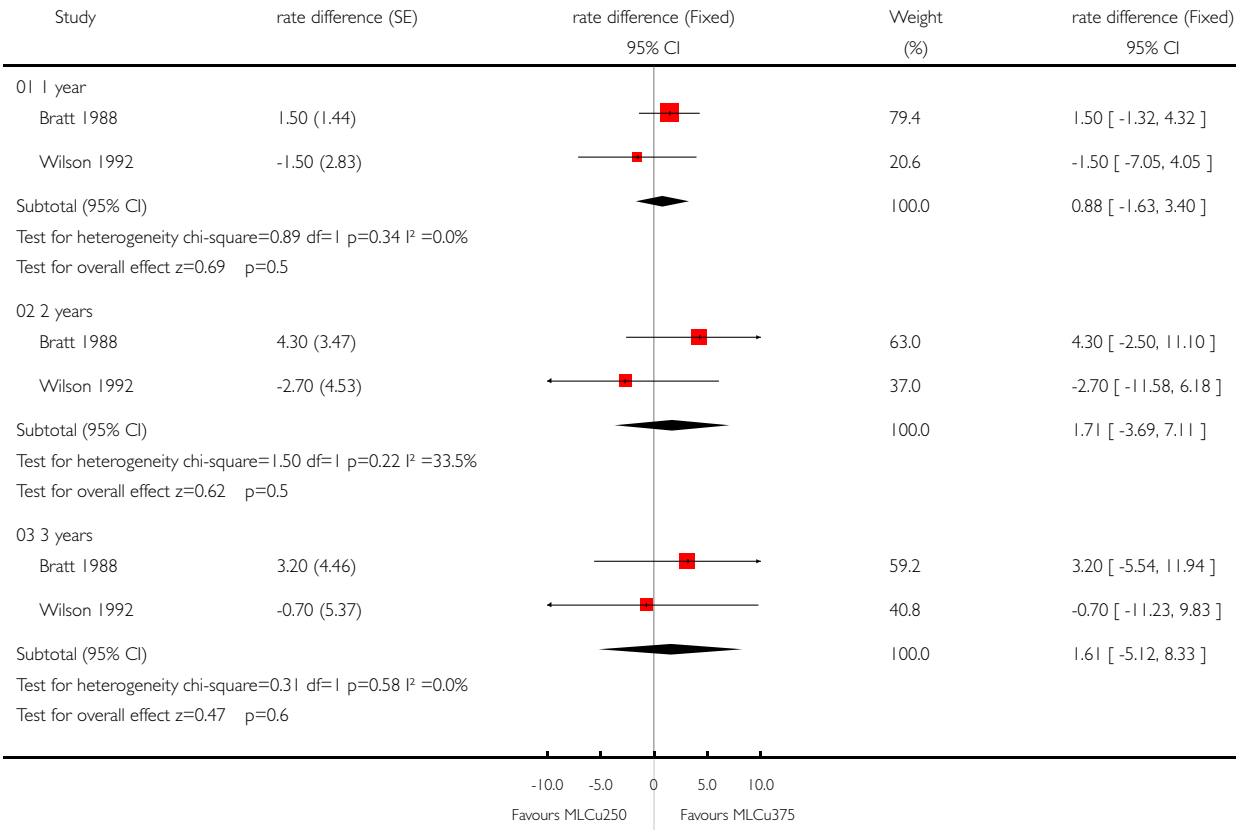


Analysis 10.06. Comparison 10 MLCu250 vs MLCu375, Outcome 06 Discontinuation: planned pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 10 MLCu250 vs MLCu375

Outcome: 06 Discontinuation: planned pregnancy

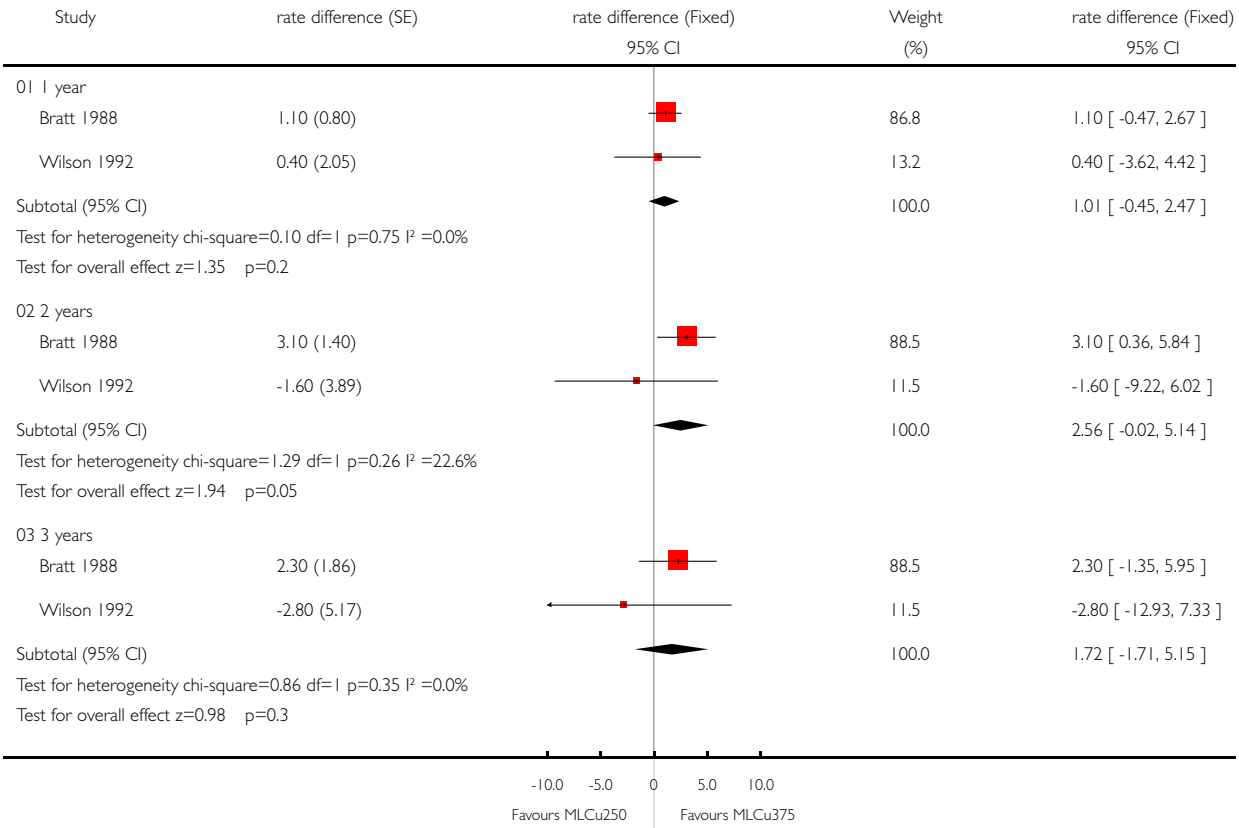


Analysis 10.07. Comparison 10 MLCu250 vs MLCu375, Outcome 07 Discontinuation: other personal reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 10 MLCu250 vs MLCu375

Outcome: 07 Discontinuation: other personal reasons

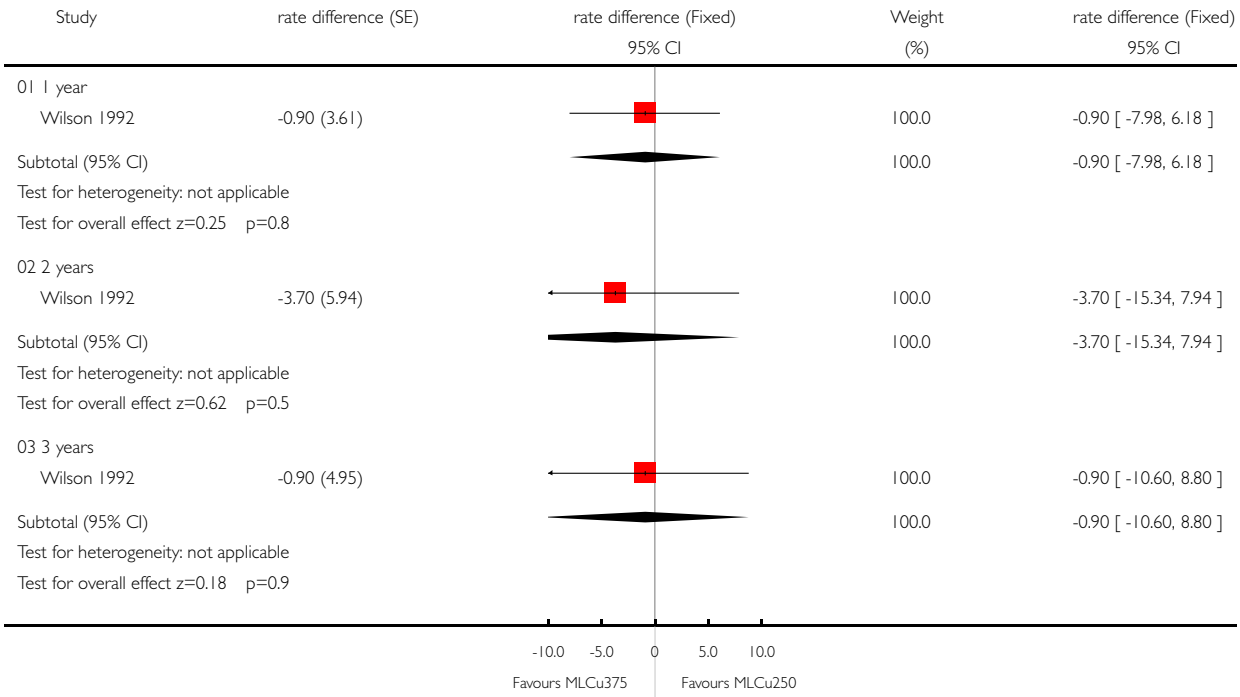


Analysis 10.08. Comparison 10 MLCu250 vs MLCu375, Outcome 08 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 10 MLCu250 vs MLCu375

Outcome: 08 Continuation



Analysis 11.01. Comparison 11 NovaT vs MLCu375, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 11 NovaT vs MLCu375

Outcome: 01 Pregnancy

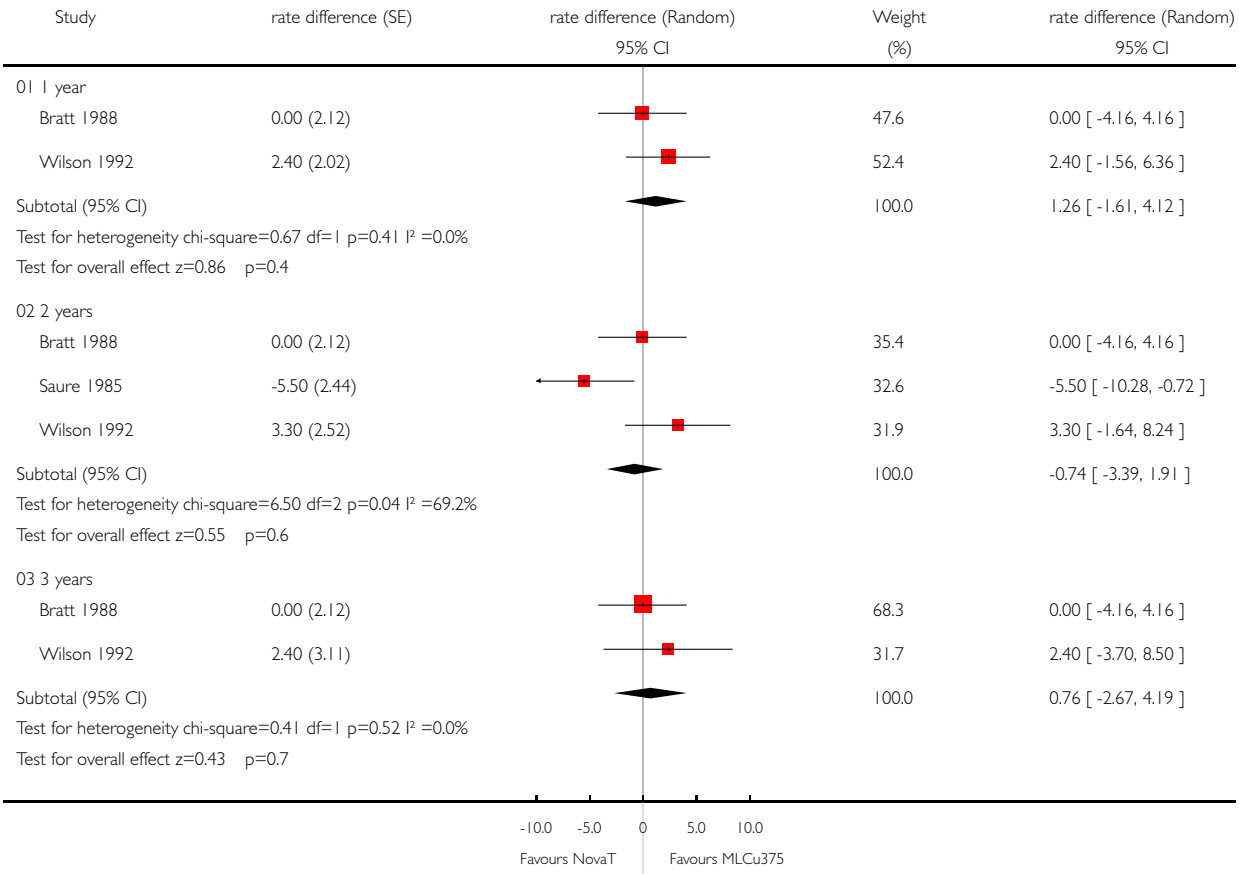
Study	rate difference (SE)	rate difference (Random) 95% CI	Weight (%)	rate difference (Random) 95% CI
01 1 year				
Bratt 1988	-0.50 (1.00)		34.2	-0.50 [-2.46, 1.46]
Saure 1985	1.70 (0.76)		46.7	1.70 [0.21, 3.19]
Wilson 1992	0.80 (1.50)		19.1	0.80 [-2.14, 3.74]
Subtotal (95% CI)			100.0	0.88 [-0.22, 1.98]
Test for heterogeneity chi-square=3.07 df=2 p=0.22 I^2 =34.9%				
Test for overall effect z=1.57 p=0.1				
02 2 years				
Bratt 1988	-1.10 (1.50)		27.6	-1.10 [-4.04, 1.84]
Saure 1985	1.40 (0.94)		58.8	1.40 [-0.44, 3.24]
Wilson 1992	2.00 (2.22)		13.5	2.00 [-2.35, 6.35]
Subtotal (95% CI)			100.0	0.84 [-0.63, 2.31]
Test for heterogeneity chi-square=2.30 df=2 p=0.32 I^2 =13.1%				
Test for overall effect z=1.13 p=0.3				
03 3 years				
Bratt 1988	-1.10 (1.50)		68.7	-1.10 [-4.04, 1.84]
Wilson 1992	3.30 (3.08)		31.3	3.30 [-2.74, 9.34]
Subtotal (95% CI)			100.0	-0.26 [-2.90, 2.39]
Test for heterogeneity chi-square=1.65 df=1 p=0.20 I^2 =39.4%				
Test for overall effect z=0.19 p=0.8				

Analysis 11.02. Comparison 11 NovaT vs MLCu375, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 11 NovaT vs MLCu375

Outcome: 02 Expulsion

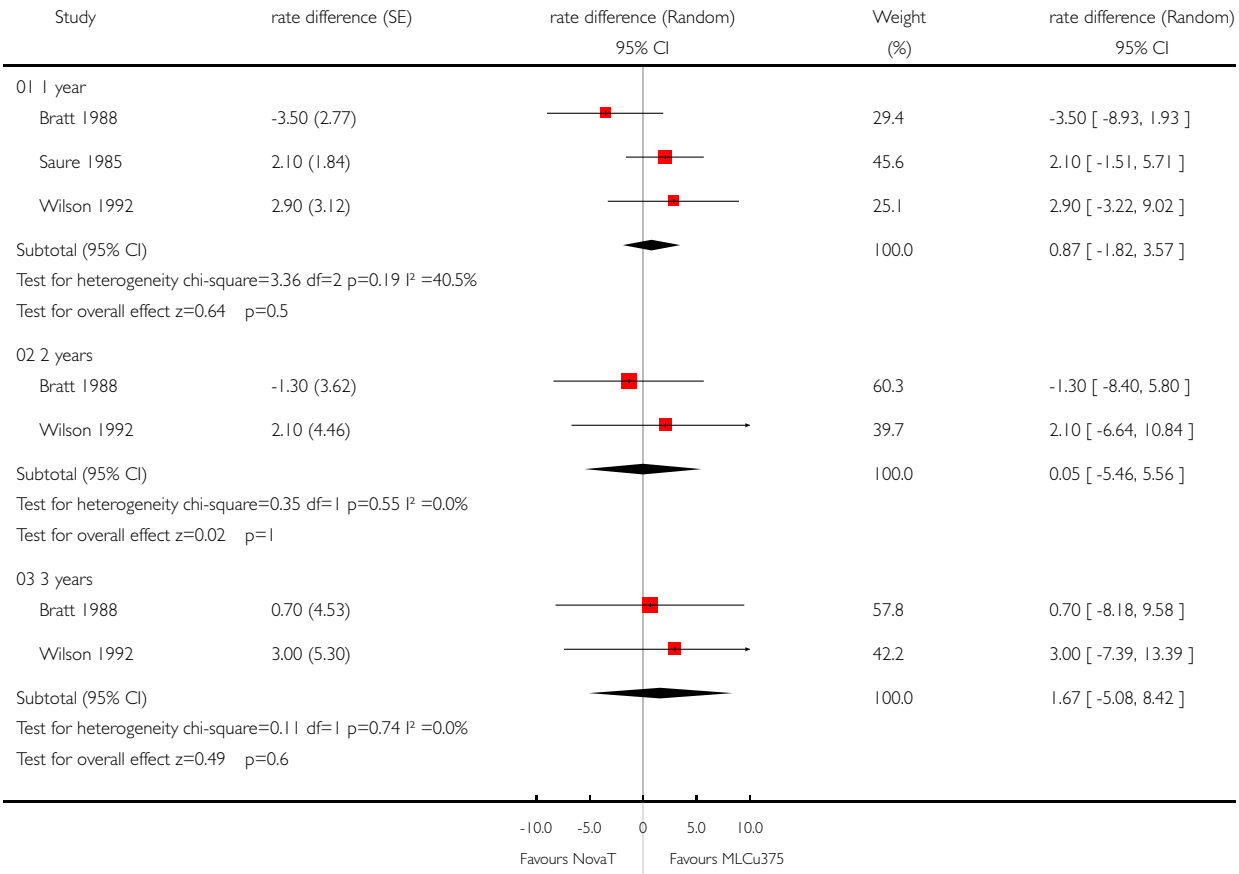


Analysis 11.03. Comparison 11 NovaT vs MLCu375, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 11 NovaT vs MLCu375

Outcome: 03 Discontinuation: bleeding and pain

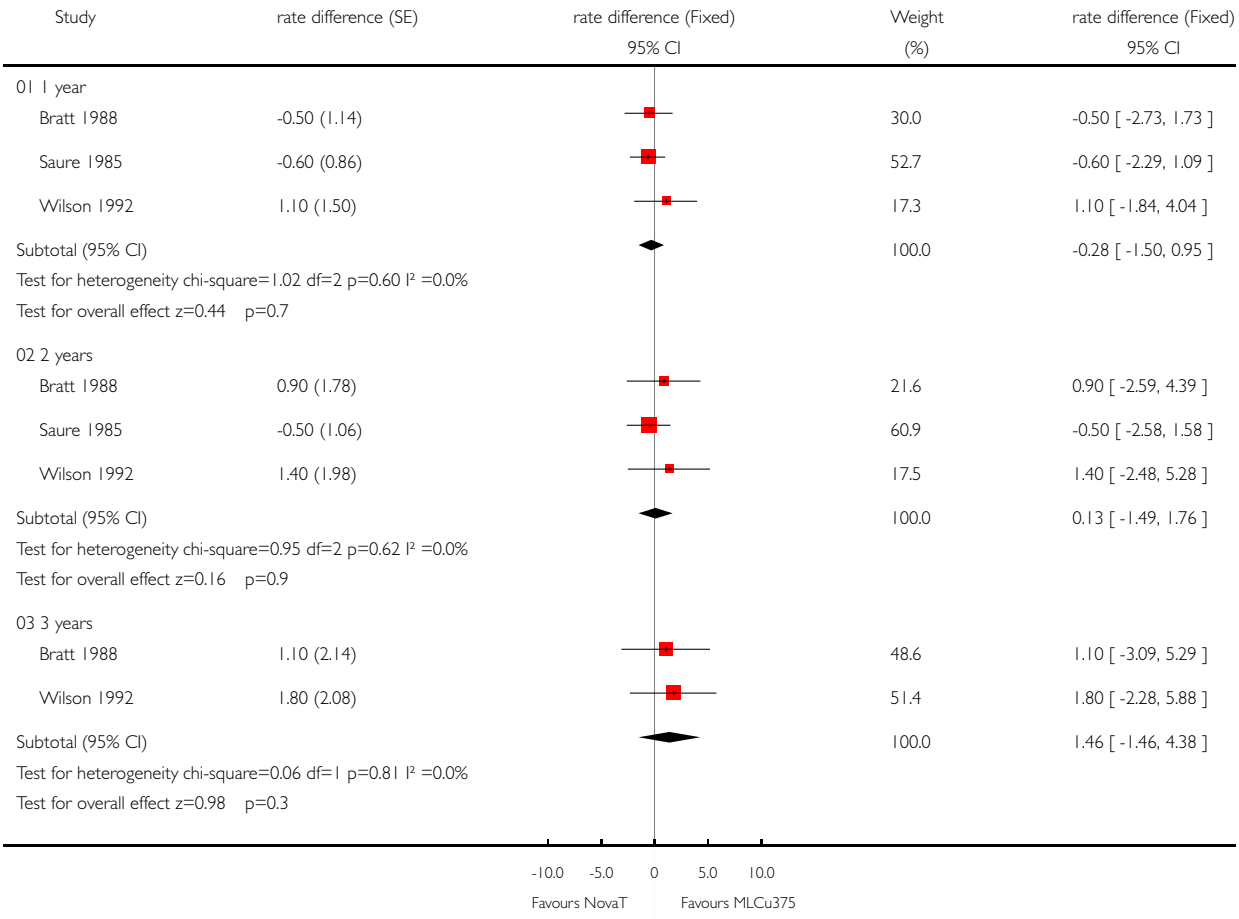


Analysis 11.04. Comparison 11 NovaT vs MLCu375, Outcome 04 Discontinuation: PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 11 NovaT vs MLCu375

Outcome: 04 Discontinuation: PID

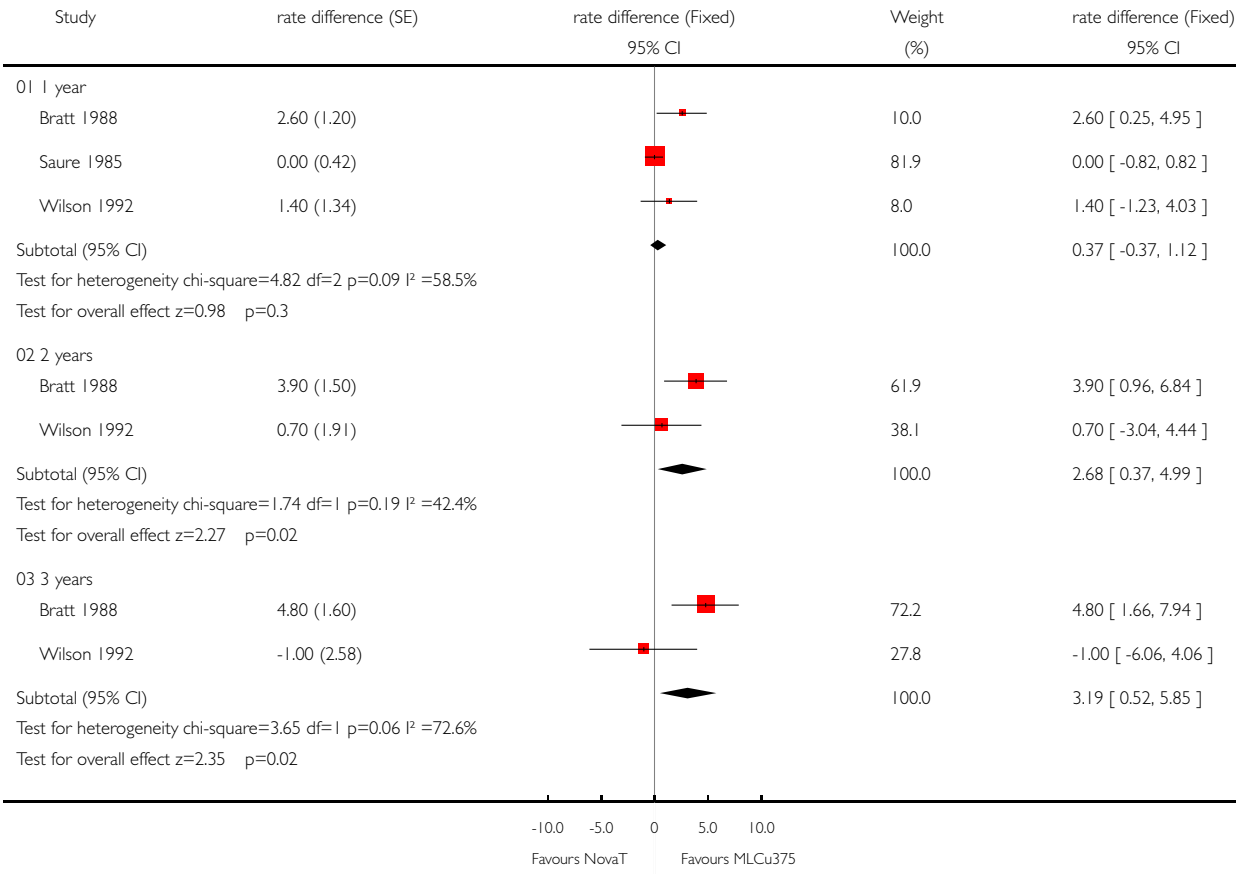


Analysis 11.05. Comparison 11 NovaT vs MLCu375, Outcome 05 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 11 NovaT vs MLCu375

Outcome: 05 Discontinuation: other medical reasons

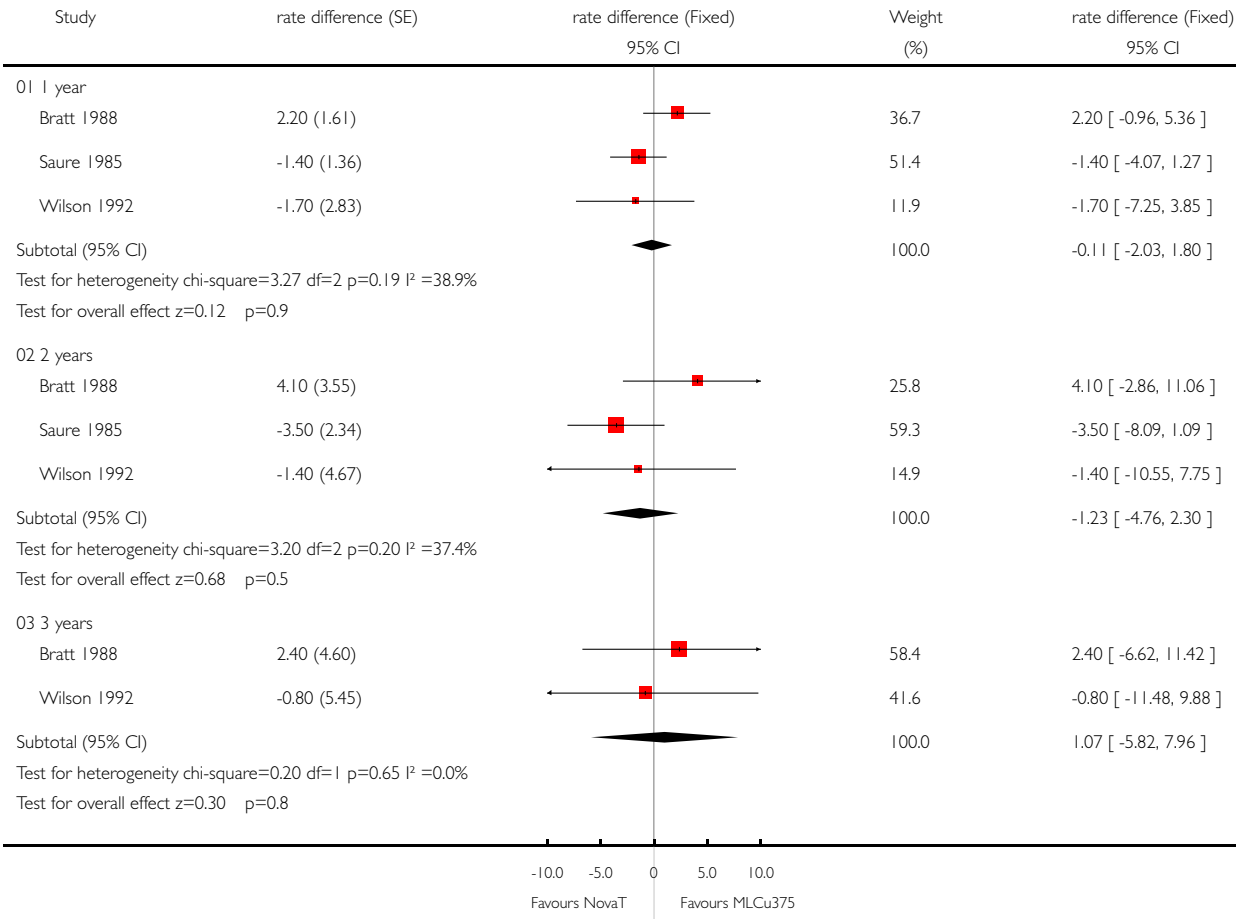


Analysis 11.06. Comparison 11 NovaT vs MLCu375, Outcome 06 Discontinuation: planned pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 11 NovaT vs MLCu375

Outcome: 06 Discontinuation: planned pregnancy

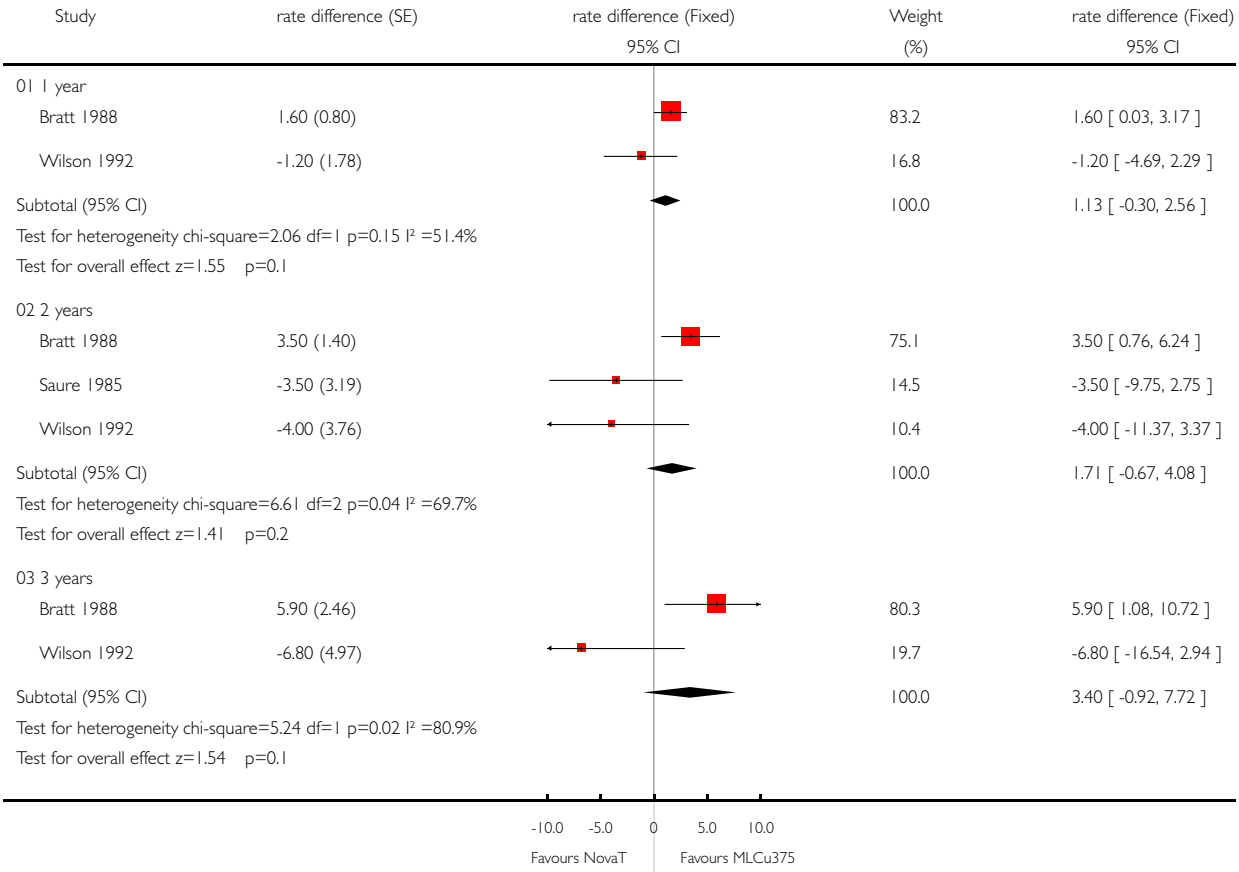


Analysis 11.07. Comparison 11 NovaT vs MLCu375, Outcome 07 Discontinuation: other personal reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 11 NovaT vs MLCu375

Outcome: 07 Discontinuation: other personal reasons

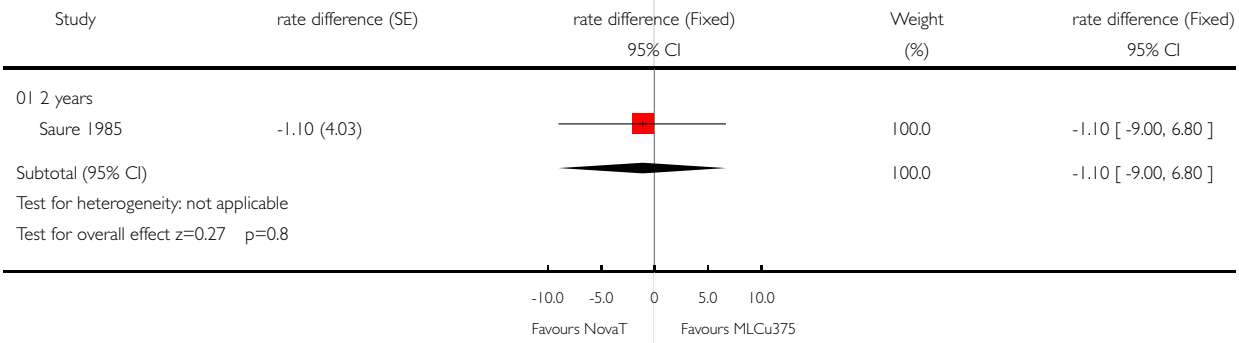


Analysis 11.08. Comparison 11 NovaT vs MLCu375, Outcome 08 Discontinuation: all

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 11 NovaT vs MLCu375

Outcome: 08 Discontinuation: all

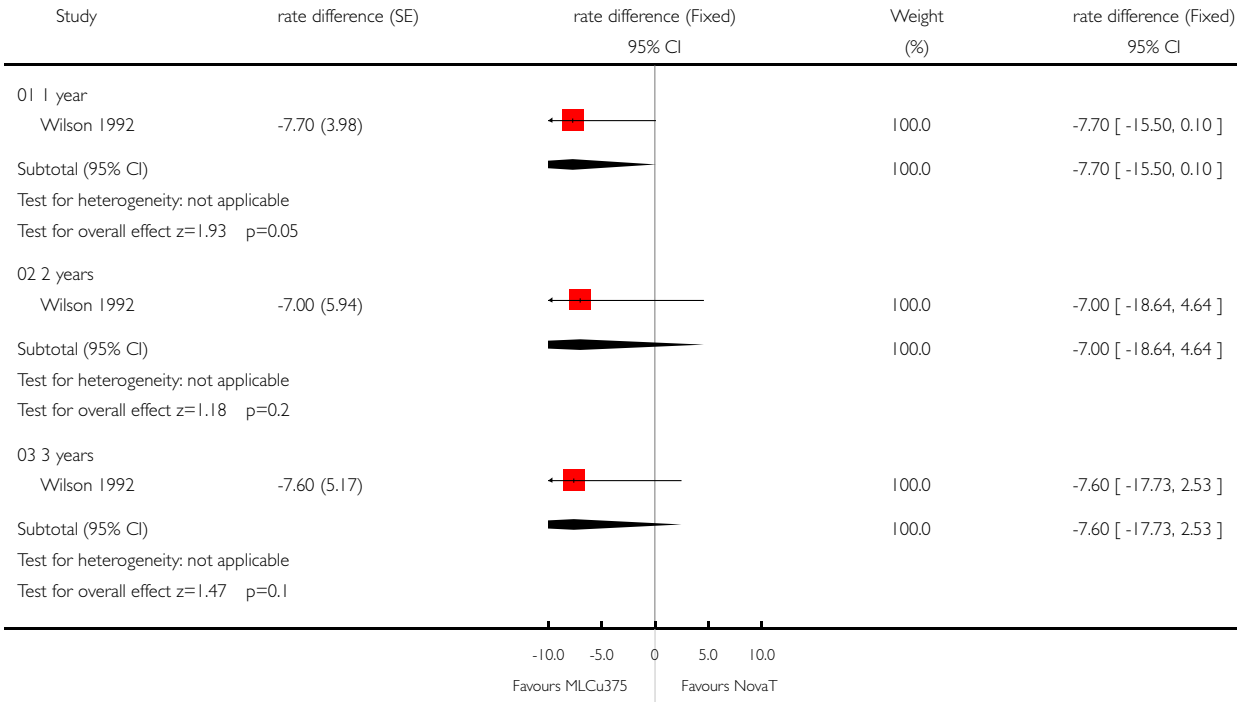


Analysis 11.09. Comparison 11 NovaT vs MLCu375, Outcome 09 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 11 NovaT vs MLCu375

Outcome: 09 Continuation

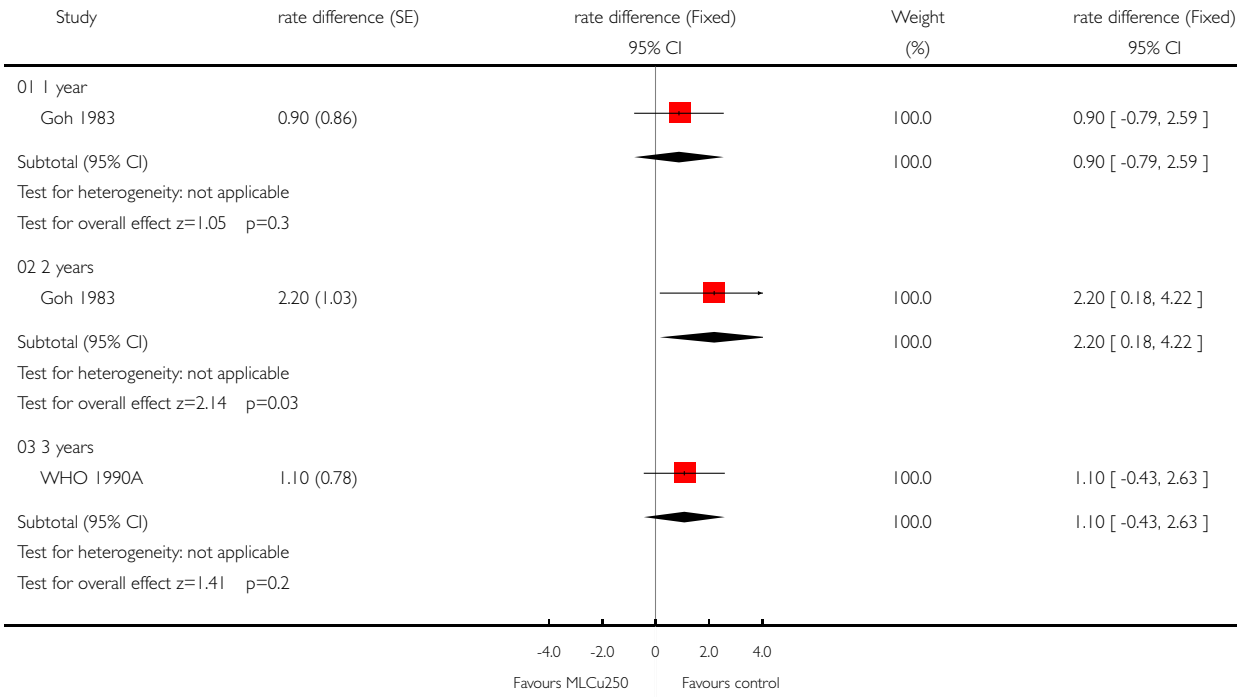


Analysis 12.01. Comparison 12 MLCu250 vs TCu220, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 12 MLCu250 vs TCu220

Outcome: 01 Pregnancy

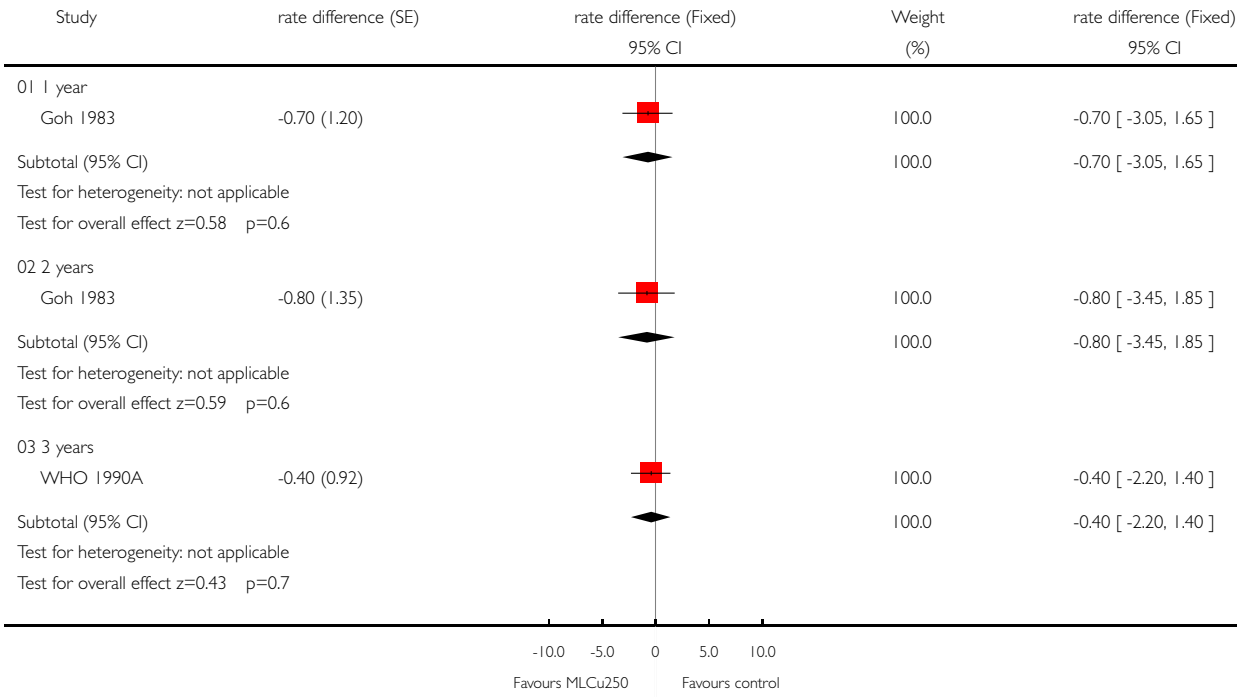


Analysis 12.02. Comparison 12 MLCu250 vs TCu220, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 12 MLCu250 vs TCu220

Outcome: 02 Expulsion

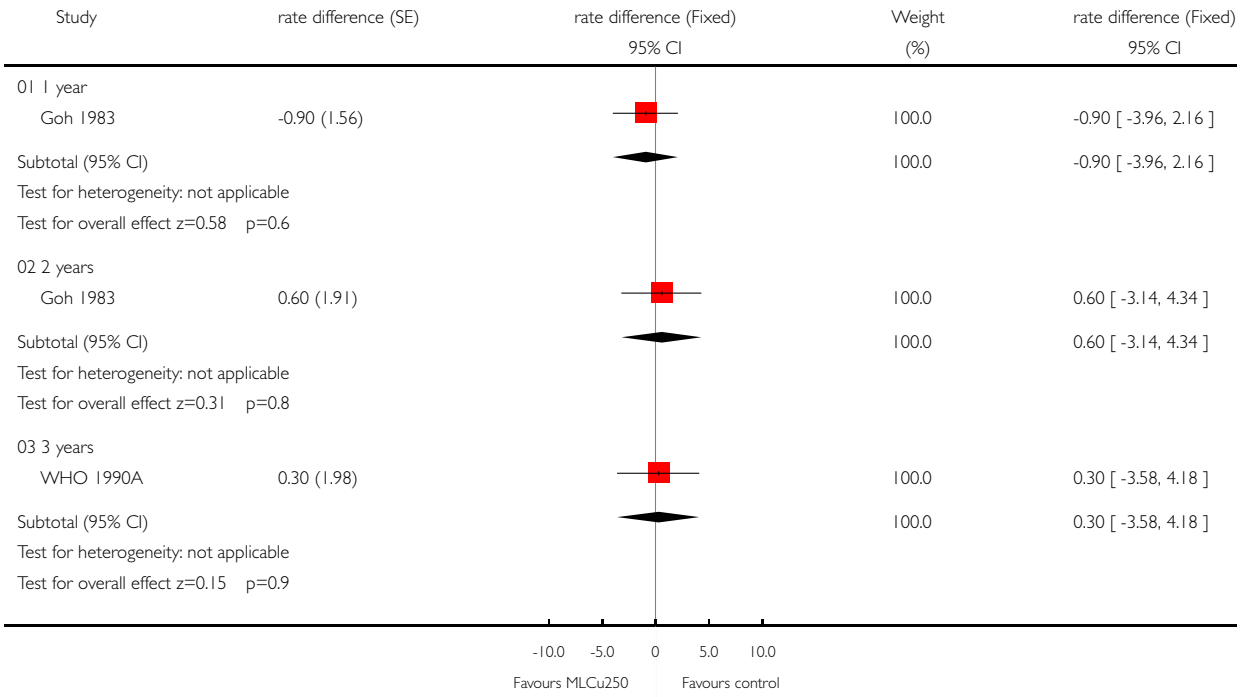


Analysis 12.03. Comparison 12 MLCu250 vs TCu220, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 12 MLCu250 vs TCu220

Outcome: 03 Discontinuation: bleeding and pain

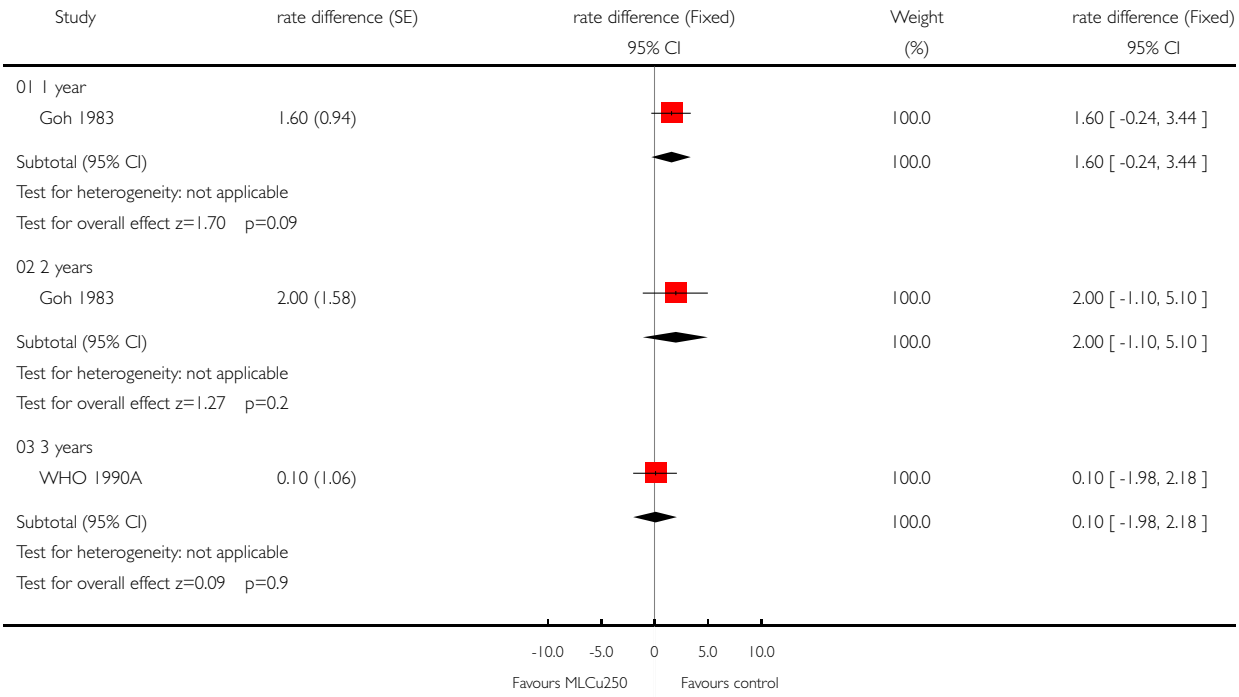


Analysis 12.04. Comparison 12 MLCu250 vs TCu220, Outcome 04 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 12 MLCu250 vs TCu220

Outcome: 04 Discontinuation: other medical reasons



Analysis 12.05. Comparison 12 MLCu250 vs TCu220, Outcome 05 Discontinuation: medical total

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 12 MLCu250 vs TCu220

Outcome: 05 Discontinuation: medical total

Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
Subtotal (95% CI)			0.0	Not estimable
Test for heterogeneity: not applicable				
Test for overall effect: not applicable				
02 2 years				
Subtotal (95% CI)			0.0	Not estimable
Test for heterogeneity: not applicable				
Test for overall effect: not applicable				
03 3 years				
WHO 1990A	0.40 (2.05)		100.0	0.40 [-3.62, 4.42]
Subtotal (95% CI)			100.0	0.40 [-3.62, 4.42]
Test for heterogeneity: not applicable				
Test for overall effect z=0.20 p=0.8				

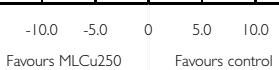
Analysis 12.06. Comparison 12 MLCu250 vs TCu220, Outcome 06 Discontinuation: non-medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 12 MLCu250 vs TCu220

Outcome: 06 Discontinuation: non-medical reasons

Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
Goh 1983	0.30 (0.92)		100.0	0.30 [-1.50, 2.10]
Subtotal (95% CI)			100.0	0.30 [-1.50, 2.10]
Test for heterogeneity: not applicable				
Test for overall effect z=0.33 p=0.7				
02 2 years				
Goh 1983	0.00 (1.28)		100.0	0.00 [-2.51, 2.51]
Subtotal (95% CI)			100.0	0.00 [-2.51, 2.51]
Test for heterogeneity: not applicable				
Test for overall effect z=0.00 p=1				
03 3 years				



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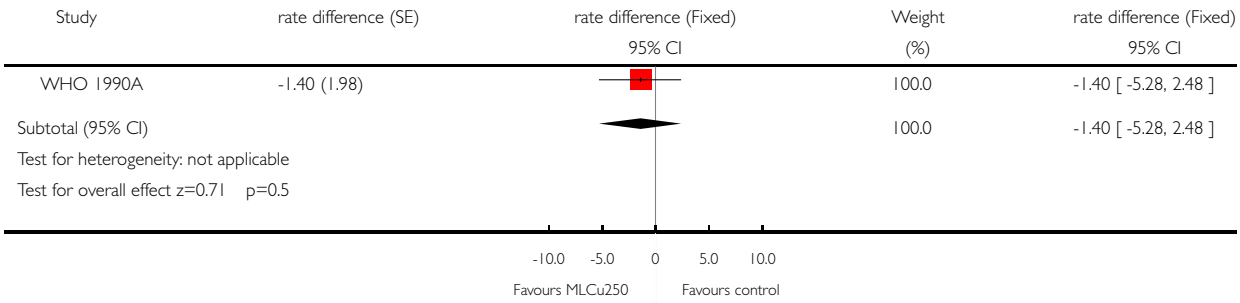
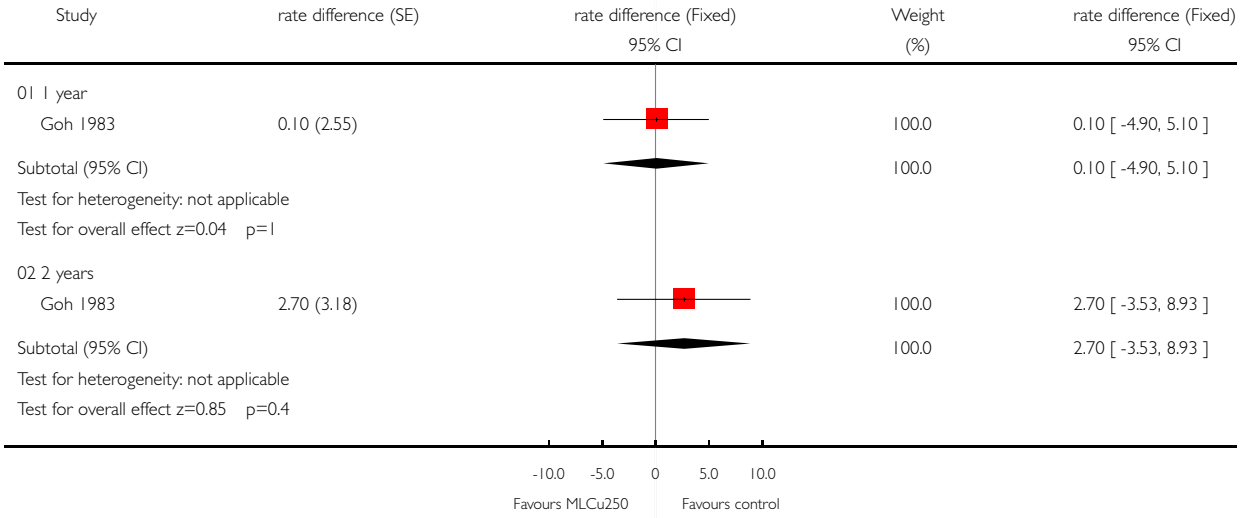


Analysis 12.07. Comparison 12 MLCu250 vs TCu220, Outcome 07 Discontinuation: total use related

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 12 MLCu250 vs TCu220

Outcome: 07 Discontinuation: total use related

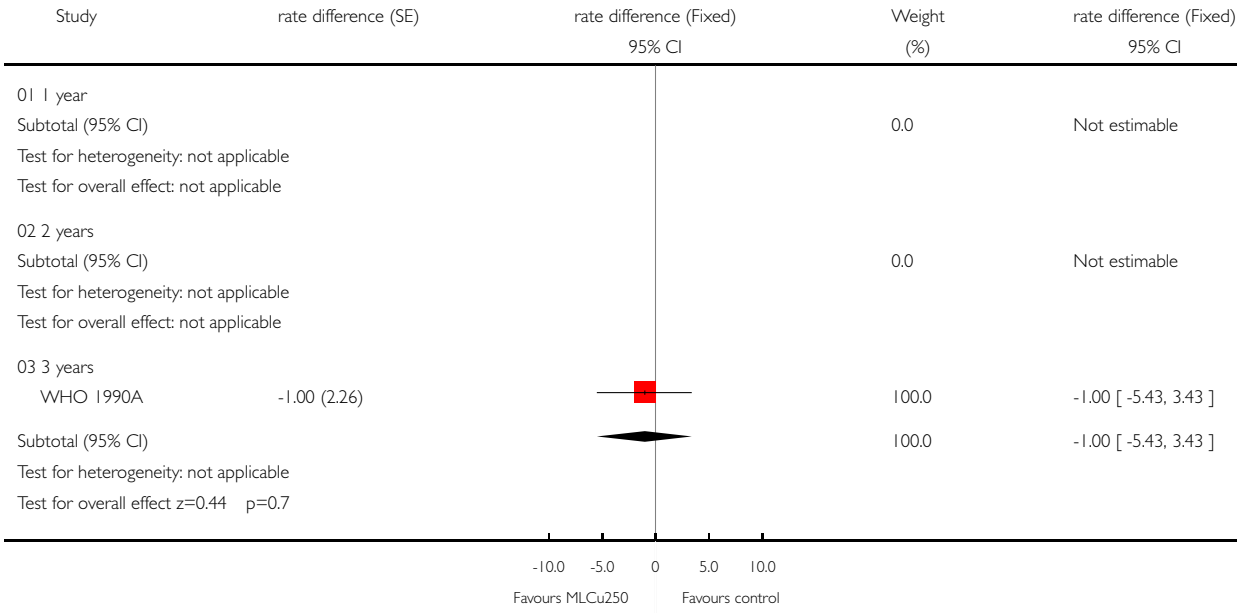


Analysis 12.08. Comparison 12 MLCu250 vs TCu220, Outcome 08 Discontinuation: all

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 12 MLCu250 vs TCu220

Outcome: 08 Discontinuation: all

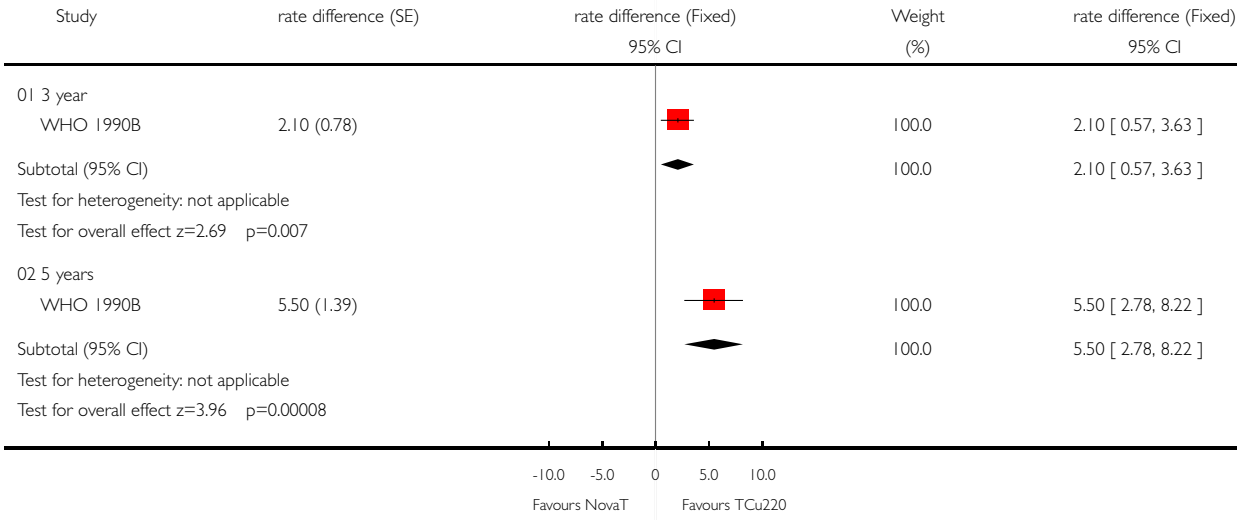


Analysis 13.01. Comparison 13 NovaT vs TCu220, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 01 Pregnancy

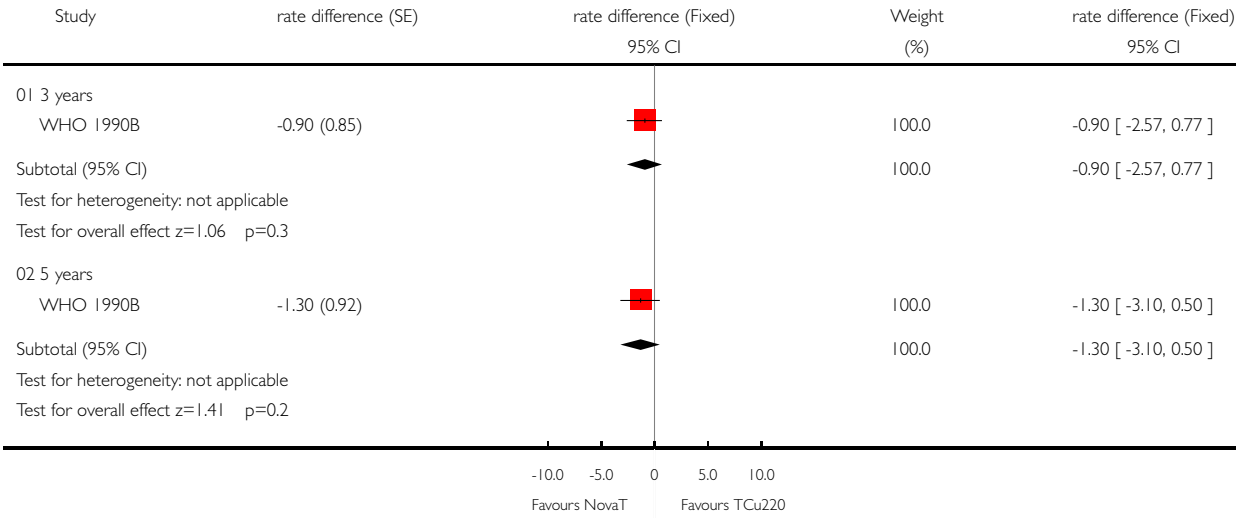


Analysis 13.02. Comparison 13 NovaT vs TCu220, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 02 Expulsion

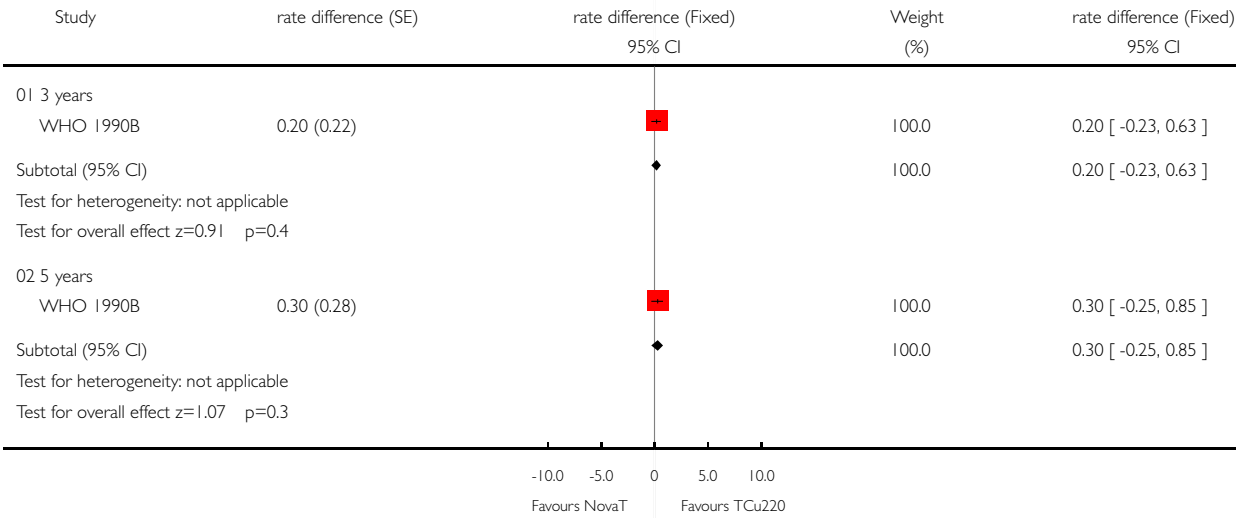


Analysis 13.03. Comparison 13 NovaT vs TCu220, Outcome 03 Ectopic pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 03 Ectopic pregnancy

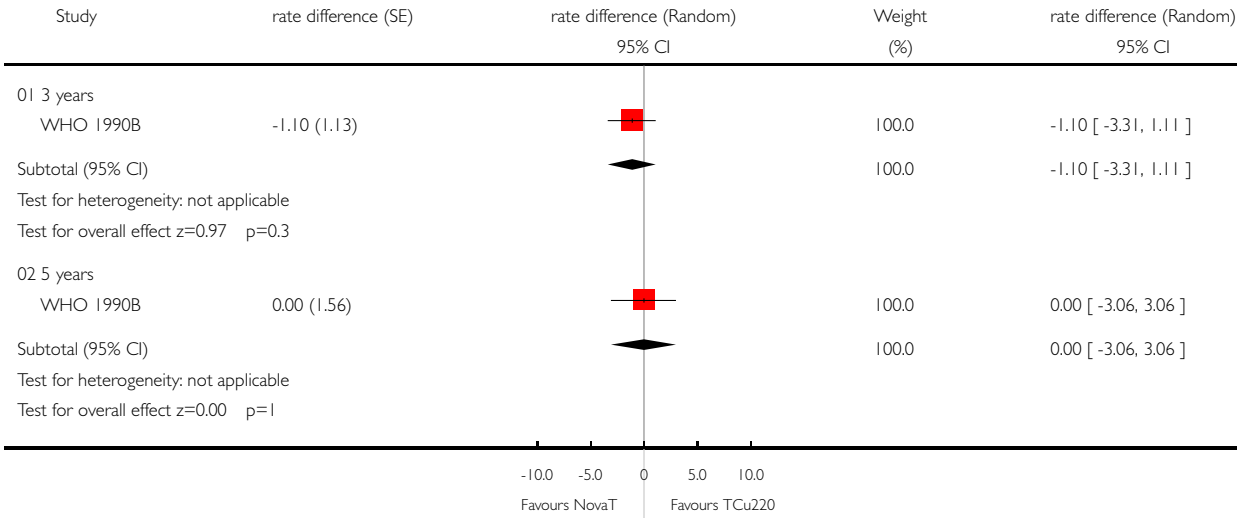


Analysis 13.04. Comparison 13 NovaT vs TCu220, Outcome 04 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 04 Discontinuation: bleeding and pain

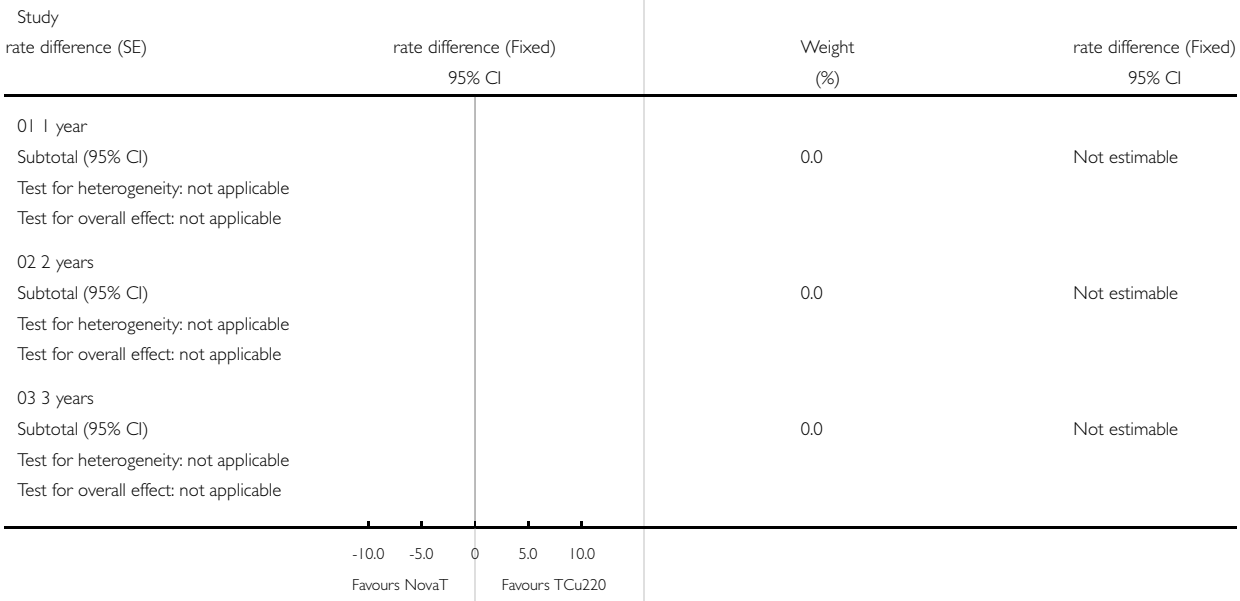


Analysis 13.05. Comparison 13 NovaT vs TCu220, Outcome 05 Discontinuation: intermenstrual bleeding

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 05 Discontinuation: intermenstrual bleeding

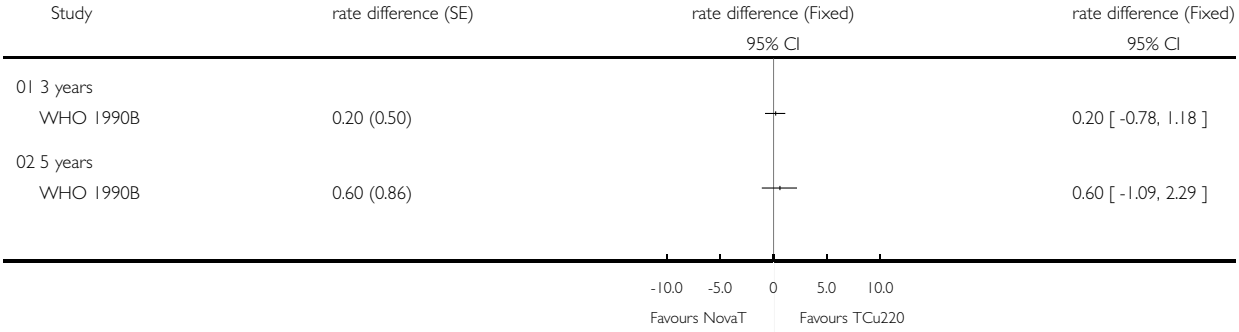


Analysis 13.06. Comparison 13 NovaT vs TCu220, Outcome 06 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 06 Discontinuation: other medical reasons

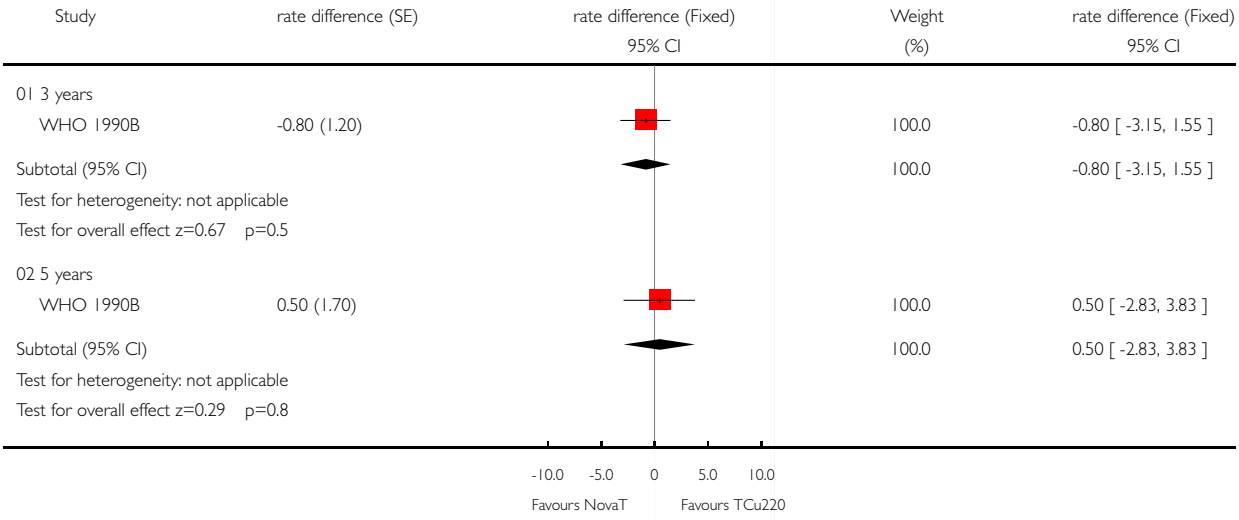


Analysis 13.07. Comparison 13 NovaT vs TCu220, Outcome 07 Discontinuation: medical total

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 07 Discontinuation: medical total

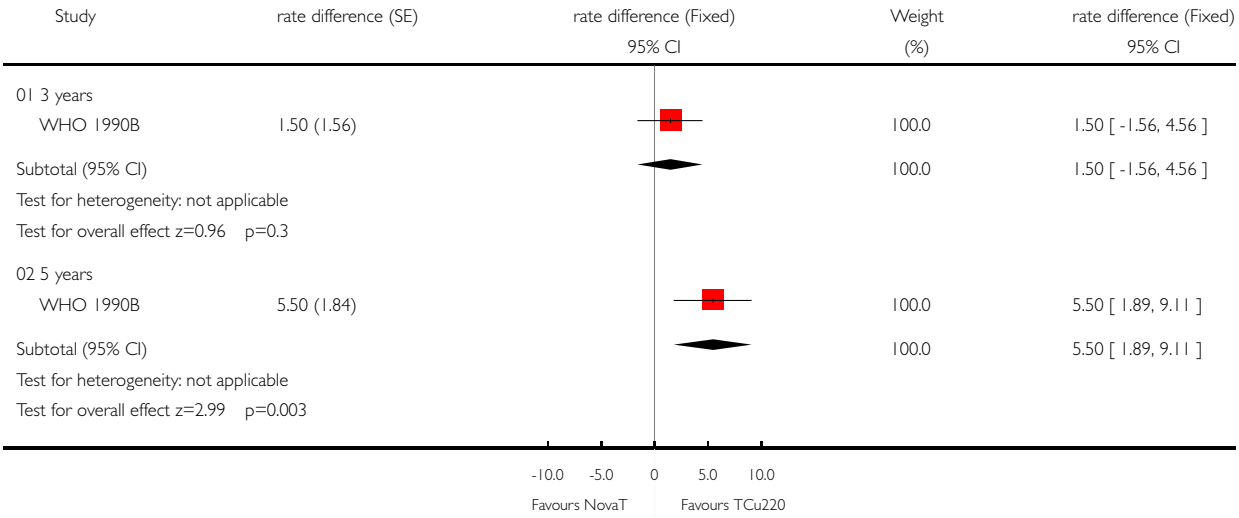


Analysis 13.08. Comparison 13 NovaT vs TCu220, Outcome 08 Discontinuation: all

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 08 Discontinuation: all

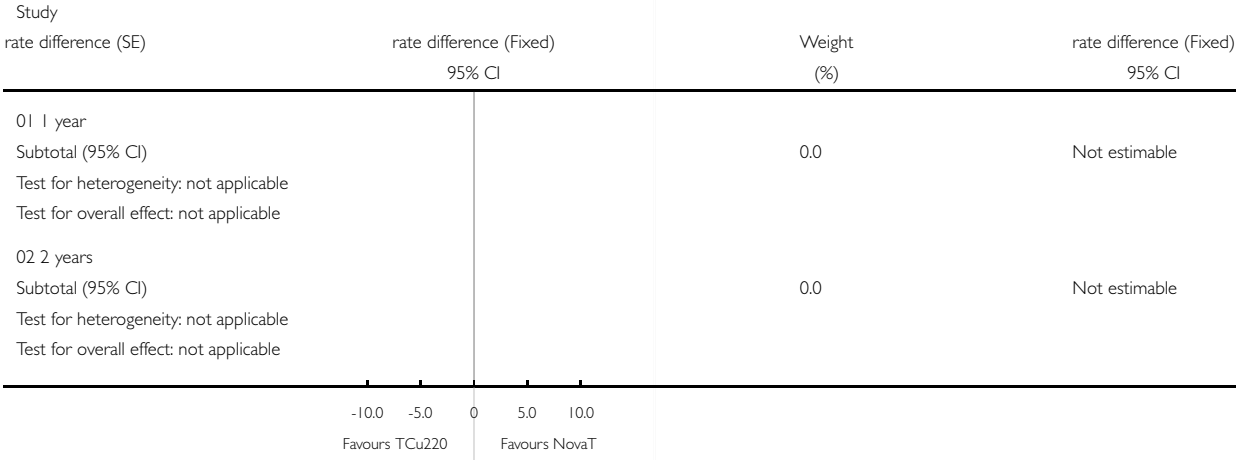


Analysis 13.09. Comparison 13 NovaT vs TCu220, Outcome 09 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 09 Continuation

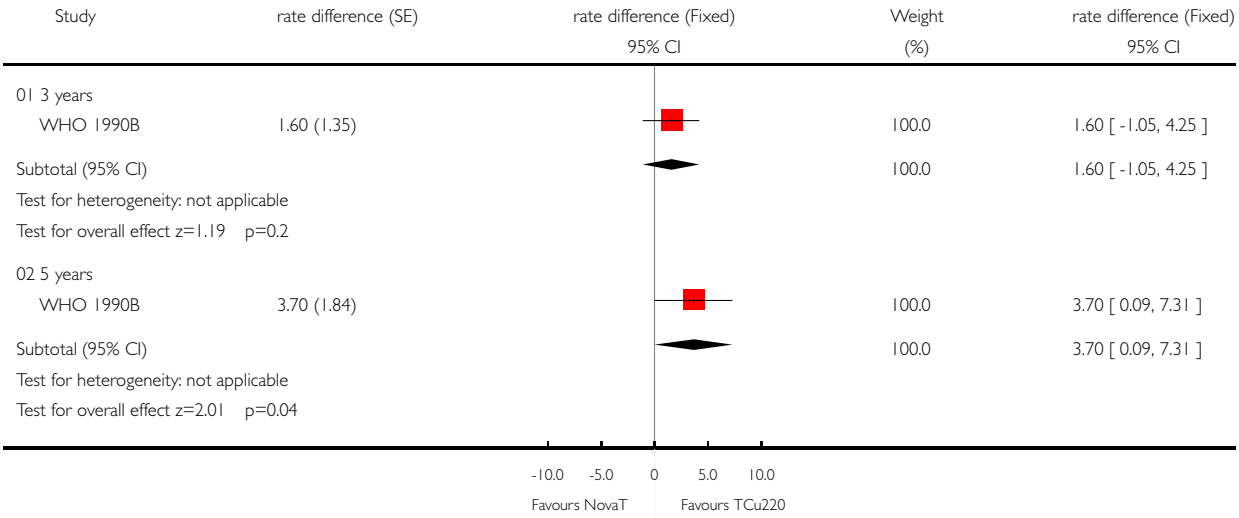


Analysis 13.10. Comparison 13 NovaT vs TCu220, Outcome 10 Discontinuation: non-medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 13 NovaT vs TCu220

Outcome: 10 Discontinuation: non-medical reasons

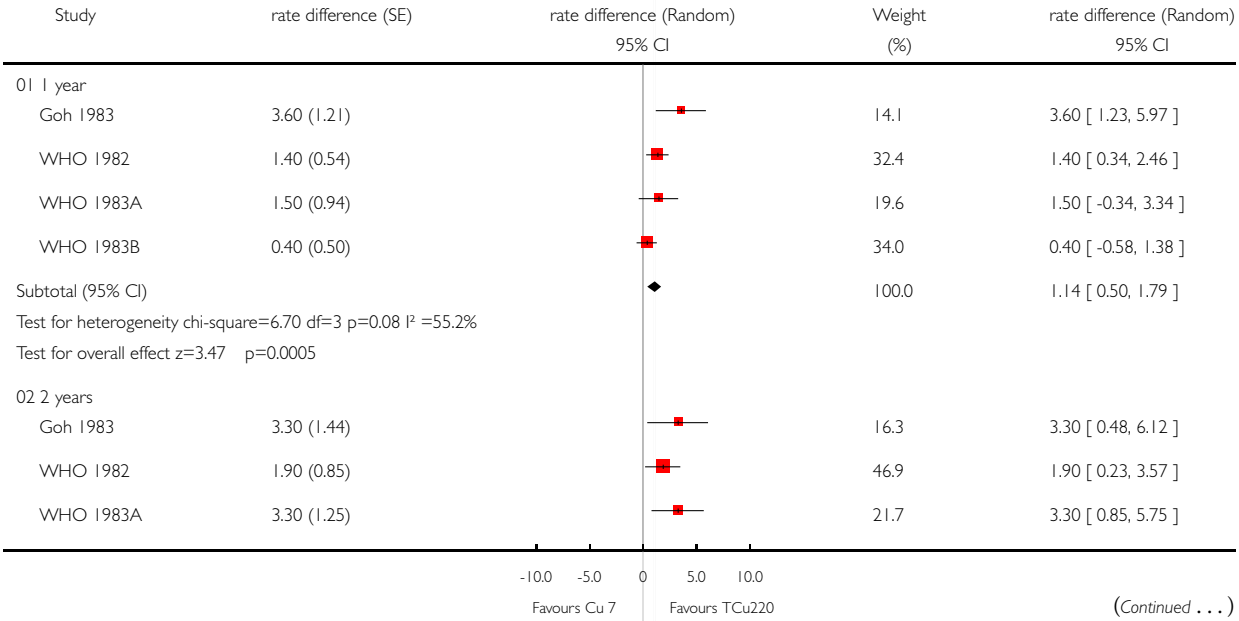


Analysis 14.01. Comparison 14 Cu 7 vs TCu220, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 01 Pregnancy



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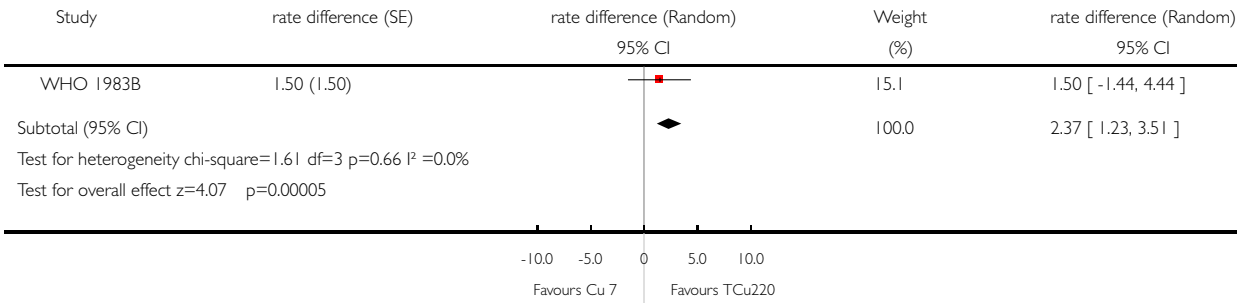
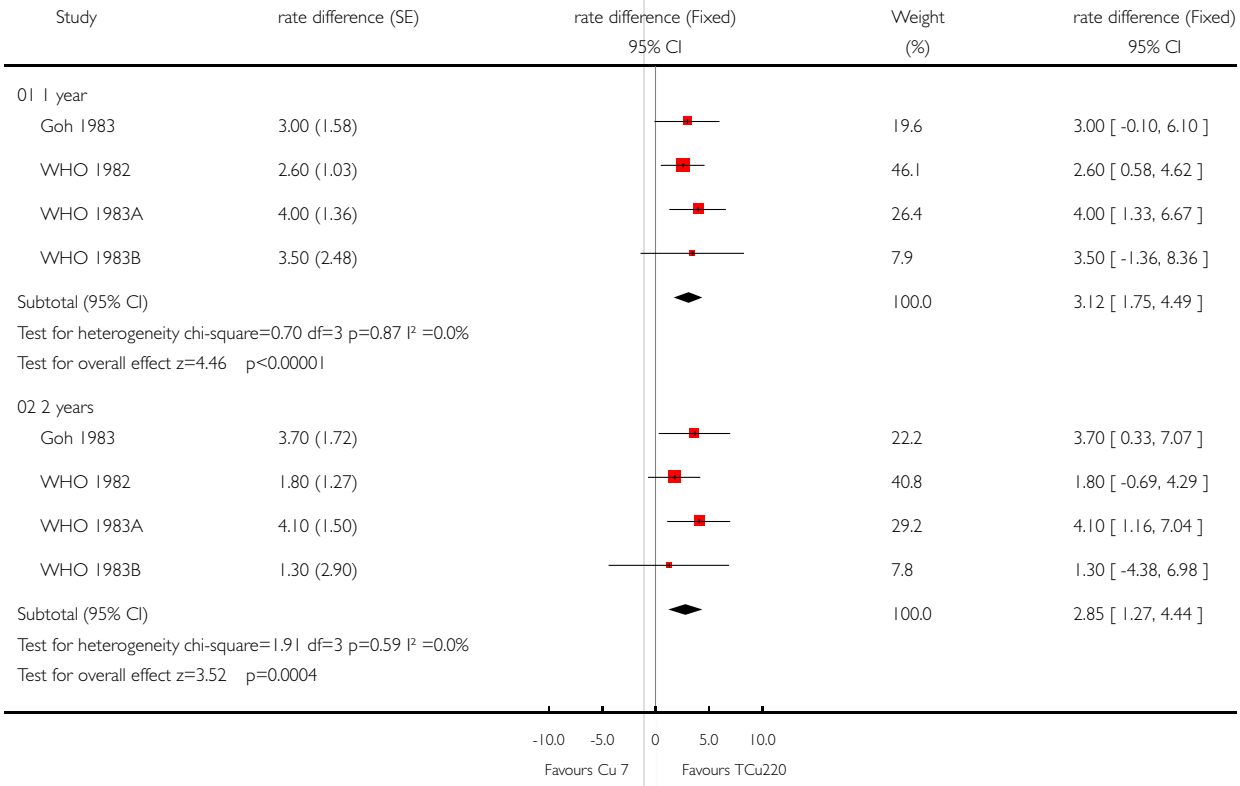


Analysis 14.02. Comparison 14 Cu 7 vs TCu220, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 02 Expulsion



Analysis 14.03. Comparison 14 Cu 7 vs TCu220, Outcome 03 Perforation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 03 Perforation

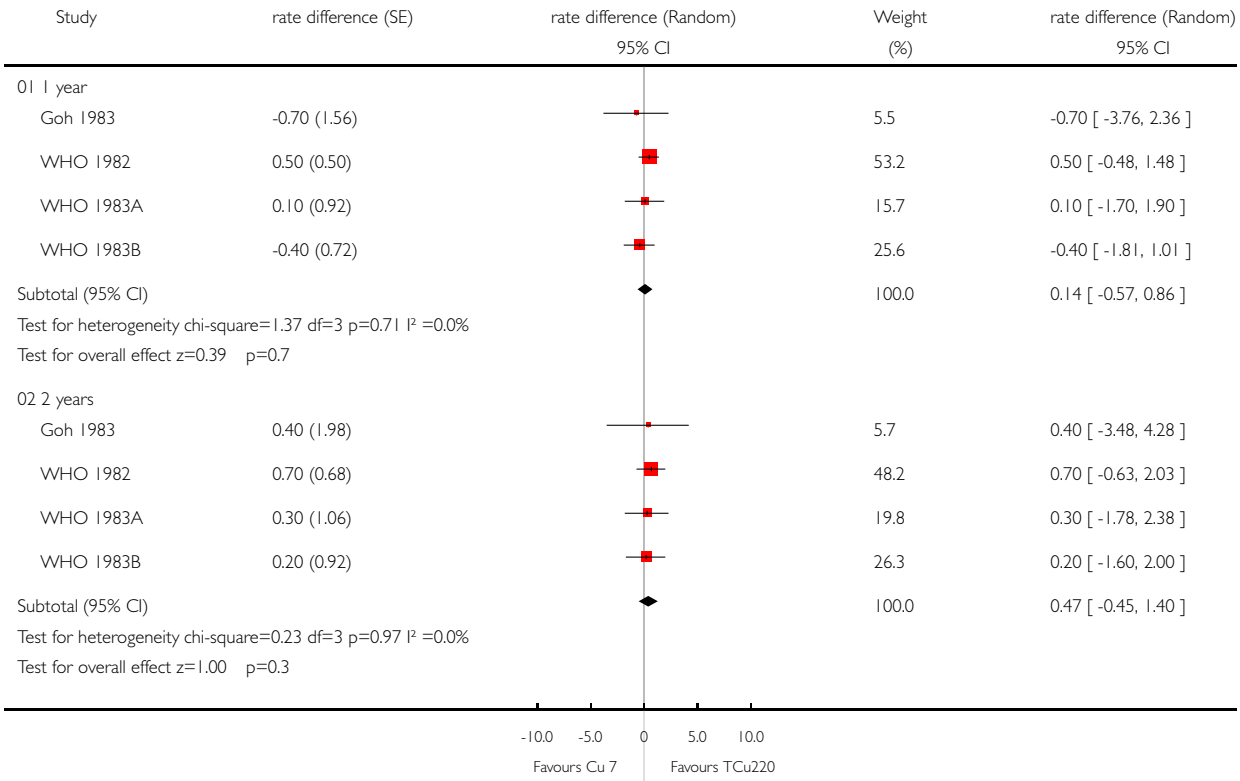
Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
WHO 1982	0.00 (0.26)		41.7	0.00 [-0.51, 0.51]
WHO 1983A	0.20 (0.22)		58.3	0.20 [-0.23, 0.63]
× WHO 1983B	0.00 (0.00)		0.0	Not estimable
Subtotal (95% CI)			100.0	0.12 [-0.21, 0.45]
Test for heterogeneity chi-square=0.34 df=1 p=0.56 I^2 =0.0%				
Test for overall effect z=0.69 p=0.5				
02 2 years				
WHO 1982	0.00 (0.26)		41.7	0.00 [-0.51, 0.51]
WHO 1983A	0.20 (0.22)		58.3	0.20 [-0.23, 0.63]
× WHO 1983B	0.00 (0.00)		0.0	Not estimable
Subtotal (95% CI)			100.0	0.12 [-0.21, 0.45]
Test for heterogeneity chi-square=0.34 df=1 p=0.56 I^2 =0.0%				
Test for overall effect z=0.69 p=0.5				

Analysis 14.04. Comparison 14 Cu 7 vs TCu220, Outcome 04 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 04 Discontinuation: bleeding and pain

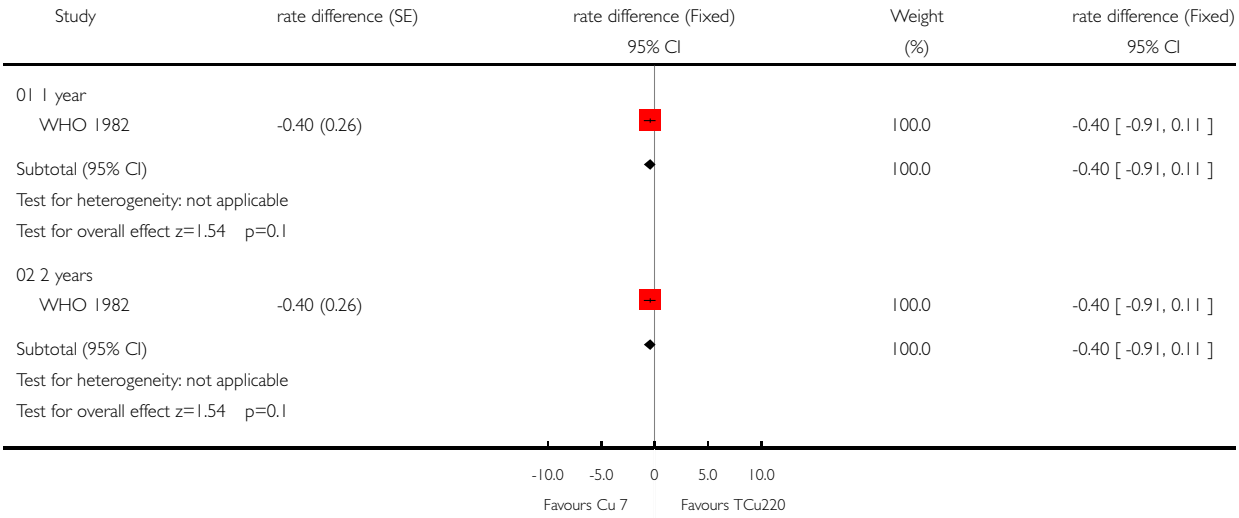


Analysis 14.05. Comparison 14 Cu 7 vs TCu220, Outcome 05 Discontinuation: intermenstrual bleeding

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 05 Discontinuation: intermenstrual bleeding

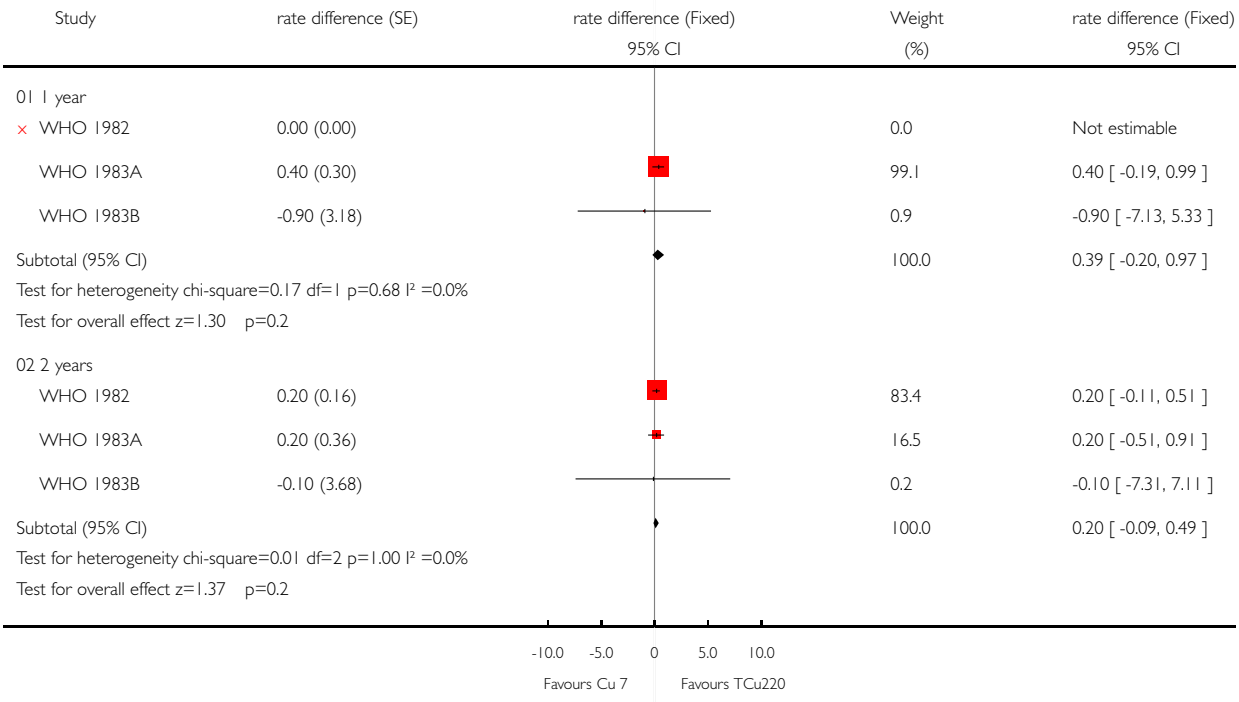


Analysis 14.06. Comparison 14 Cu 7 vs TCu220, Outcome 06 Ectopic pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 06 Ectopic pregnancy

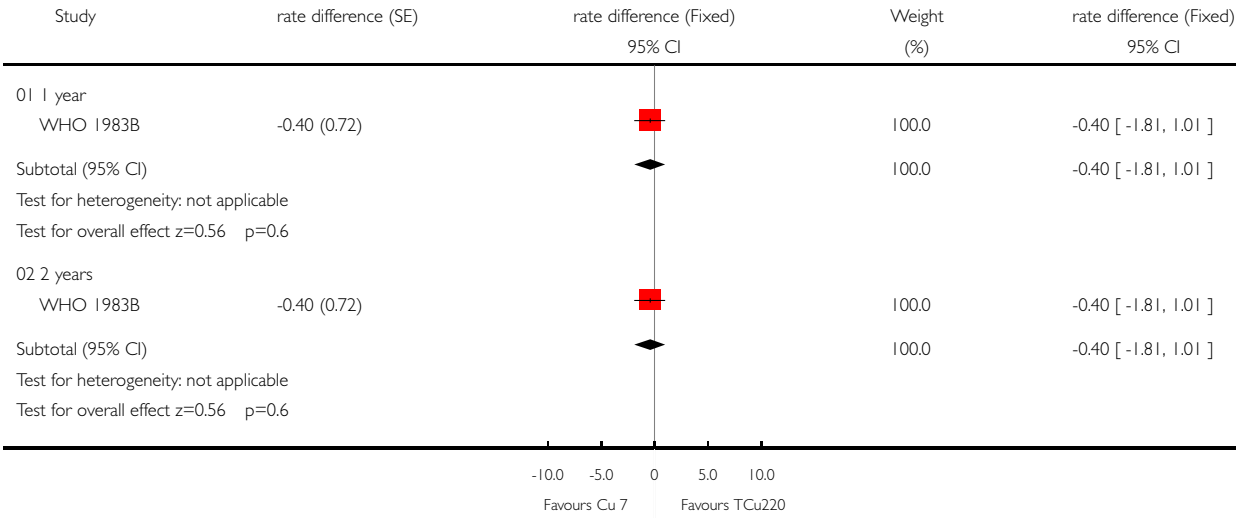


Analysis 14.07. Comparison 14 Cu 7 vs TCu220, Outcome 07 Discontinuation: infection/PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 07 Discontinuation: infection/PID

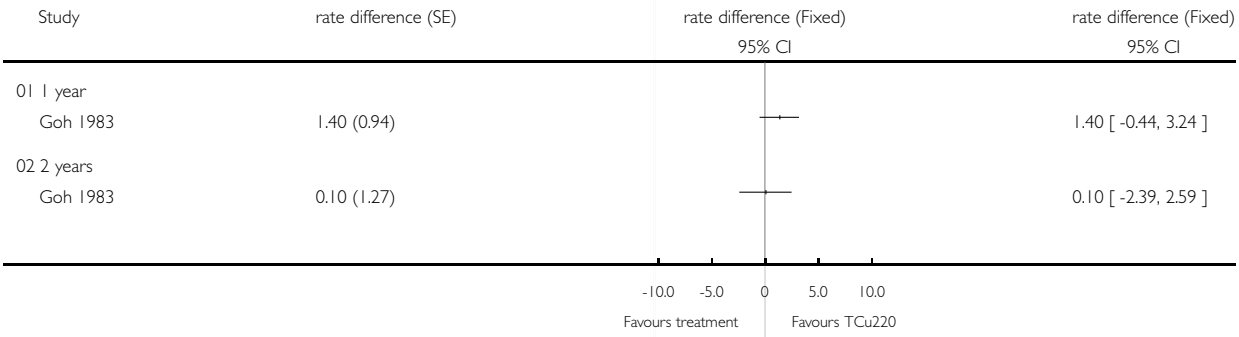


Analysis 14.08. Comparison 14 Cu 7 vs TCu220, Outcome 08 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 08 Discontinuation: other medical reasons

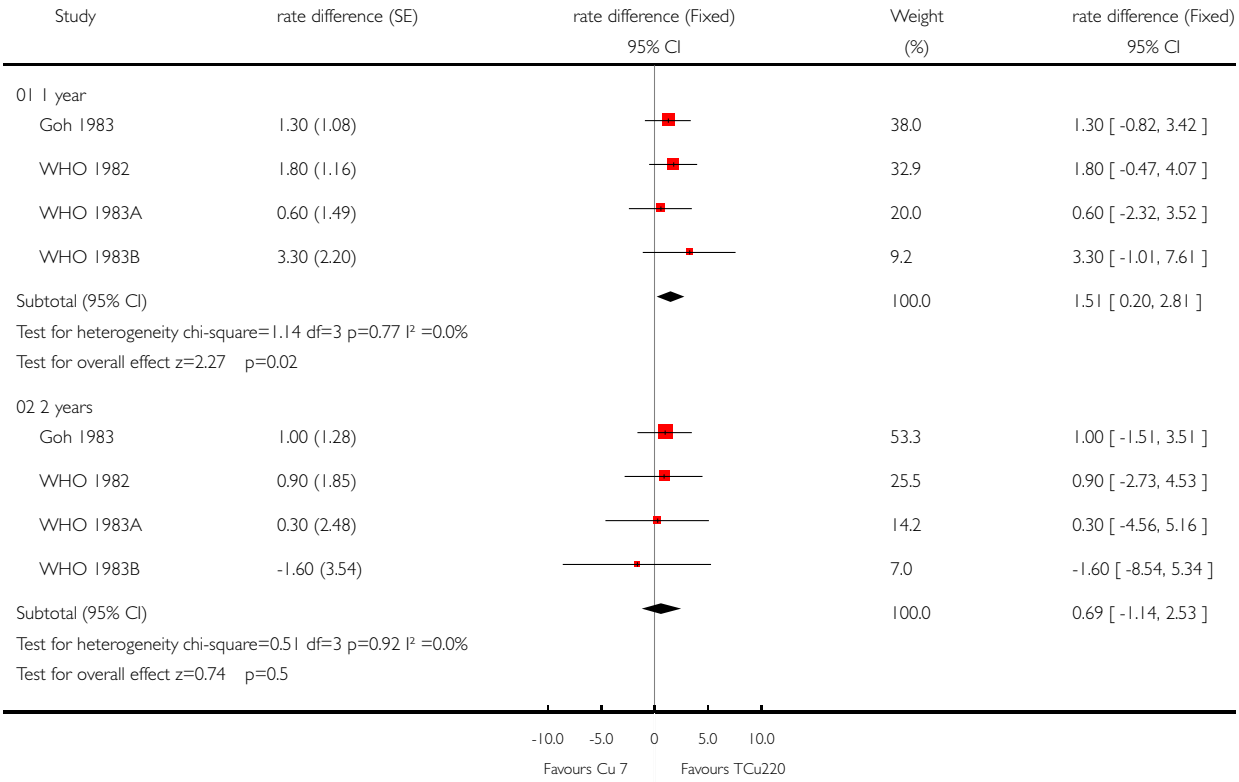


Analysis 14.09. Comparison 14 Cu 7 vs TCu220, Outcome 09 Discontinuation: non-medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 09 Discontinuation: non-medical reasons

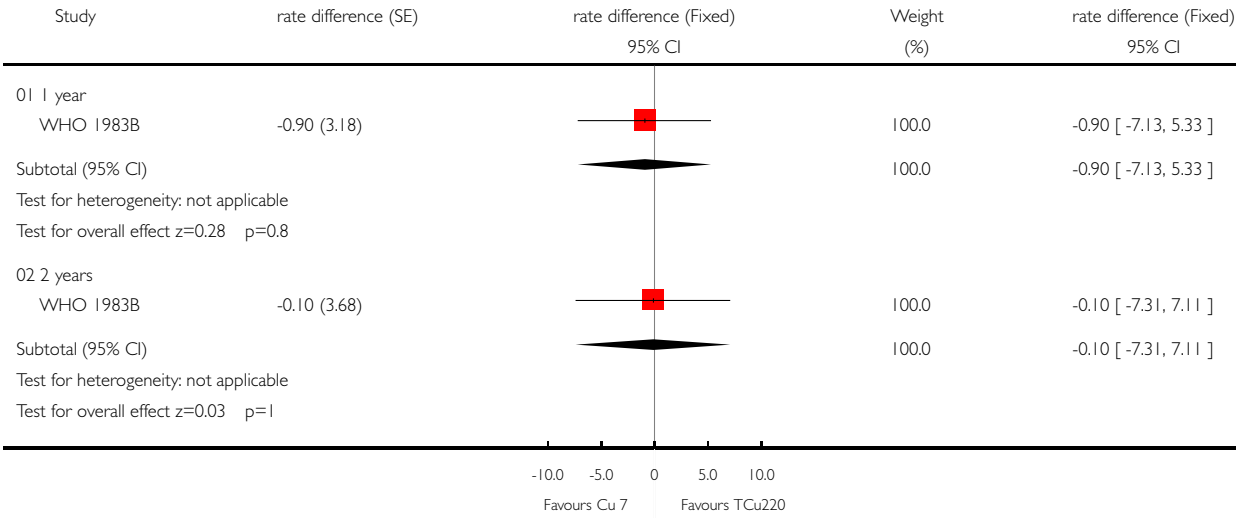


Analysis 14.10. Comparison 14 Cu 7 vs TCu220, Outcome 10 Discontinuation: all

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 10 Discontinuation: all

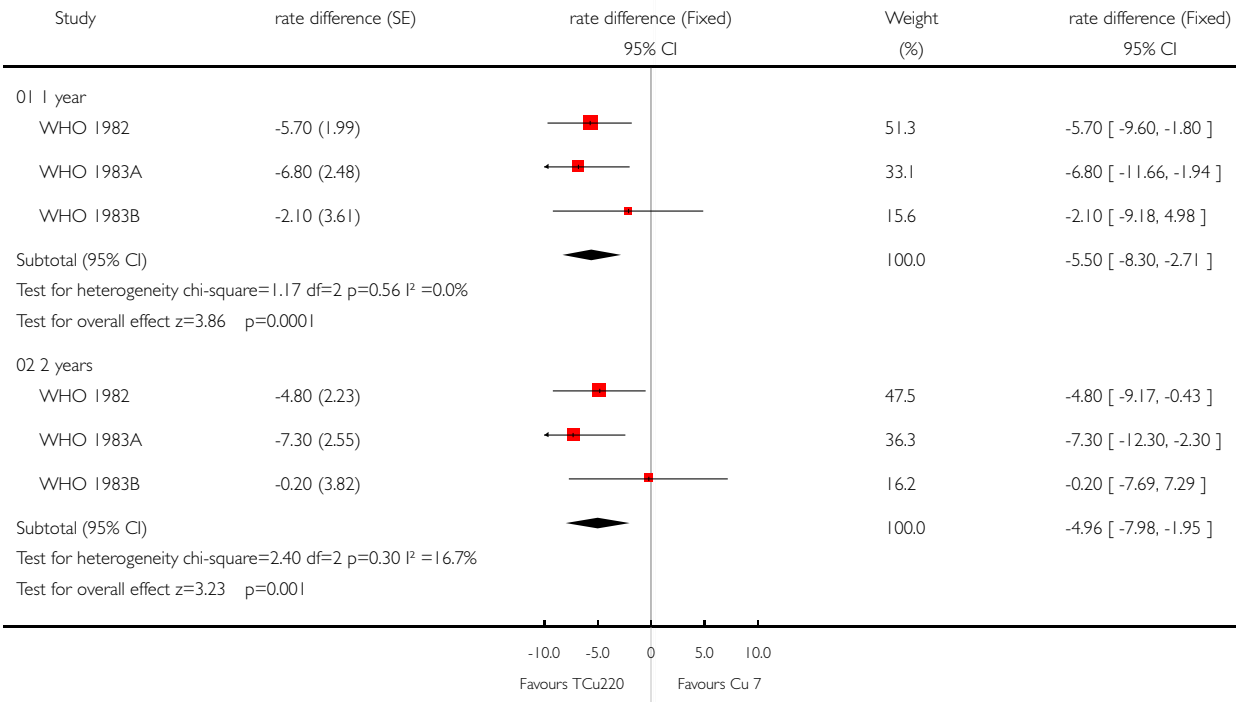


Analysis 14.11. Comparison 14 Cu 7 vs TCu220, Outcome 11 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 11 Continuation



Analysis 14.12. Comparison 14 Cu 7 vs TCu220, Outcome 12 Discontinuation: total use related

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 12 Discontinuation: total use related

Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
Goh 1983	6.30 (2.77)		24.5	6.30 [0.87, 11.73]
WHO 1982	5.40 (1.58)		75.5	5.40 [2.30, 8.50]
Subtotal (95% CI)			100.0	5.62 [2.93, 8.31]
Test for heterogeneity chi-square=0.08 df=1 p=0.78 I^2 =0.0%				
Test for overall effect z=4.10 p=0.00004				
02 2 years				
Goh 1983	5.40 (3.26)		27.7	5.40 [-0.99, 11.79]
WHO 1982	6.90 (2.02)		72.3	6.90 [2.94, 10.86]
Subtotal (95% CI)			100.0	6.48 [3.12, 9.85]
Test for heterogeneity chi-square=0.15 df=1 p=0.70 I^2 =0.0%				
Test for overall effect z=3.78 p=0.0002				

Analysis 14.13. Comparison 14 Cu 7 vs TCu220, Outcome 13 Discontinuation: total medical

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 14 Cu 7 vs TCu220

Outcome: 13 Discontinuation: total medical

Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
WHO 1982	1.80 (0.94)		71.4	1.80 [-0.04, 3.64]
WHO 1983A	0.10 (1.91)		17.3	0.10 [-3.64, 3.84]
WHO 1983B	-5.10 (2.36)		11.3	-5.10 [-9.73, -0.47]
Subtotal (95% CI)			100.0	0.72 [-0.83, 2.28]
Test for heterogeneity chi-square=7.51 df=2 p=0.02 I^2 =73.4%				
Test for overall effect z=0.91 p=0.4				
02 2 years				
WHO 1982	3.90 (1.73)		50.9	3.90 [0.51, 7.29]
WHO 1983A	1.10 (2.19)		31.8	1.10 [-3.19, 5.39]

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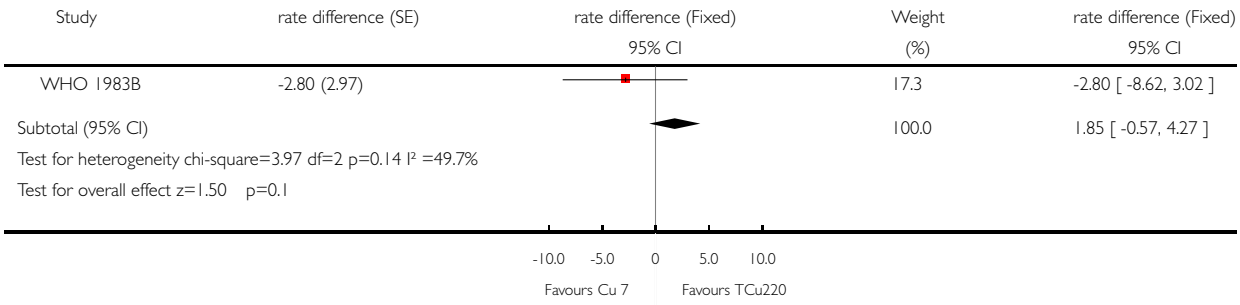
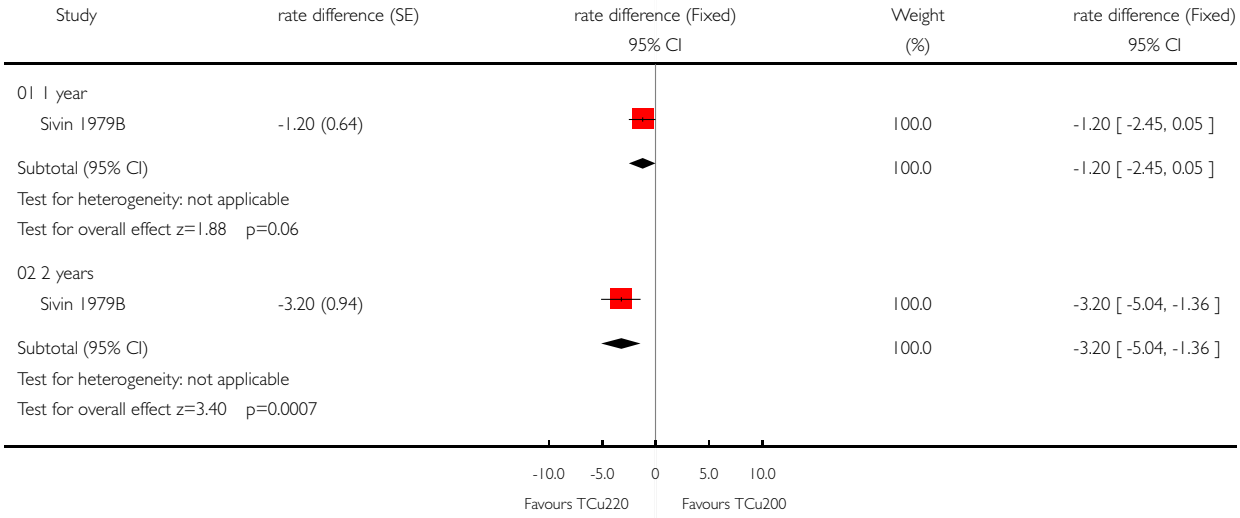


Analysis 15.01. Comparison 15 TCu220 vs TCu200, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 15 TCu220 vs TCu200

Outcome: 01 Pregnancy

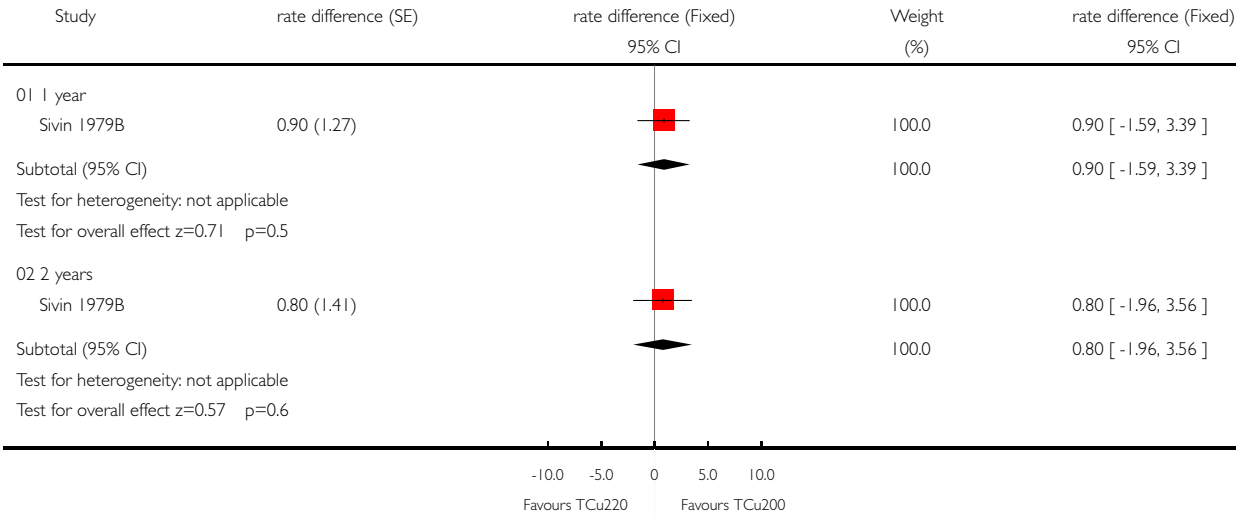


Analysis 15.02. Comparison 15 TCu220 vs TCu200, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 15 TCu220 vs TCu200

Outcome: 02 Expulsion

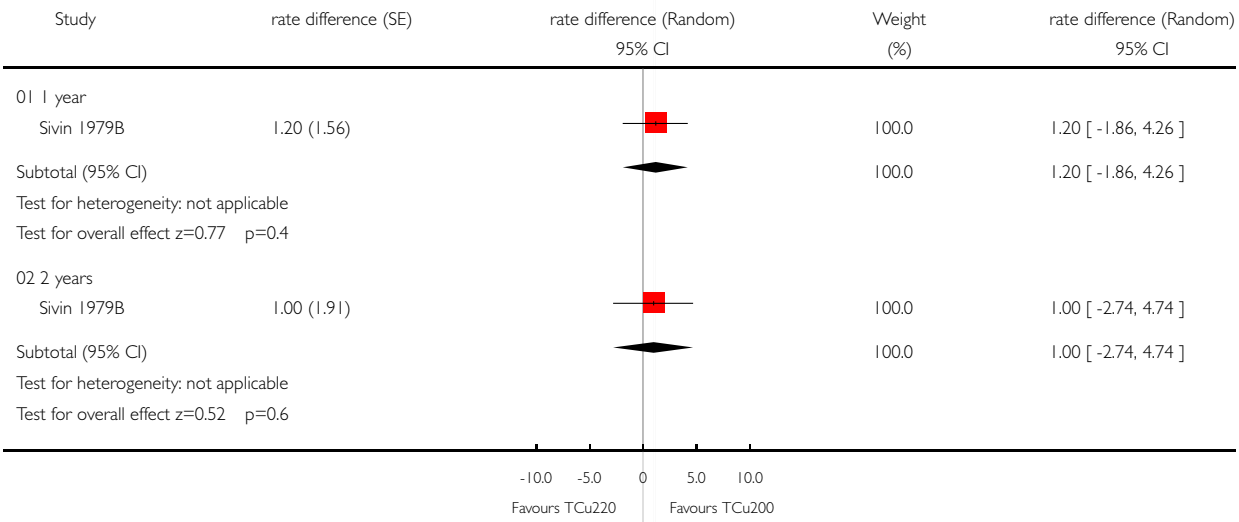


Analysis 15.03. Comparison 15 TCu220 vs TCu200, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 15 TCu220 vs TCu200

Outcome: 03 Discontinuation: bleeding and pain

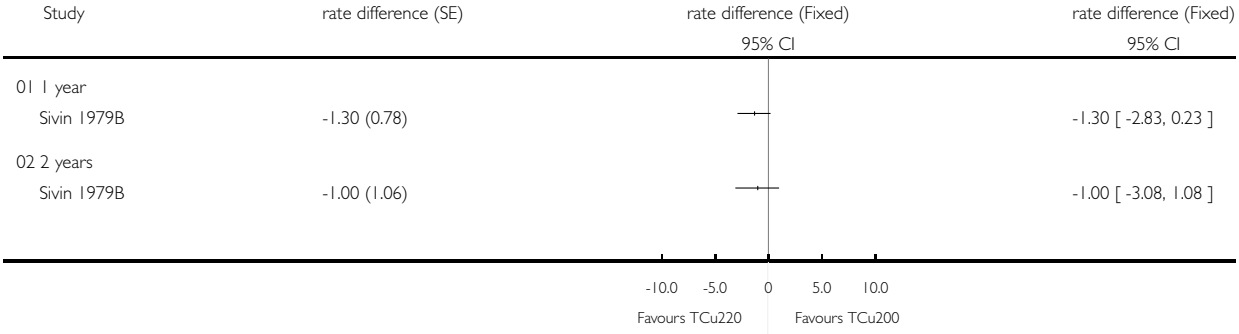


Analysis 15.04. Comparison 15 TCu220 vs TCu200, Outcome 04 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 15 TCu220 vs TCu200

Outcome: 04 Discontinuation: other medical reasons

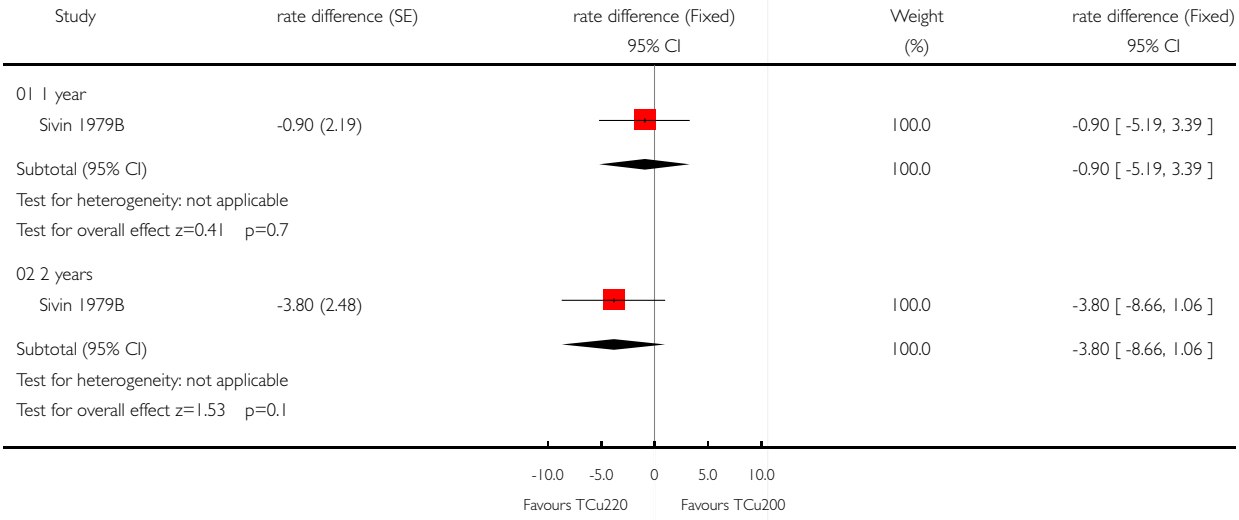


Analysis 15.05. Comparison 15 TCu220 vs TCu200, Outcome 05 Discontinuation: all

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 15 TCu220 vs TCu200

Outcome: 05 Discontinuation: all

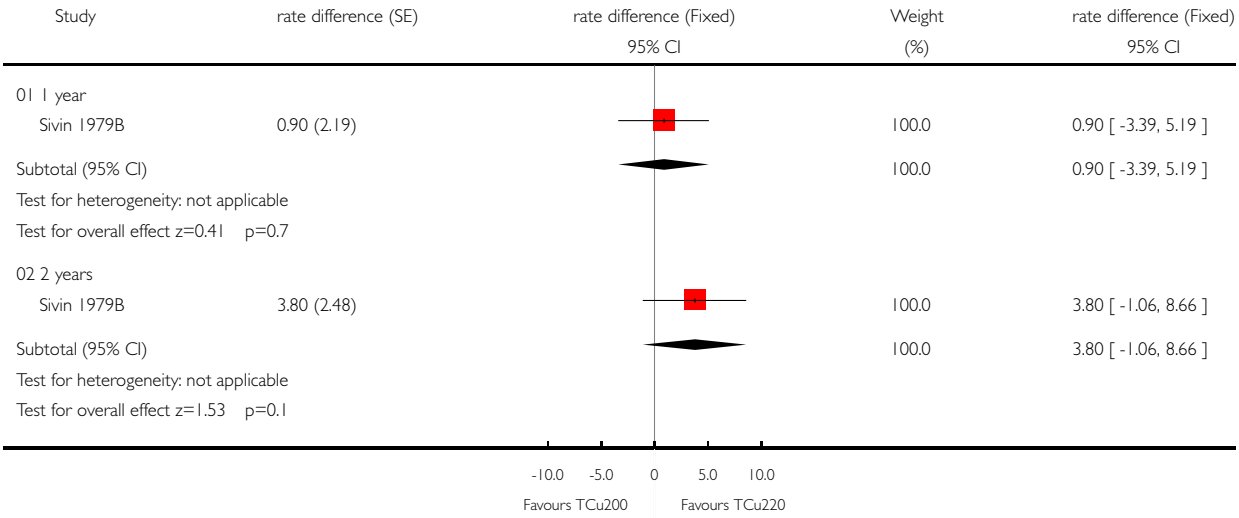


Analysis 15.06. Comparison 15 TCu220 vs TCu200, Outcome 06 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 15 TCu220 vs TCu200

Outcome: 06 Continuation

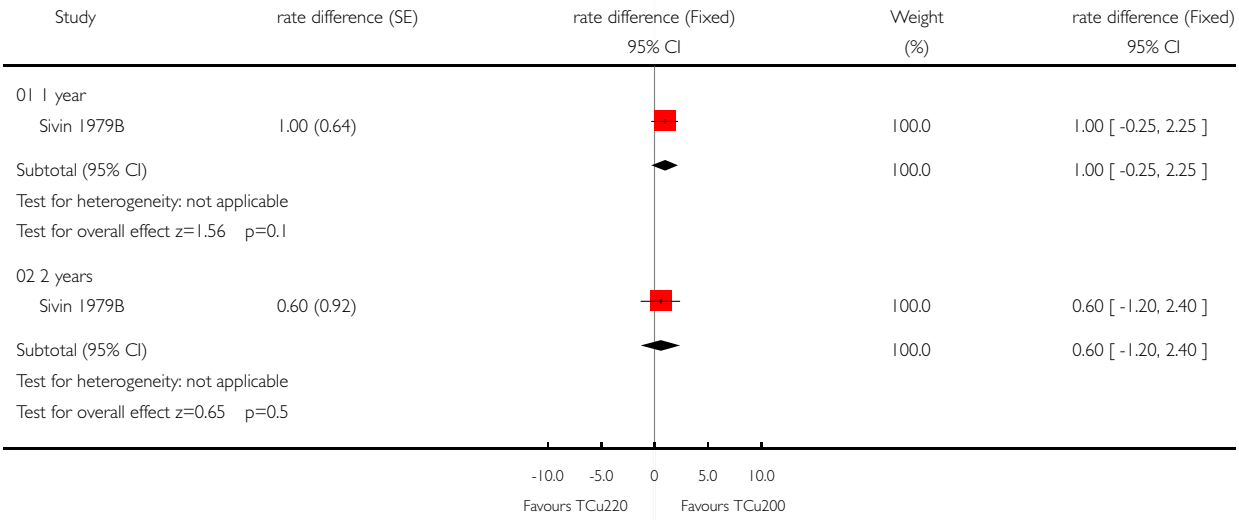


Analysis 15.07. Comparison 15 TCu220 vs TCu200, Outcome 07 Discontinuation: planned pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 15 TCu220 vs TCu200

Outcome: 07 Discontinuation: planned pregnancy

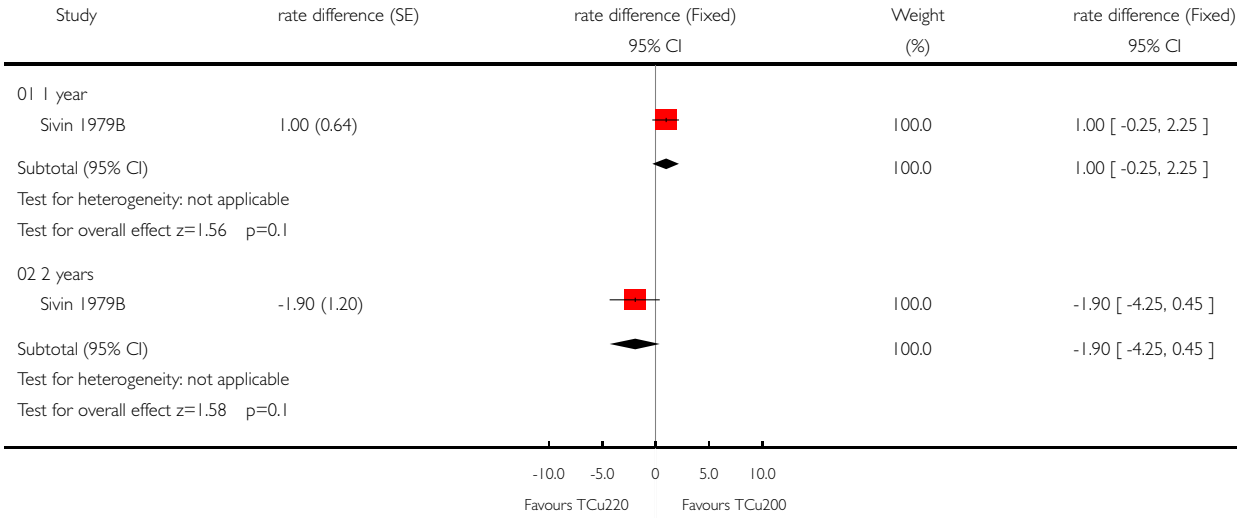


Analysis 15.08. Comparison 15 TCu220 vs TCu200, Outcome 08 Discontinuation: other personal reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 15 TCu220 vs TCu200

Outcome: 08 Discontinuation: other personal reasons

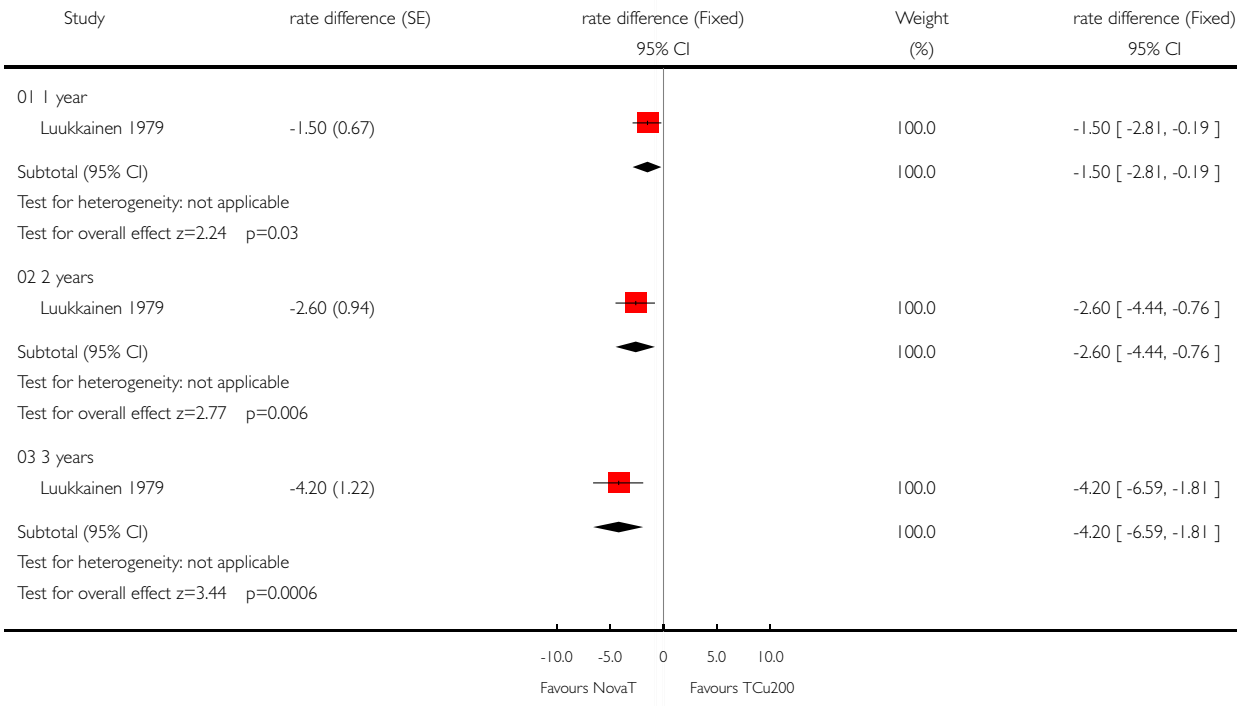


Analysis 16.01. Comparison 16 NovaT vs TCu200, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 16 NovaT vs TCu200

Outcome: 01 Pregnancy

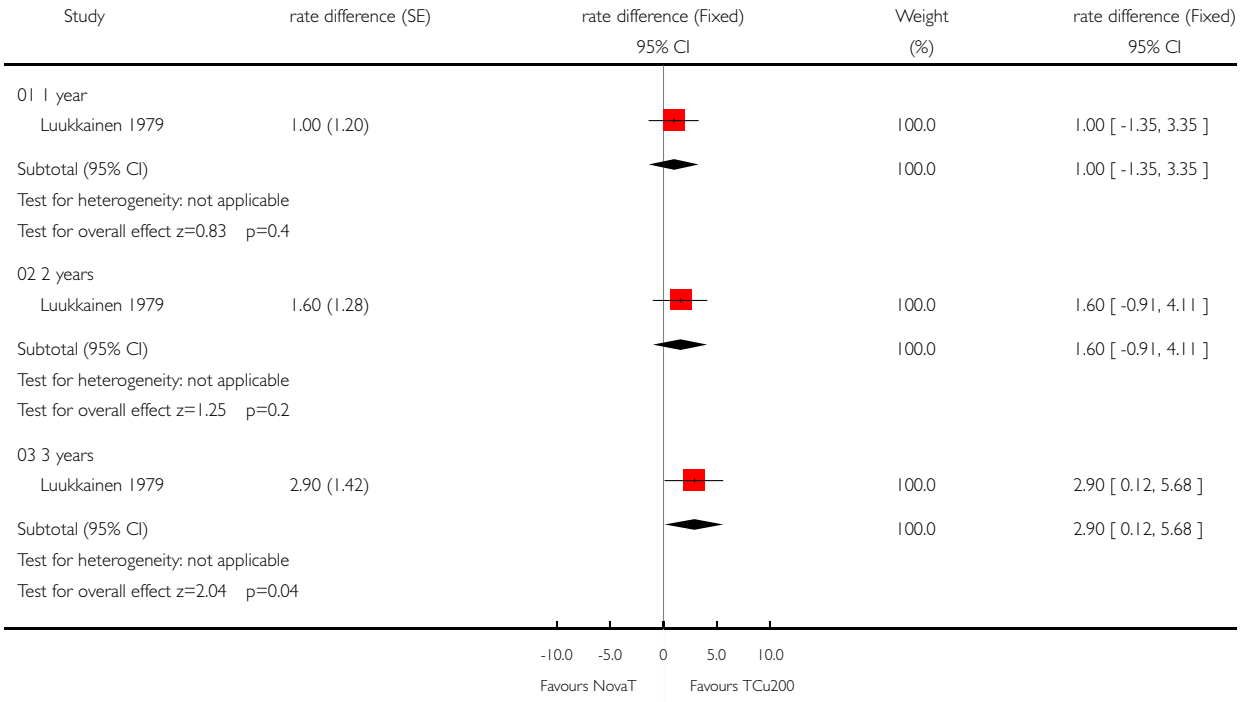


Analysis 16.02. Comparison 16 NovaT vs TCu200, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 16 NovaT vs TCu200

Outcome: 02 Expulsion

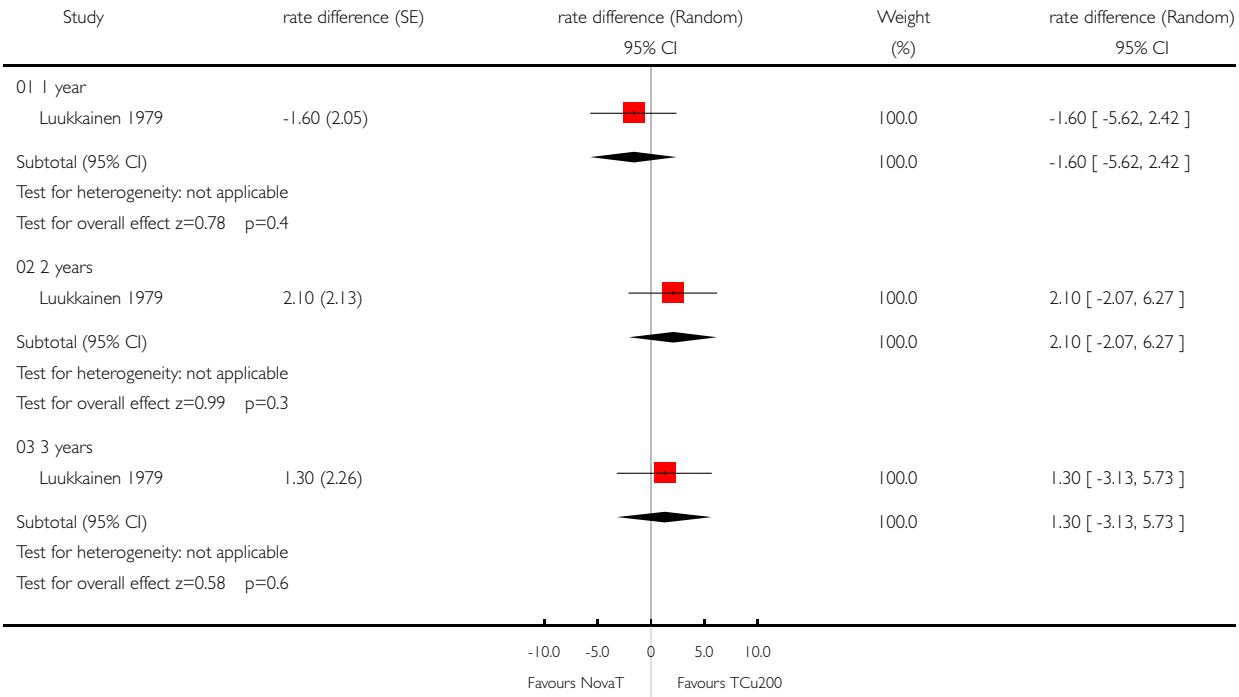


Analysis 16.03. Comparison 16 NovaT vs TCu200, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 16 NovaT vs TCu200

Outcome: 03 Discontinuation: bleeding and pain

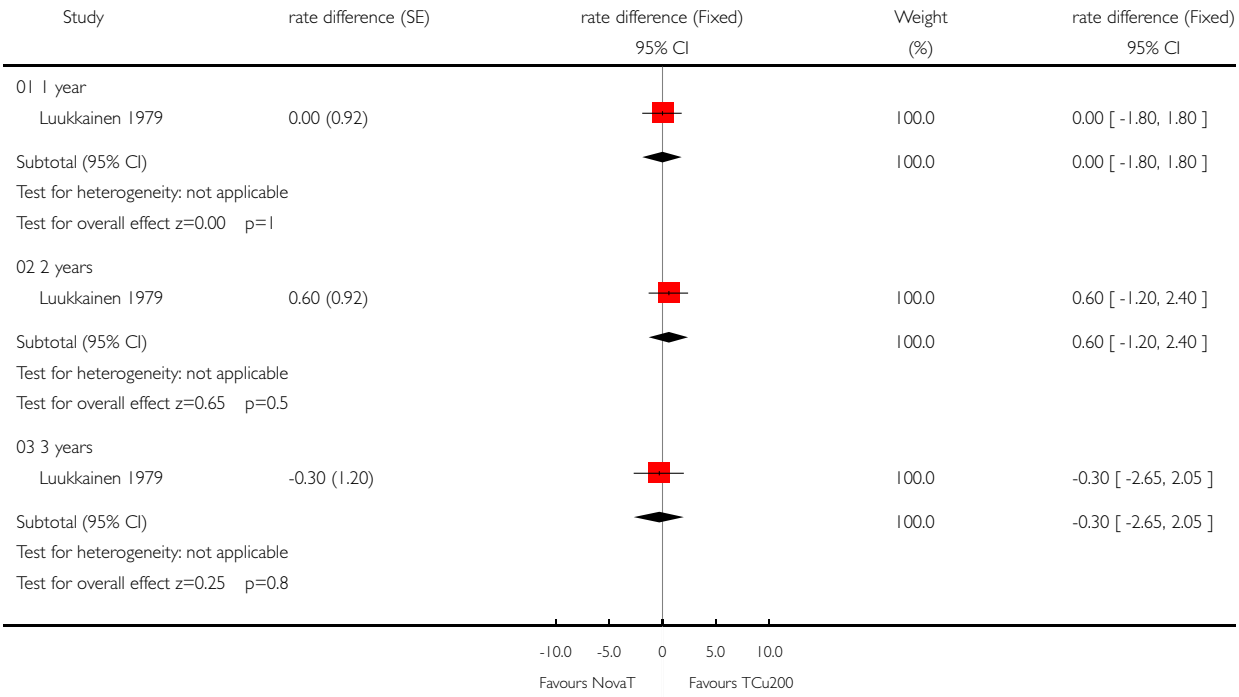


Analysis 16.04. Comparison 16 NovaT vs TCu200, Outcome 04 Discontinuation: infection/PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 16 NovaT vs TCu200

Outcome: 04 Discontinuation: infection/PID

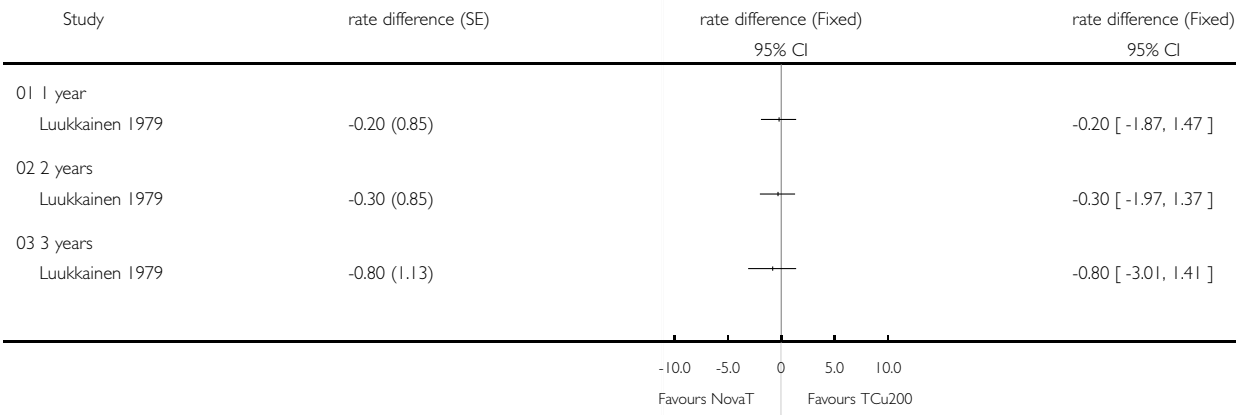


Analysis 16.05. Comparison 16 NovaT vs TCu200, Outcome 05 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 16 NovaT vs TCu200

Outcome: 05 Discontinuation: other medical reasons

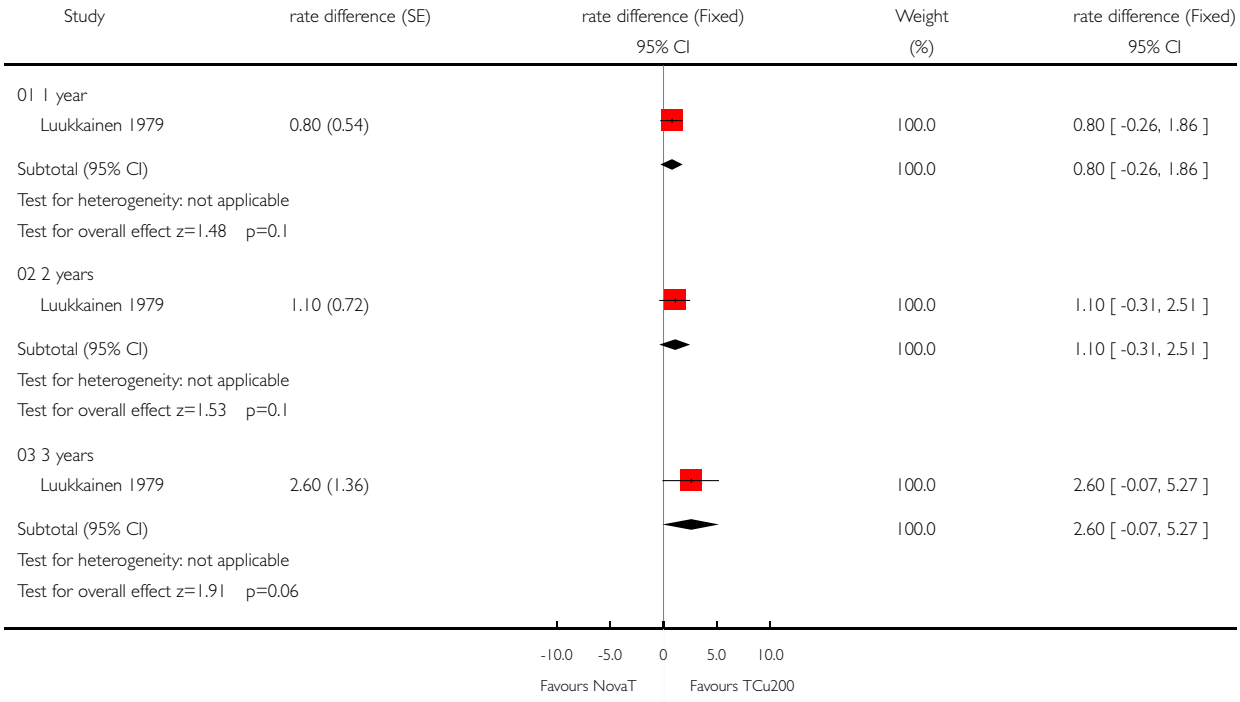


Analysis 16.06. Comparison 16 NovaT vs TCu200, Outcome 06 Discontinuation: non-medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 16 NovaT vs TCu200

Outcome: 06 Discontinuation: non-medical reasons

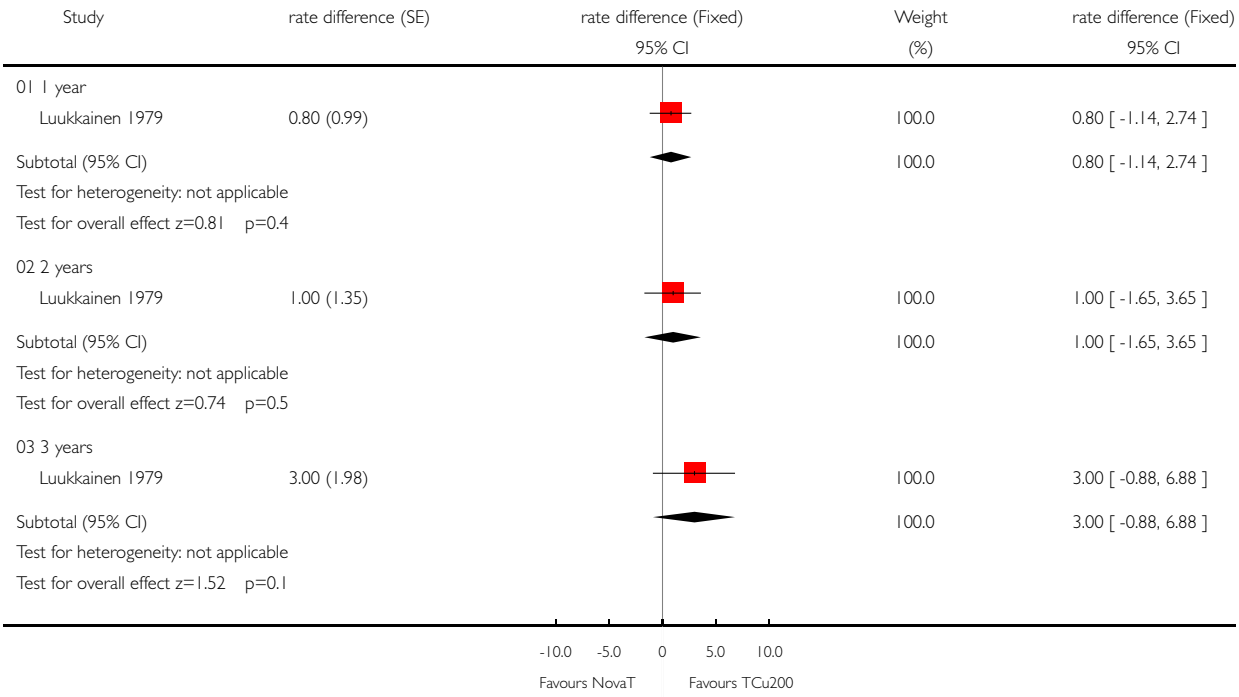


Analysis 16.07. Comparison 16 NovaT vs TCu200, Outcome 07 Discontinuation: planned pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 16 NovaT vs TCu200

Outcome: 07 Discontinuation: planned pregnancy

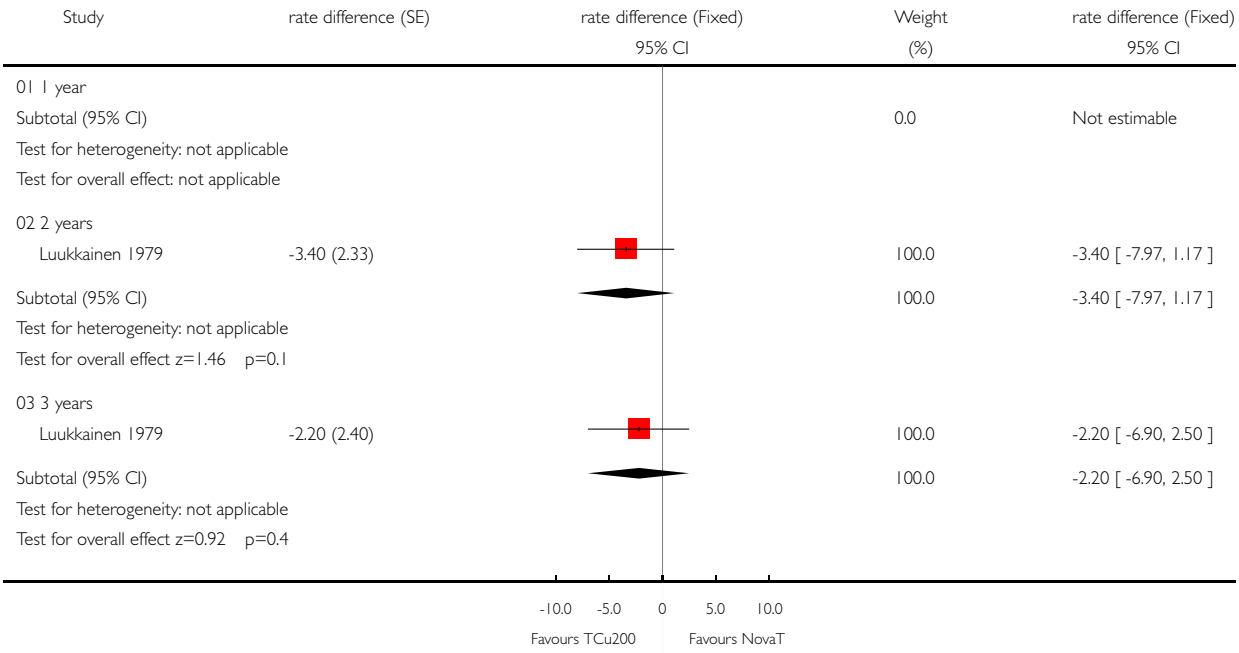


Analysis 16.08. Comparison 16 NovaT vs TCu200, Outcome 08 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 16 NovaT vs TCu200

Outcome: 08 Continuation

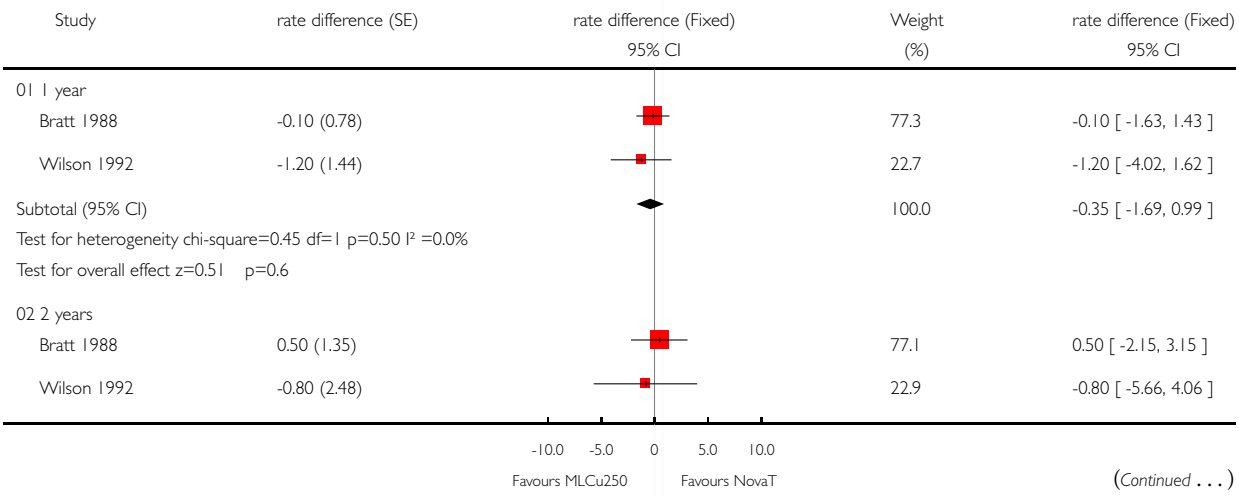


Analysis 17.01. Comparison 17 MLCu 250 vs NovaT, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 17 MLCu 250 vs NovaT

Outcome: 01 Pregnancy



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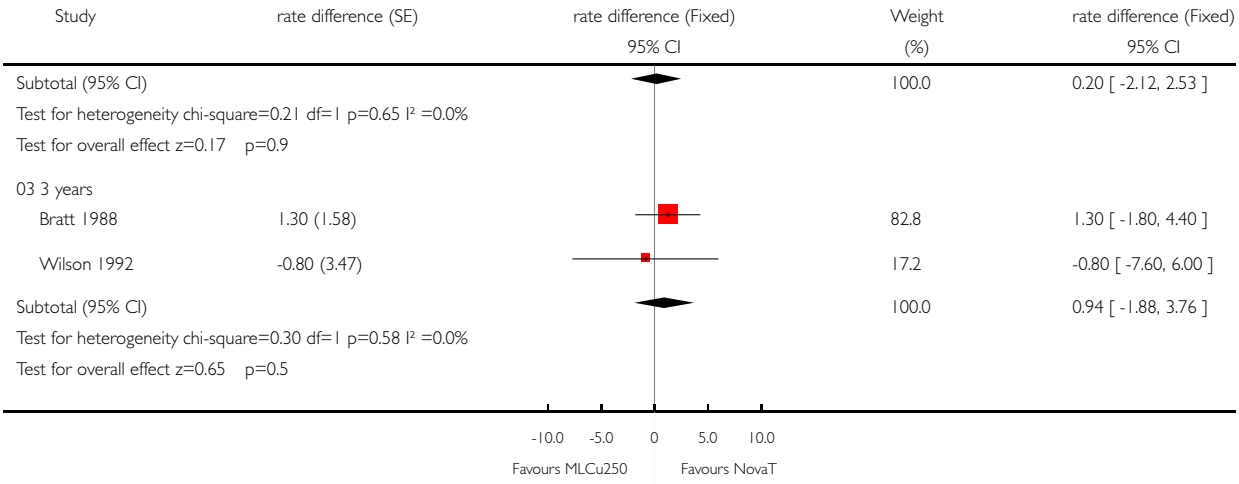
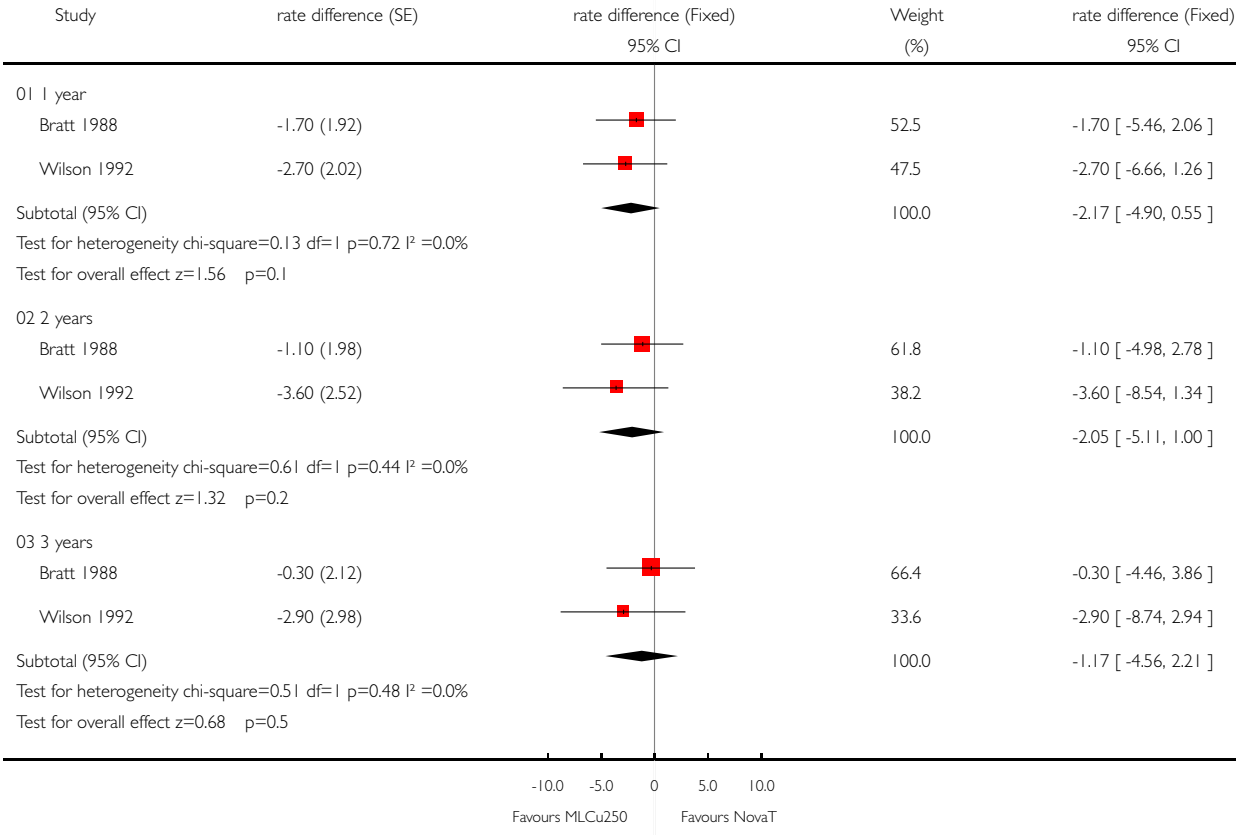


Analysis 17.02. Comparison 17 MLCu 250 vs NovaT, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 17 MLCu 250 vs NovaT

Outcome: 02 Expulsion

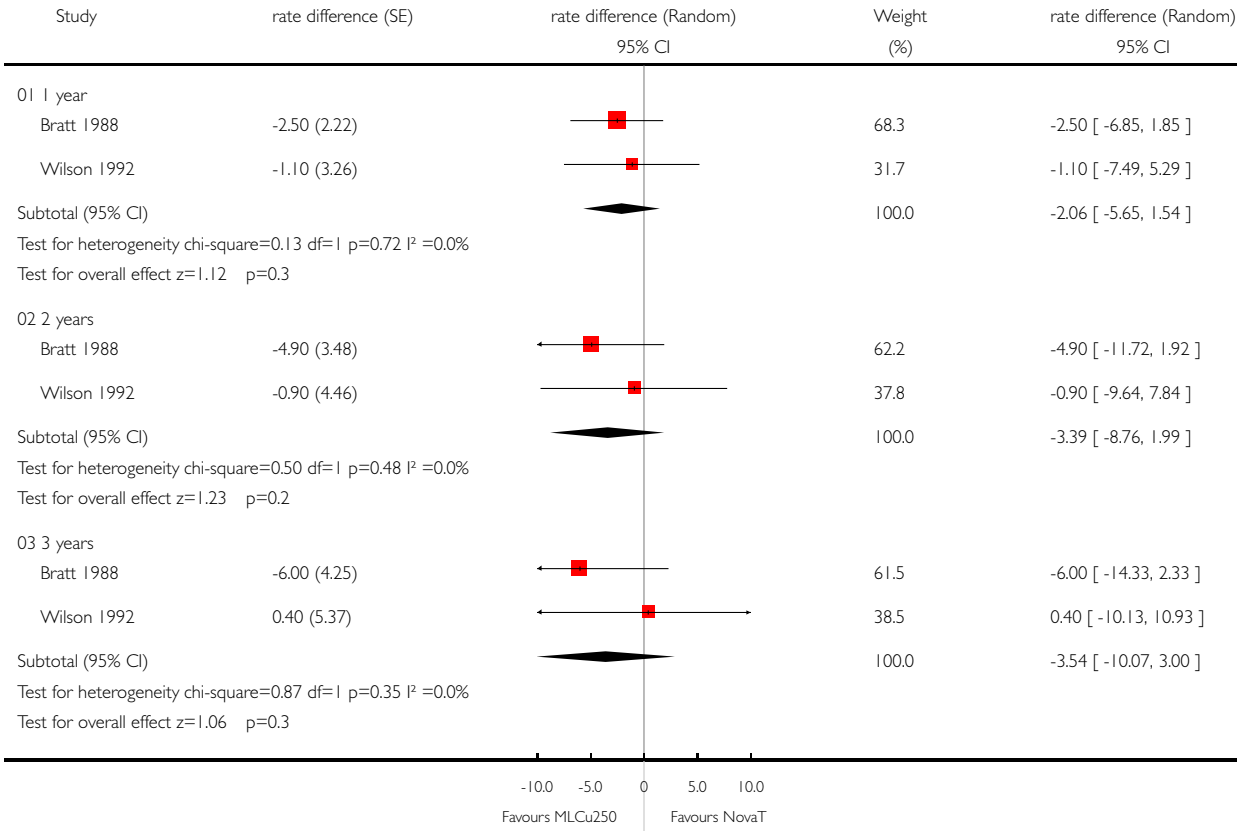


Analysis 17.03. Comparison 17 MLCu 250 vs NovaT, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 17 MLCu 250 vs NovaT

Outcome: 03 Discontinuation: bleeding and pain



Analysis 17.04. Comparison 17 MLCu 250 vs NovaT, Outcome 04 Discontinuation: infection/PID

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 17 MLCu 250 vs NovaT

Outcome: 04 Discontinuation: infection/PID

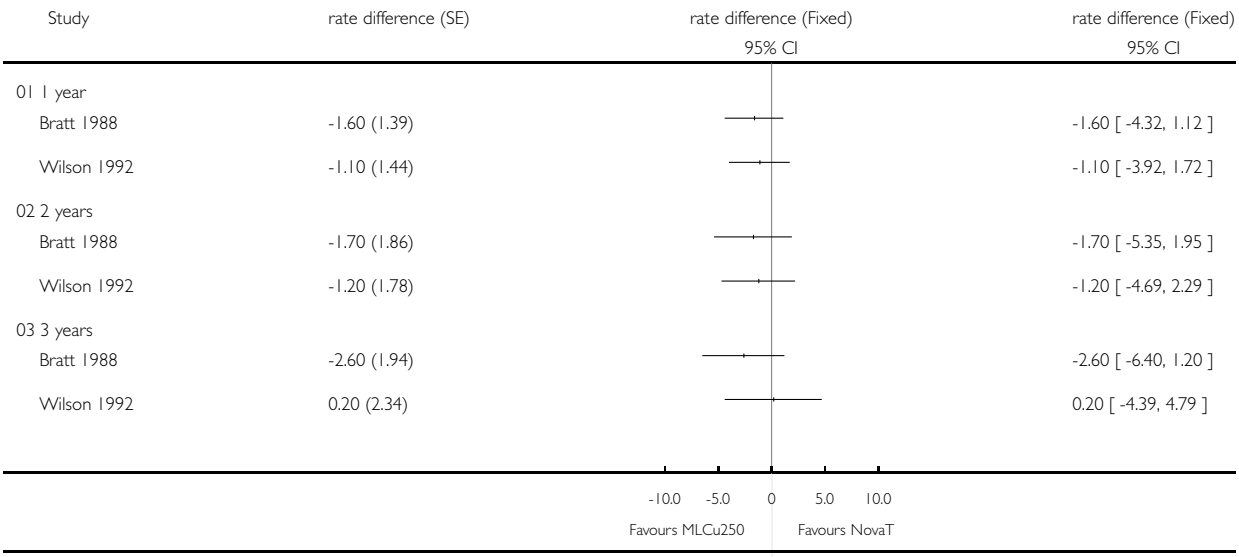
Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
Bratt 1988	-0.60 (0.86)		70.8	-0.60 [-2.29, 1.09]
Wilson 1992	-1.70 (1.34)		29.2	-1.70 [-4.33, 0.93]
Subtotal (95% CI)			100.0	-0.92 [-2.34, 0.50]
Test for heterogeneity chi-square=0.48 df=1 p=0.49 I^2 =0.0%				
Test for overall effect z=1.27 p=0.2				
02 2 years				
Bratt 1988	-2.00 (1.61)		54.2	-2.00 [-5.16, 1.16]
Wilson 1992	-2.10 (1.75)		45.8	-2.10 [-5.53, 1.33]
Subtotal (95% CI)			100.0	-2.05 [-4.37, 0.28]
Test for heterogeneity chi-square=0.00 df=1 p=0.97 I^2 =0.0%				
Test for overall effect z=1.73 p=0.08				
03 3 years				
Bratt 1988	-2.20 (2.02)		52.9	-2.20 [-6.16, 1.76]
Wilson 1992	-1.90 (2.14)		47.1	-1.90 [-6.09, 2.29]
Subtotal (95% CI)			100.0	-2.06 [-4.94, 0.82]
Test for heterogeneity chi-square=0.01 df=1 p=0.92 I^2 =0.0%				
Test for overall effect z=1.40 p=0.2				

Analysis 17.05. Comparison 17 MLCu 250 vs NovaT, Outcome 05 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 17 MLCu 250 vs NovaT

Outcome: 05 Discontinuation: other medical reasons

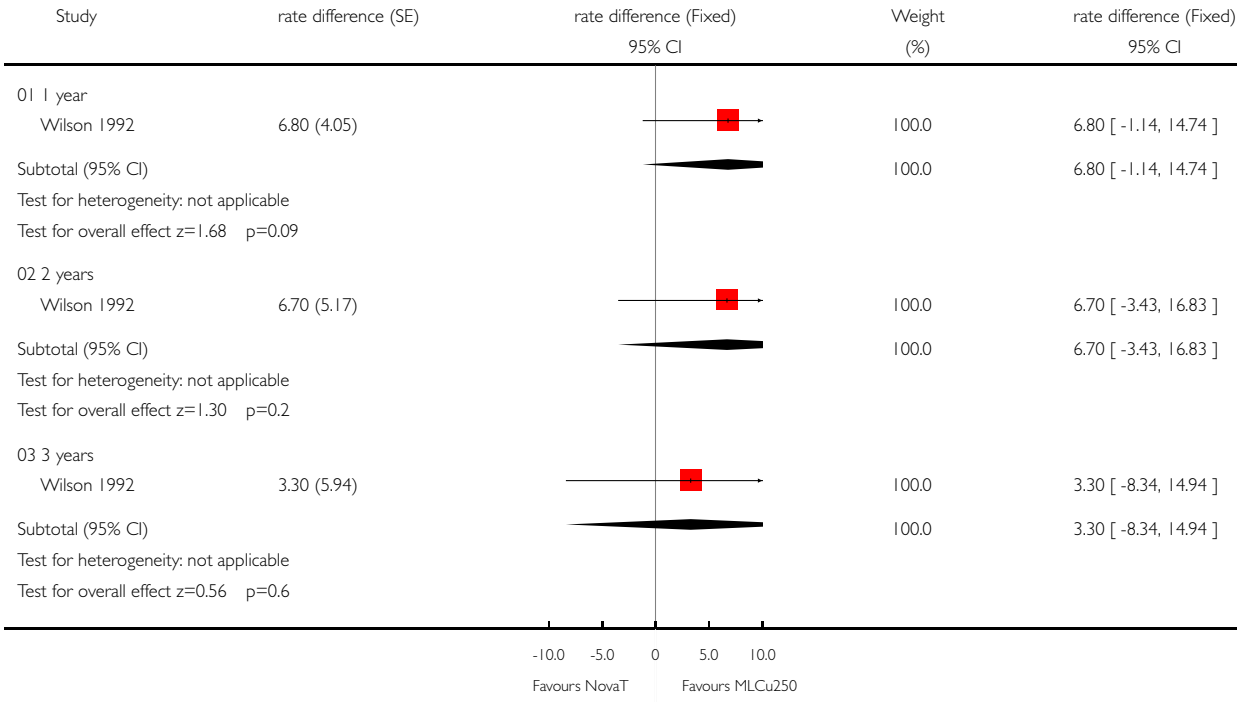


Analysis 17.06. Comparison 17 MLCu 250 vs NovaT, Outcome 06 Continuation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 17 MLCu 250 vs NovaT

Outcome: 06 Continuation

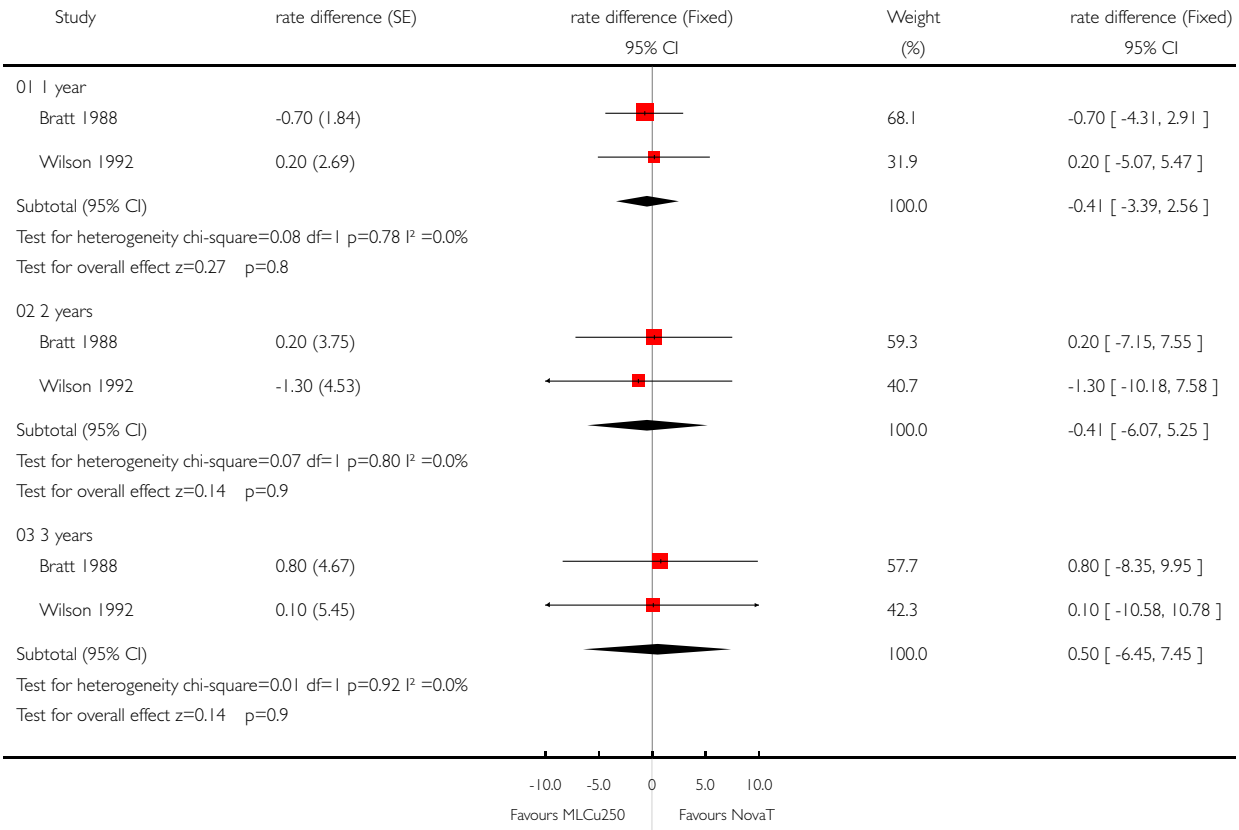


Analysis 17.07. Comparison 17 MLCu 250 vs NovaT, Outcome 07 Discontinuation: planned pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 17 MLCu 250 vs NovaT

Outcome: 07 Discontinuation: planned pregnancy

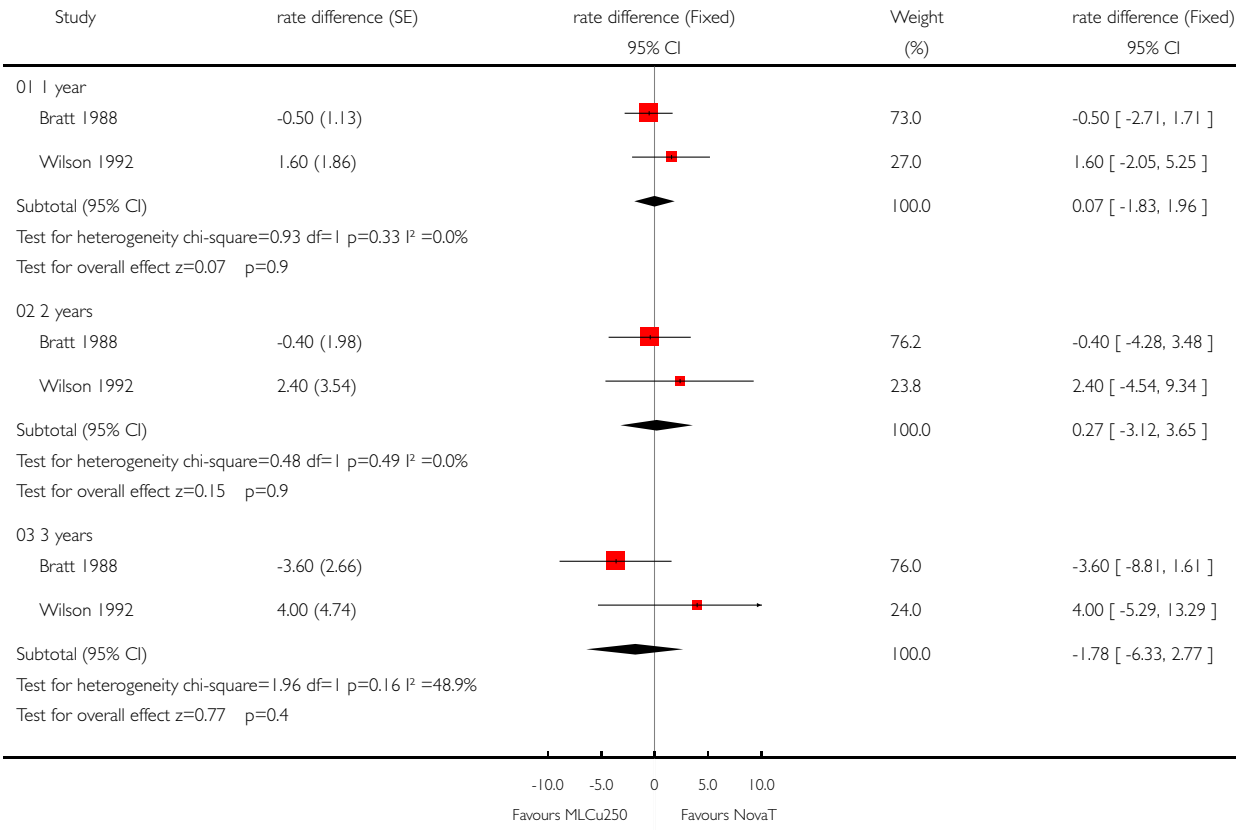


Analysis 17.08. Comparison 17 MLCu 250 vs NovaT, Outcome 08 Discontinuation: other personal reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 17 MLCu 250 vs NovaT

Outcome: 08 Discontinuation: other personal reasons

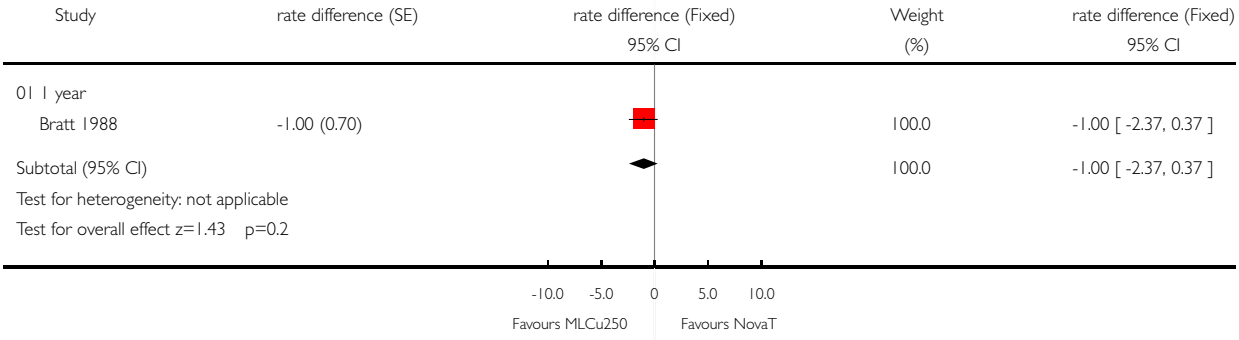


Analysis 17.09. Comparison 17 MLCu 250 vs NovaT, Outcome 09 Perforation

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 17 MLCu 250 vs NovaT

Outcome: 09 Perforation



Analysis 18.01. Comparison 18 MLCu 250 vs Cu 7, Outcome 01 Pregnancy

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 18 MLCu 250 vs Cu 7

Outcome: 01 Pregnancy

Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
Goh 1983	-2.70 (1.30)		100.0	-2.70 [-5.25, -0.15]
Subtotal (95% CI)			100.0	-2.70 [-5.25, -0.15]
Test for heterogeneity: not applicable				
Test for overall effect z=2.08 p=0.04				
02 2 years				
Goh 1983	-2.40 (1.50)		100.0	-2.40 [-5.34, 0.54]
Subtotal (95% CI)			100.0	-2.40 [-5.34, 0.54]
Test for heterogeneity: not applicable				
Test for overall effect z=1.60 p=0.1				
03 3 years				
Subtotal (95% CI)			0.0	Not estimable
Test for heterogeneity: not applicable				
Test for overall effect: not applicable				

Analysis 18.02. Comparison 18 MLCu 250 vs Cu 7, Outcome 02 Expulsion

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 18 MLCu 250 vs Cu 7

Outcome: 02 Expulsion

Study	rate difference (SE)	rate difference (Fixed) 95% CI	Weight (%)	rate difference (Fixed) 95% CI
01 1 year				
Goh 1983	-3.70 (1.53)		100.0	-3.70 [-6.70, -0.70]
Subtotal (95% CI)			100.0	-3.70 [-6.70, -0.70]
Test for heterogeneity: not applicable				
Test for overall effect z=2.42 p=0.02				
02 2 years				
Goh 1983	-4.50 (1.66)		100.0	-4.50 [-7.75, -1.25]
Subtotal (95% CI)			100.0	-4.50 [-7.75, -1.25]
Test for heterogeneity: not applicable				

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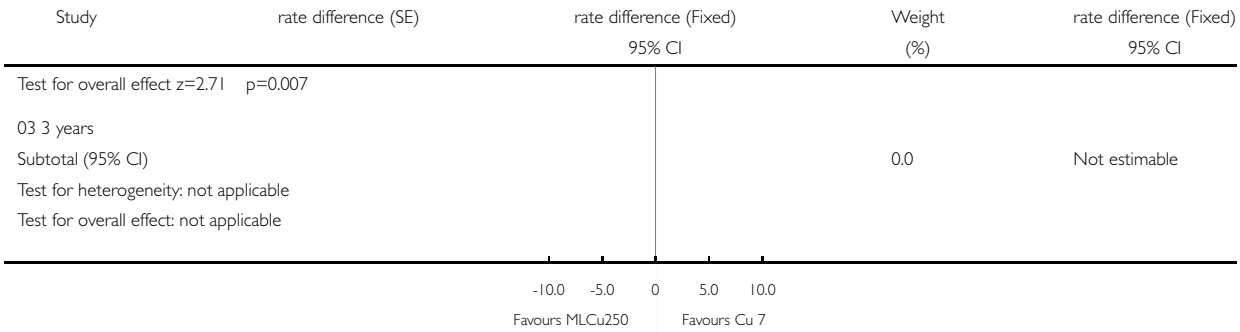
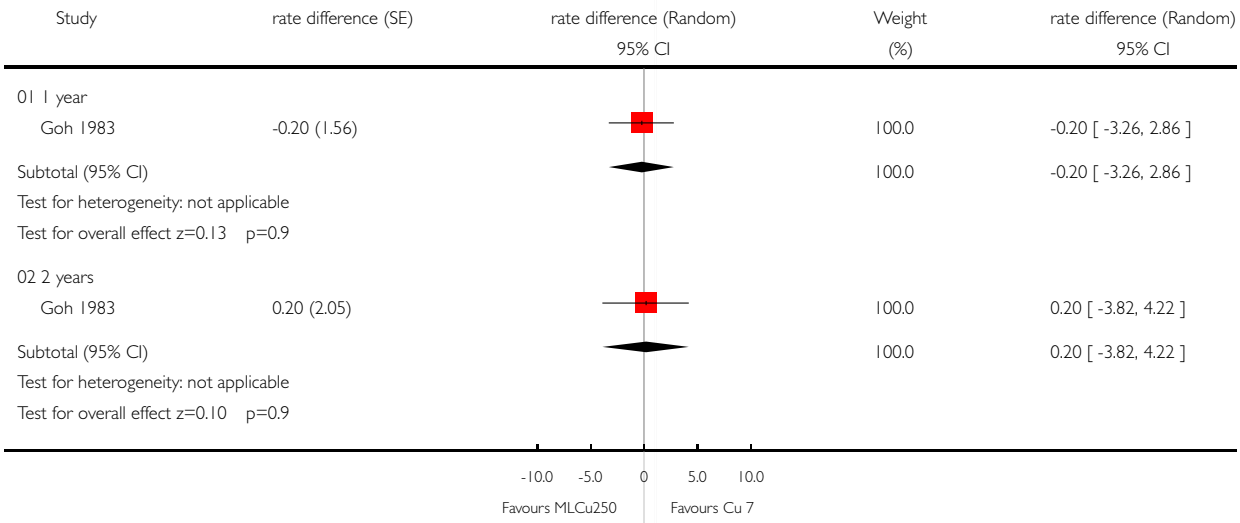


Analysis 18.03. Comparison 18 MLCu 250 vs Cu 7, Outcome 03 Discontinuation: bleeding and pain

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 18 MLCu 250 vs Cu 7

Outcome: 03 Discontinuation: bleeding and pain

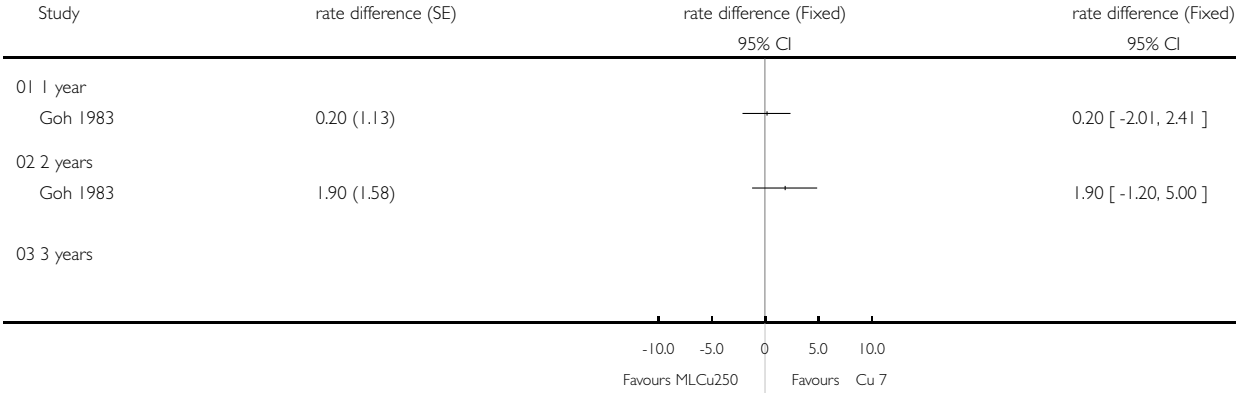


Analysis 18.05. Comparison 18 MLCu 250 vs Cu 7, Outcome 05 Discontinuation: other medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 18 MLCu 250 vs Cu 7

Outcome: 05 Discontinuation: other medical reasons

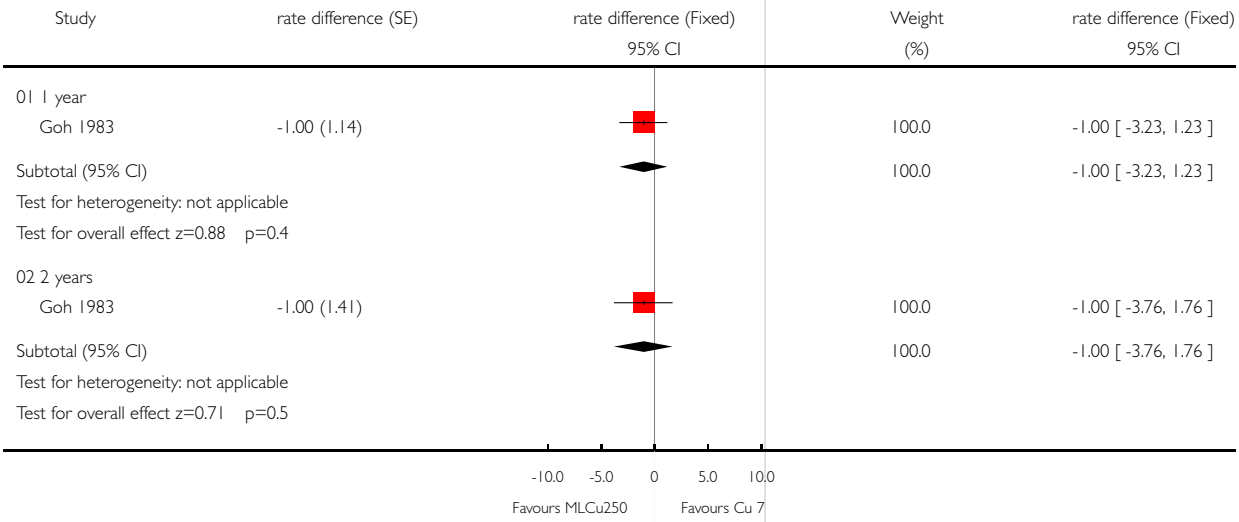


Analysis 18.06. Comparison 18 MLCu 250 vs Cu 7, Outcome 06 Discontinuation: non-medical reasons

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 18 MLCu 250 vs Cu 7

Outcome: 06 Discontinuation: non-medical reasons



Analysis 18.07. Comparison 18 MLCu 250 vs Cu 7, Outcome 07 Discontinuation: all use related

Review: Copper containing, framed intra-uterine devices for contraception

Comparison: 18 MLCu 250 vs Cu 7

Outcome: 07 Discontinuation: all use related