

Treatment options for heavy menstrual bleeding: Systematic review, pairwise and network meta-analysis

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INTRODUCTION

- Heavy menstrual bleeding (HMB) affects 1 in 3 women of reproductive age
- There are many treatment options available for HMB, but evidence of treatment efficacy and safety is limited

OBJECTIVE

- To provide up-to-date, comprehensive evidence on medical and surgical treatment options for women with heavy menstrual bleeding through systematic review, meta-analysis and network meta-analysis

METHODS

- Systematic searches were conducted up to August 2024
- Random-effects pairwise and network meta-analyses

Inclusion Criteria

- Randomised Controlled Trials (RCTs)
- Women with HMB
- Comparing any medical or surgical treatment compared to placebo or other active treatments

Primary Outcomes:

- Menstrual blood loss (MBL)
- Quality of Life (QoL)
- Adverse events (AEs)

Secondary Outcomes:

- Amenorrhea, Haemoglobin, Dysmenorrhea, Satisfaction, Treatment failure

RESULTS

1 Medical treatments for HMB due to uterine fibroids

3 main treatment groups:

- GnRH analogues (e.g. elagolix, linzagolix)
- GnRH analogues + hormone replacement therapy (e.g. UPA, vilaprisan)
- SPRMs (e.g. UPA, vilaprisan)

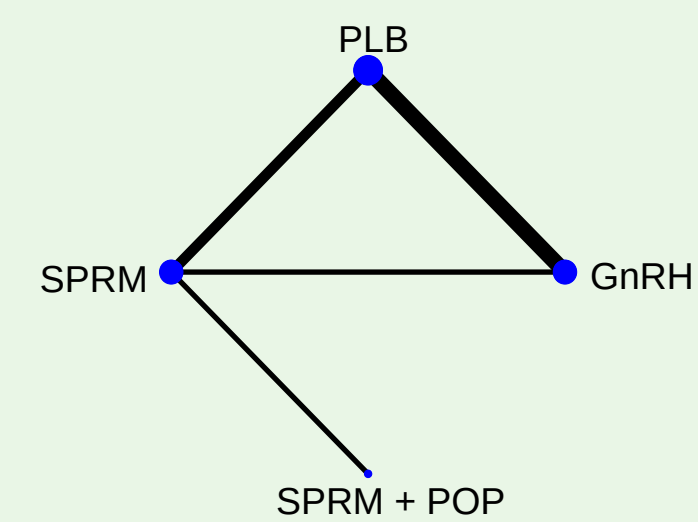


Figure 1: Network connectivity diagram

Menstrual blood loss:

Treatment group	Reduction in mL MD (95% CI)	No trials	No patients
SPRMs	218 (141 – 295)	2	1094
GnRH analogues	167 (103 – 230)	4	362
GnRH analogues + HRT	207 (174 – 241)	2	135

Table 1: Reduction in MBL for medical treatment of HMB due to uterine fibroids compared with placebo (pairwise meta-analysis)

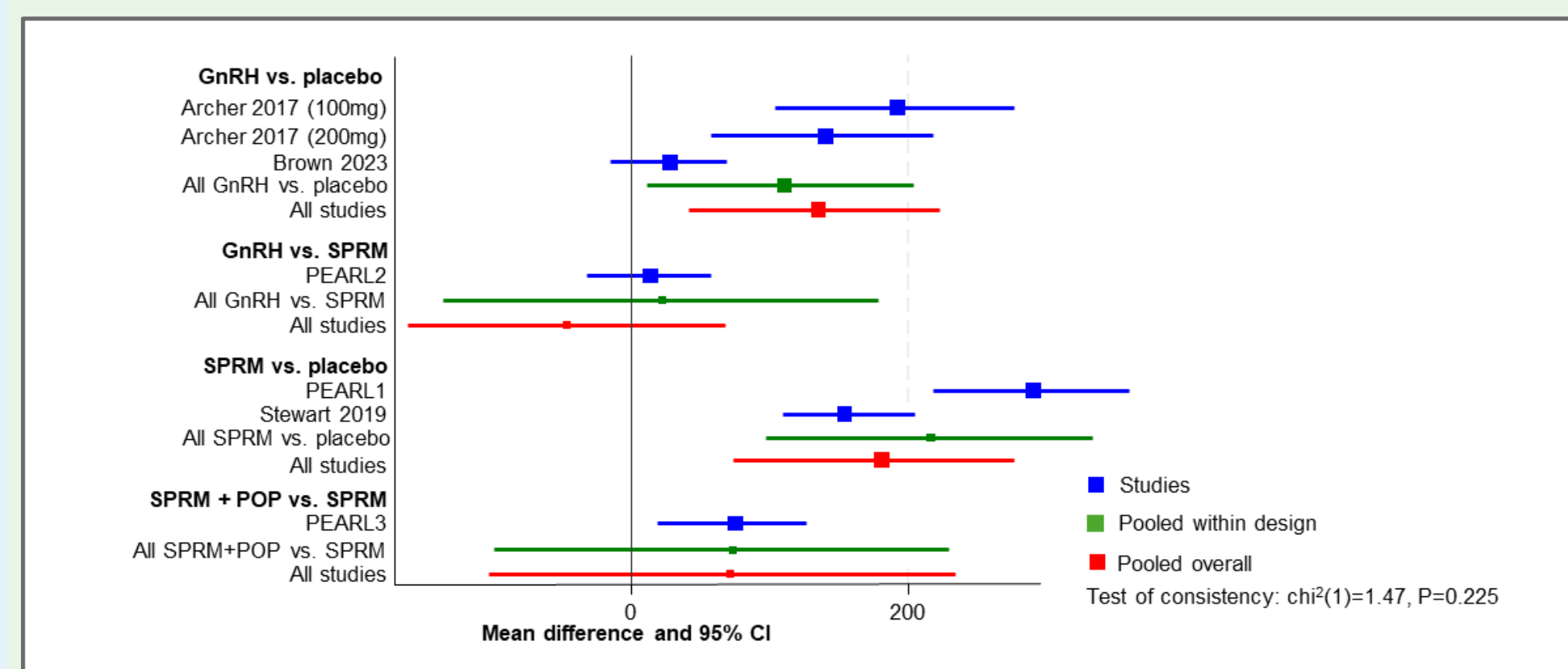


Figure 2: Reduction in MBL of medical treatments for HMB due to uterine fibroids compared with each other (network meta-analysis)

Quality of Life: SPRMs, GnRH analogues and GnRH analogues with hormone replacement therapy all improve quality of life compared to placebo.

Safety: GnRH analogues alone significantly increase the risk of AEs compared to placebo (RR 1.28; 95%CI 1.20-1.36). No strong evidence that SPRMs or GnRH analogues + hormone replacement increase risk of AEs compared with placebo

2 Medical treatments for HMB due to unknown causes

Variety of treatments:

- Hormonal therapies (e.g. combined hormonal contraceptives (CHCs), progesterone-only pills (POPs), LNG-IUS)
- Non-hormonal therapies (e.g. tranexamic acid, NSAIDs)

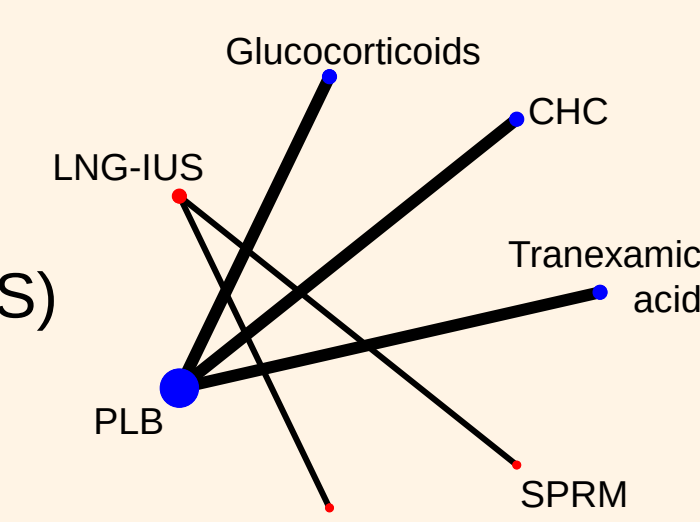


Figure 3: Network connectivity diagram

Menstrual blood loss:

Treatment group	Reduction in mL MD (95% CI)	No trials	No patients
CHCs	285 (141 – 429)	2	509
Tranexamic acid	49 (39 – 58)	2	548
Glucocorticoids	15 (-8 – 38)	1	97

Table 2: Reduction in MBL for medical treatment of HMB due to unknown causes compared with placebo (pairwise meta-analysis)

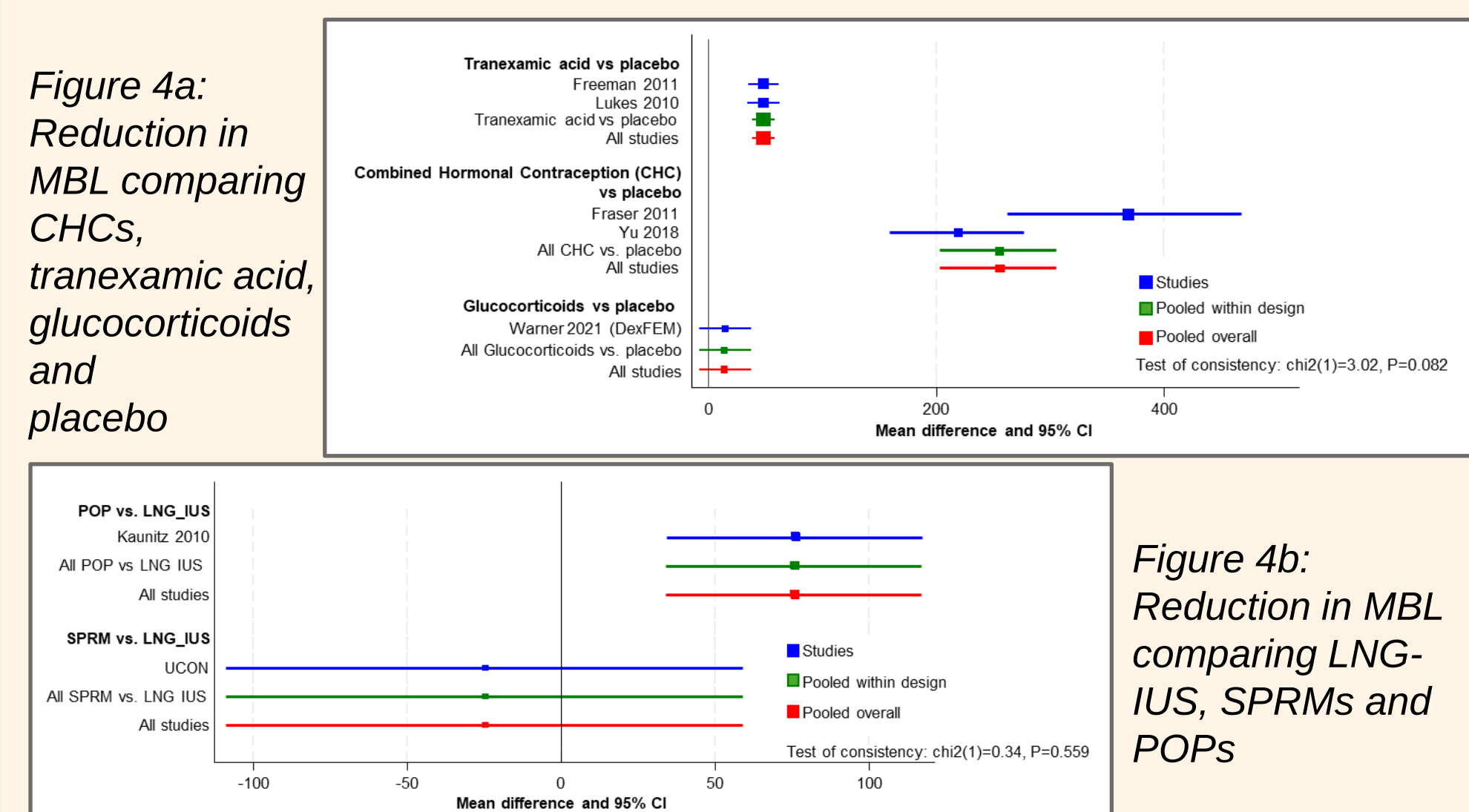


Figure 4a: Reduction in MBL comparing CHCs, tranexamic acid, glucocorticoids and placebo

Figure 4b: Reduction in MBL comparing LNG-IUS, SPRMs and POPs

Quality of Life: LNG-IUS and SPRMs seem to improve quality of life compared to placebo and compared to combined hormonal contraceptives.

Safety: No strong evidence that risk of AEs differs between combined hormonal contraceptives, tranexamic acid or placebo. There is no strong evidence that the risk of AEs differs between LNG-IUS, tranexamic acid and progesterone-only pills.

3 Surgeries or Procedures for HMB due to unknown causes

3 main treatment groups:

- Endometrial ablation techniques (1st Generation or 2nd Generation)
- Hysterectomy
- LNG-IUS (commonly used as a comparator for surgical treatments)

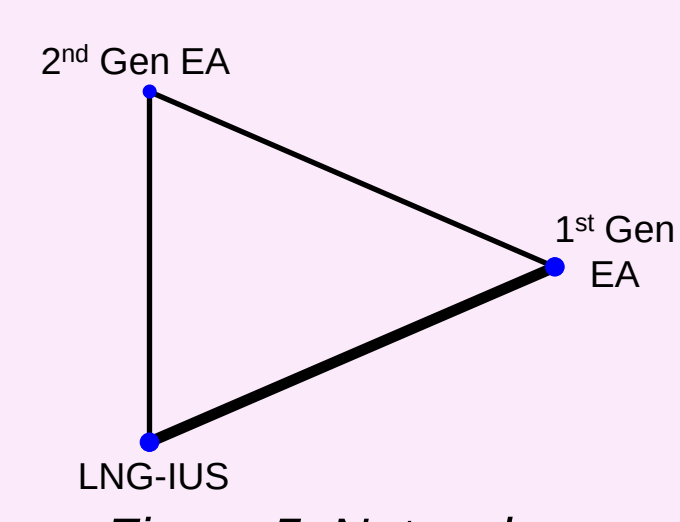


Figure 5: Network connectivity diagram

Menstrual blood loss:

Treatment group	Reduction in mL MD (95% CI)	No trials	No patients
1 st Gen EA vs LNG-IUS	34 (2 – 66)	2	152
2 nd Gen EA vs LNG-IUS	45 (34 – 57)	1	67
2 nd Gen EA vs 1 st Gen EA	15 (7 – 23)	1	139

Table 3: Reduction in MBL for medical treatment of HMB due to unknown causes compared with each other (pairwise meta-analysis)

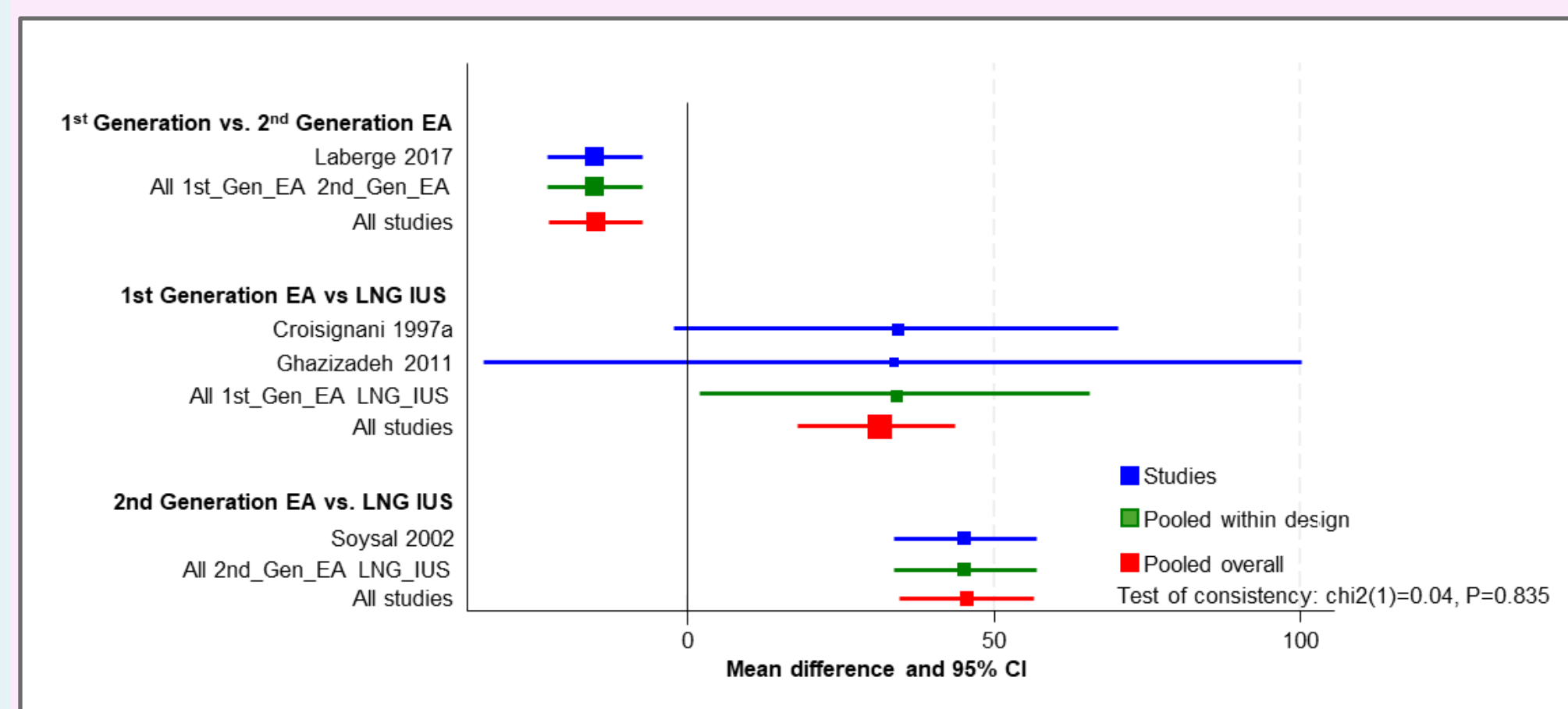


Figure 6: Reduction in MBL for surgical treatments for HMB due to unknown causes compared with each other (network meta-analysis)

Quality of Life: LNG-IUS seems to improve quality of life compared to endometrial ablation techniques, although across all eligible trials, the reported quality of life data is very sparse.

Safety: Both 1st Generation and 2nd Generation endometrial ablation reduce the risk of AEs compared to LNG-IUS, but data is sparse. The risk of AEs seems lower with 2nd Generation compared to 1st Generation endometrial ablation (RR 0.55; 95% CI 0.34-0.89).

BASELINE DATA

	1 Medical - Fibroids	2 Medical – Unknown Cause	3 Surgical – Unknown Cause
No trials	23	29	35
No patients	6715	4192	5292
Age (years)	42.2 (38.9 – 44.7)	38 (27.8 – 43.3)	42.6 (39.4 – 47.5)
Ethnicity	44% White 40% Black 14% Asian 2% Other/Unknown	68% White 11% Black 16% Asian 5% Other/Unknown	Only reported in 5/35 trials identified
MBL (mL)	245 (165 – 434)	267 (112 – 492)	454 (107 – 937)
BMI (kg/m ²)	28.7 (20.8 – 36.5)	26.5 (22.6 – 31.1)	28.0 (22.9 – 35.6)

Table 4: Key baseline characteristics of included participants

CONCLUSION

- Compared to placebo, all the medical treatments assessed appear to reduce menstrual blood loss both in HMB due to fibroids and unknown causes
- Endometrial ablation techniques reduce menstrual blood loss to a greater degree than LNG-IUS
- Despite identifying many eligible trials, uncertainty remains. This is due to:
 - Sparse data for treatment comparisons
 - Many different treatment comparisons
 - Inconsistent measurement and reporting of outcomes

Next steps:

- Complete analyses of secondary outcomes and sensitivity analyses to include data across all timepoints and treatment dosages
- Explore methods to include more available HMB trial data in meta-analyses
- Seek to improve consistency of outcome measurement and reporting in future trials