Birmingham Women's NHS
NHS Foundation Trust

UNIVERSITY OF BIRMINGHAM

AUB management: How do systematic reviews & meta-analysis help?

T Justin Clark

Consultant Gynaecologist
Birmingham Women's Hospital

Honorary Professor
University of Birmingham

Endometriosis and Women's Reproductive Life:

Session: Abnormal Uterine Bleeding

1st Congress of the Society of Endometriosis and Uterine Disorders

[Thursday 7 – Saturday 9 May 2015]

AUB management: How do systematic reviews & meta-analyses help us?

DEFINITIONS & RATIONALE

TJ Clark, Birmingham Women's Hospital & University of Birmingham

What is a systematic review?

- A literature review focused on a research question that tries to identify, appraise, select and synthesize all high quality research evidence relevant to that question.
  - Systematic reviews of high-quality randomized controlled trials are crucial to evidence-based medicine
- Systematic reviews usually summarise randomised controlled trial data of therapeutic interventions BUT methodologies have been developed to synthesise observational data
- Systematic reviews can also be used to address questions relating to diagnosis, disease prevalence, prognosis and qualitative issues

Why systematic reviews?

- Replaced traditional narrative reviews and expert commentaries as a way of summarising research evidence without bias.
  - Narrative reviews are inherently biased
    - Lack explicit criteria for article selection
    - No evaluation of selected articles for validity
    - Authors frequently have expert opinions (and biases) and find studies to support their positions (selection bias)

- Systematic reviews attempt to bring the same level of rigour to reviewing research evidence as should be used in producing that research evidence in the first place.
  - Based on a peer-reviewed protocol so that they can be replicated if necessary

What is a high quality systematic review?

- High quality systematic reviews seek to:
  - Identify all relevant published and unpublished evidence
  - Select studies or reports for inclusion
  - Assess the quality of each study or report
  - Synthesise the findings from individual studies or reports in an unbiased way
  - Interpret the findings and present a balanced and impartial summary of the findings with due consideration of any flaws in the evidence

Systematic reviews and identification of research needs

- Systematic reviews do not just provide clinical findings that can direct clinical practice BUT identify **research** questions and direct areas for further study
  - Relevant research
  - Rationally allocate research funding
  - Encourage collaboration (multicentre working)

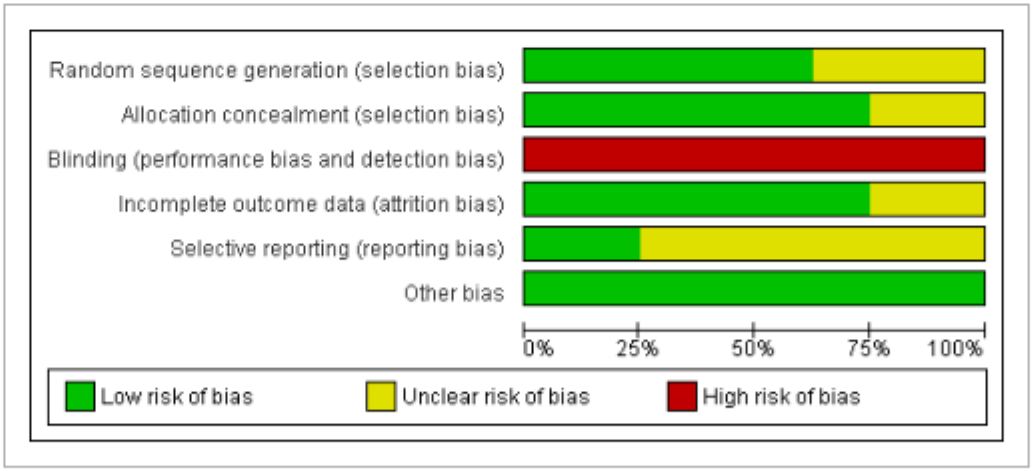
Caution with systematic reviews

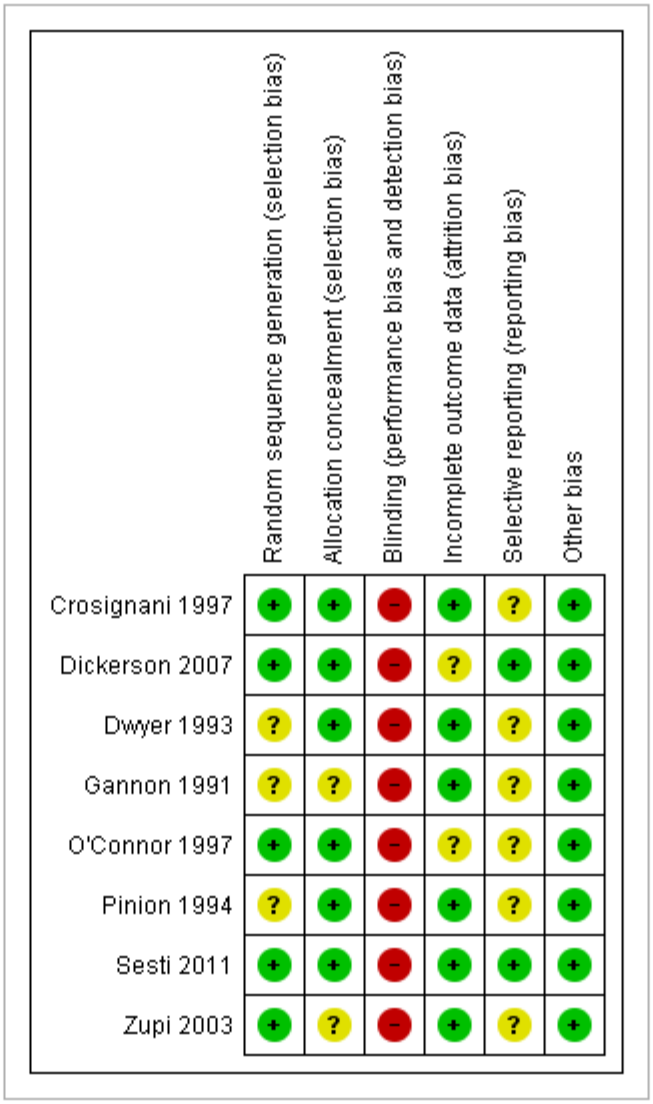
- Not all published systematic reviews have been produced with meticulous care
  - findings may sometimes mislead
  - Interrogating published reports by asking a series of questions can uncover deficiencies (critical appraisal)

- Proponents of systematic reviews argue that they accumulate wisdom
- Opponents of systematic reviews suggest that they propagate ignorance!!!??

Assessing bias of studies included in systematic reviews

- Use tools e.g. Cochrane collaboration 'risk





What is a meta-analysis?

- Refers to statistical methods for contrasting and combining results from different studies
- In its simplest form, meta-analysis is done by identifying a common statistical measure that is shared among studies, such as an effect size, and calculating a weighted average of that common measure.
  - This weighting is usually related to the sample sizes of the individual studies
- **Why meta-analysis?**
  - The aim of a meta-analysis is to aggregate information in order to achieve a higher statistical power for the measure of interest, as opposed to a less precise measure derived from a single study.
  - In addition meta-analysis may:
    - identify patterns among study results
    - sources of variation (heterogeneity)
    - other interesting relationships

Meta-analysis: Bias

- Usually conducted as part of a systematic review
- Bias possible when performing a meta-analysis arising from:
  - Search and study selection strategies
  - Dealing with incomplete data
  - Data analysis
  - Accounting for publication bias
- The decision not aggregate data statistically should be carefully considered in light of these possible sources of bias
  - Don't compare 'apples and pears'

Appraising and reporting systematic reviews & meta-analyses?

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a struc participants, ar implications of	
INTRODUCTION			
Rationale	3	Describe the ra	
Objectives	4	Provide an exp outcomes, and	
METHODS			
Protocol and registration	5	Indicate if a rev registration infc	
Eligibility criteria	6	Specify study c language, publ	
Information sources	7	Describe all inf additional studi	
Search	8	Present full ele repeated.	
Study selection	9	State the proce included in the	
Data collection process	10	Describe meth for obtaining ar	
Data items	11	List and define simplifications	
Risk of bias in individual studies	12	Describe meth done at the stu	
Summary measures	13	State the princi	
Synthesis of results	14	Describe the m (e.g., I^2) for eac	

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

AUB management: How do systematic reviews & meta-analyses help us?

ACCESS TO REVIEWS IN AUB

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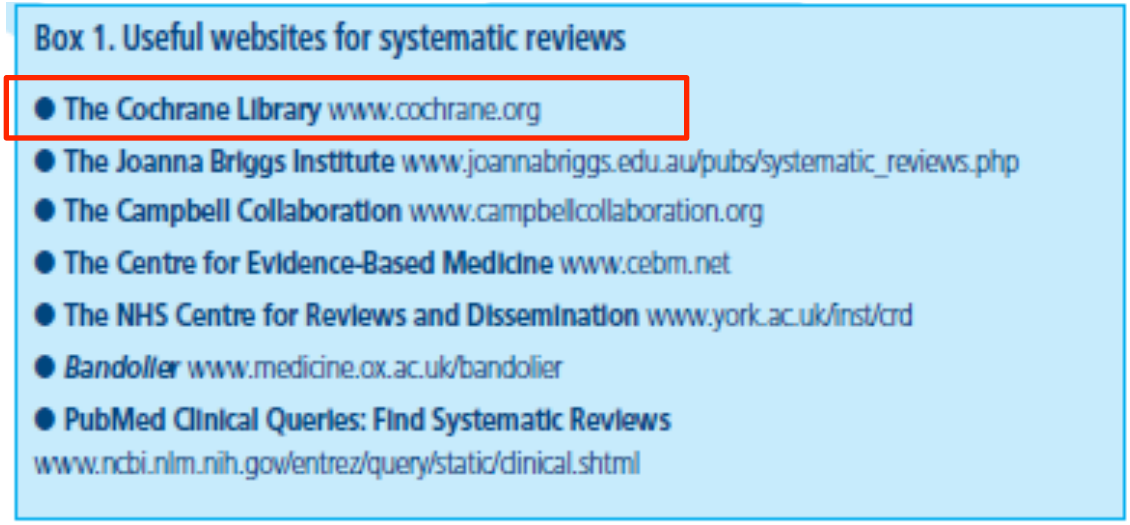
How can we access high quality systematic reviews?

- Medical journals
- Databases
- Other electronic sources.



Box 1. Useful websites for systematic reviews

- **The Cochrane Library** www.cochrane.org
- **The Joanna Briggs Institute** www.joannabriggs.edu.au/pubs/systematic_reviews.php
- **The Campbell Collaboration** www.campbellcollaboration.org
- **The Centre for Evidence-Based Medicine** www.cebm.net
- **The NHS Centre for Reviews and Dissemination** www.york.ac.uk/inst/crd
- ***Bandolier*** www.medicine.ox.ac.uk/bandolier
- **PubMed Clinical Queries: Find Systematic Reviews** www.ncbi.nlm.nih.gov/entrez/query/static/clinical.shtml

C ase

Cochrane Library

Trusted evidence.
Informed decisions.
Better health.

Cochrane Reviews ▼ Trials ▼

Cochrane Library

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Better health.

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Truste
Inform
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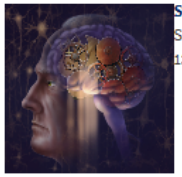
Cochrane Reviews ▼ Trials ▼

Editorials | Highlighted Reviews

Regulatory agencies hold the ke
drugs
Jeppe Schroll, Lisa Bero
20 April 2015

Should hormone therapy be rec
cardiovascular disease?
Helen Roberts, Martha Hickey
12 March 2015



Systematic reviews of case mar
Sascha Köpke & Jenny McCleery
13 January 2015

The emerging epidemic of endo
Emma Crosbie & Jo Morrison
22 December 2014

Browse by Cochrane Review G

Browse the *Cochrane Database of Systematic Reviews* by Coch

- Acute Respiratory Infections Group
- Airways Group
- Anaesthesia Group
- Back Group
- Bone, Joint and Muscle Trauma Group
- Breast Cancer Group
- Childhood Cancer Group
- Colorectal Cancer Group
- Consumers and Communication Group
- Cystic Fibrosis and Genetic Disorders Group
- Dementia and Cognitive Improvement Group
- Depression, Anxiety and Neurosis Group
- Developmental, Psychosocial and Learning Problems Group
- Drugs and Alcohol Group
- Ear, Nose and Throat Disorders Group
- Effective Practice and Organisation of Care Group
- Epilepsy Group
- Eyes and Vision Group
- Fertility Regulation Group
- Gynaecological Cancer Group
- Haematological Malignancies Group
- Heart Group
- Hepato-Biliary Group
- HIV/AIDS Group
- Hypertension Group
- Sexually Transmitted Infections Group

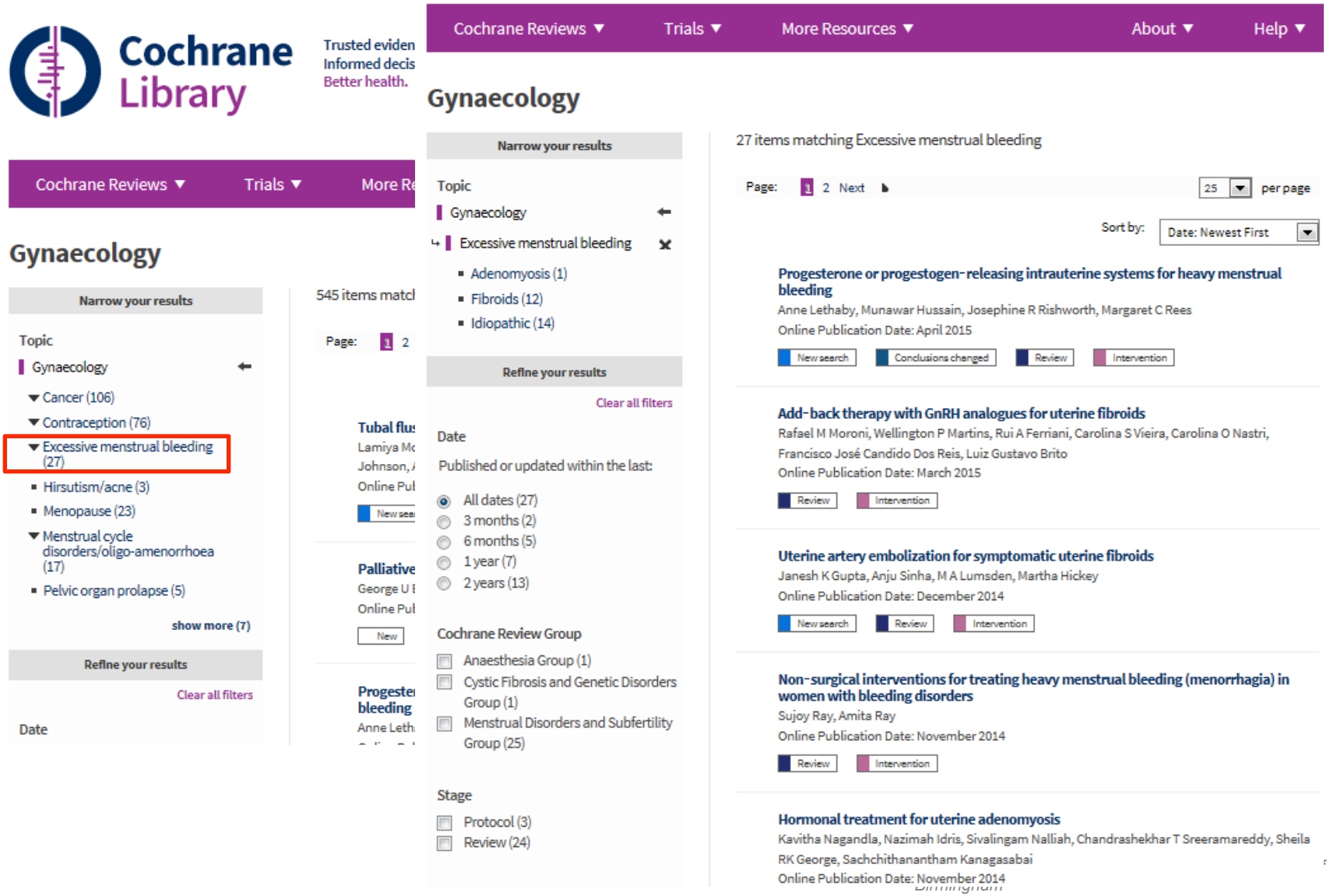
Cochrane Reviews ▼ Trials ▼ More Resources ▼

Browse by Topic

Browse the *Cochrane Database of Systematic Reviews* by Topic...

- Blood disorders
- Cancer
- Child health
- Complementary & alternative medicine
- Consumer & communication strategies
- Dentistry & oral health
- Developmental, psychosocial & learning problems
- Diagnosis
- Ear, nose & throat
- Effective practice/health systems
- Endocrine & metabolic
- Eyes & vision
- Gastroenterology
- Genetic disorders
- Gynaecology
- Health & safety at work
- Heart & circulation
- Infectious disease
- Kidney disease
- Lungs & airways
- Mental health
- Methodology
- Neonatal care
- Neurology
- Orthopaedics & trauma
- Pain & anaesthesia
- Pregnancy & childbirth
- Public health
- Rheumatology
- Skin
- Tobacco, drugs & alcohol
- Urology
- Wounds

Cochrane database



AUB management: How do systematic reviews & meta-analyses help us?

SURGICAL TREATMENT OF HMB

SEUD 2015

TJ Clark, Birmingham Women's Hospital & University of Birmingham

TCRE vs. hysterectomy

Cochrane Library
Cochrane Database of Systematic Reviews

Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding

New search | Review | Intervention

Rosalie J Fergusson, Anne Lethaby, Sasha Shepperd, Cindy Farquhar

First published: 29 November 2013 Full publication history

Assessed as up-to-date: 30 October 2013

Editorial Group: Cochrane Menstrual Disorders and Subfertility Group

DOI: 10.1002/14651858.CD000329.pub2

Cited by: 2 articles Refresh Citing literature

- 8 trials comparing endometrial resection and ablation:
  - Both procedures are effective, and satisfaction rates are high
  - Hysterectomy is associated with longer operating time (particularly for the laparoscopic route), a longer recovery period and higher rates of postoperative complications BUT it offers permanent relief from heavy menstrual bleeding
  - The initial cost of endometrial destruction is significantly lower than that of hysterectomy, but, because retreatment is often necessary, the cost difference narrows over time

- Future research
  - More studies are needed to assess rates of uterine rupture, occurrence of thromboembolism, need for repeat myomectomy and hysterectomy at a later stage.

TJ Clark, Birmingham Women's Hospital & University of Birmingham

TCRE vs. hysterectomy:

Forest plots (meta-analysis data presentatic

- **Outcome**: Proportion satisfied with treatment

Cochrane Library
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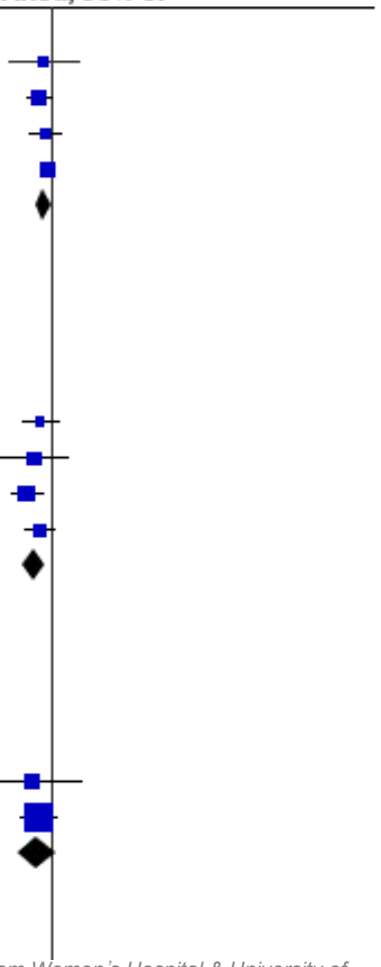
Study or Subgroup	TCRE/ablation Events	Total	Hysterectomy Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 At one year of follow-up						
Dickerson 2007	53	107	54	103	18.6%	0.94 [0.72, 1.23]
Dwyer 1993	84	99	89	95	30.7%	0.91 [0.82, 1.00]
O'Connor 1997	90	104	42	46	19.7%	0.95 [0.84, 1.07]
Pinion 1994	92	96	88	89	30.9%	0.97 [0.92, 1.02]
Subtotal (95% CI)		**406**		**333**	**100.0%**	**0.94 [0.88, 1.00]**
Total events	319		273			
Heterogeneity: Chi² = 2.11, df = 3 (P = 0.55); I² = 0%						
Test for overall effect: Z = 1.87 (P = 0.06)						
1.4.2 At two years of follow-up						
Crosignani 1997	33	38	37	39	16.7%	0.92 [0.79, 1.06]
Dickerson 2007	51	106	59	107	26.9%	0.87 [0.67, 1.13]
Dwyer 1993	64	81	69	72	33.5%	0.82 [0.73, 0.93]
O'Connor 1997	74	86	36	38	22.9%	0.91 [0.81, 1.02]
Subtotal (95% CI)		**311**		**256**	**100.0%**	**0.87 [0.80, 0.95]**
Total events	222		201			
Heterogeneity: Chi² = 1.75, df = 3 (P = 0.63); I² = 0%						
Test for overall effect: Z = 3.04 (P = 0.002)						
1.4.3 At four years of follow-up						
Dickerson 2007	23	47	29	51	29.7%	0.86 [0.59, 1.26]
Pinion 1994	61	76	64	72	70.3%	0.90 [0.79, 1.04]
Subtotal (95% CI)		**123**		**123**	**100.0%**	**0.89 [0.77, 1.03]**
Total events	84		93			
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%						



TCRE vs. hysterectomy:

Forest plots (meta-analysis data presentatic

- **Outcome:** Improvement in bleeding symptoms

Cochrane Library
Cochrane Database of Systematic Reviews

Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding

New search | Review | Intervention

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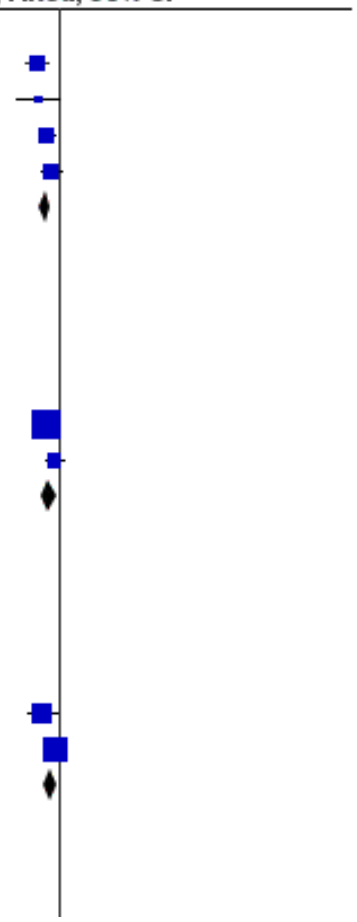
Study or Subgroup	TCRE/ablation Events	Total	Hysterectomy Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Within one year of follow-up						
Pinion 1994	80	96	97	97	30.4%	0.83 [0.76, 0.91]
Gannon 1991	21	25	26	26	8.1%	0.84 [0.70, 1.01]
Dwyer 1993	90	99	97	97	30.8%	0.91 [0.85, 0.97]
Dickerson 2007	94	107	96	103	30.6%	0.94 [0.86, 1.03]
Subtotal (95% CI)		**327**		**323**	**100.0%**	**0.89 [0.85, 0.93]**
Total events	285		316			
Heterogeneity: Chi² = 4.33, df = 3 (P = 0.23); I² = 31%						
Test for overall effect: Z = 4.92 (P < 0.00001)						
1.1.2 At two years of follow-up						
Dickerson 2007	90	106	101	107	71.8%	0.90 [0.82, 0.99]
Crosignani 1997	34	35	44	44	28.2%	0.97 [0.90, 1.04]
Subtotal (95% CI)		**141**		**151**	**100.0%**	**0.92 [0.86, 0.99]**
Total events	124		145			
Heterogeneity: Chi² = 2.13, df = 1 (P = 0.14); I² = 53%						
Test for overall effect: Z = 2.39 (P = 0.02)						
1.1.3 At four years of follow-up						
Dickerson 2007	40	47	50	51	40.7%	0.87 [0.77, 0.98]
Pinion 1994	71	73	66	66	59.3%	0.97 [0.93, 1.02]
Subtotal (95% CI)		**120**		**117**	**100.0%**	**0.93 [0.88, 0.99]**
Total events	111		116			
Heterogeneity: Chi² = 4.65, df = 1 (P = 0.03); I² = 79%						
Test for overall effect: Z = 2.47 (P = 0.01)						



TCRE vs. hysterectomy:

Forest plots (meta-analysis data presentatic

- **Outcome**: Requirement for further surgery

Cochrane Library
Cochrane Database of Systematic Reviews

Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding

New search | Review | Intervention

Rosalie J Fergusson, Anne Lethaby, Sasha Shepperd, Cindy Farquhar

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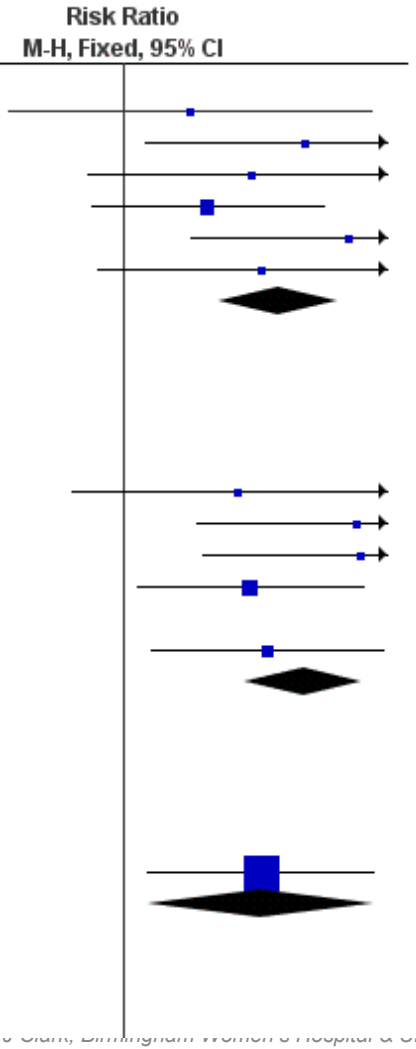
DOI: 10.1002/14651858.CD000329.pub2
Cited by: 2 articles Refresh Citing literature

Study or Subgroup	TCRE/ablation Events	Total	Hysterectomy Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 Within one year after surgery						
Crosignani 1997	1	41	0	44	12.6%	3.21 [0.13, 76.74]
Dwyer 1993	12	99	0	97	13.2%	24.50 [1.47, 408.14]
Gannon 1991	4	25	0	26	12.8%	9.35 [0.53, 165.12]
O'Connor 1997	9	116	1	56	35.1%	4.34 [0.56, 33.46]
Pinion 1994	28	105	0	97	13.5%	52.70 [3.26, 851.56]
Zupi 2003	5	89	0	92	12.8%	11.37 [0.64, 202.59]
Subtotal (95% CI)		**475**		**412**	**100.0%**	**14.94 [5.24, 42.57]**
Total events	59		1			
Heterogeneity: Chi² = 3.35, df = 5 (P = 0.65); I² = 0%						
Test for overall effect: Z = 5.06 (P < 0.00001)						
1.3.2 At two years after surgery						
Crosignani 1997	3	41	0	44	12.7%	7.50 [0.40, 140.91]
Dickerson 2007	27	110	0	118	12.7%	58.96 [3.64, 955.12]
Dwyer 1993	32	99	0	97	13.3%	63.70 [3.96, 1025.88]
O'Connor 1997	19	116	1	56	35.5%	9.17 [1.26, 66.80]
Sesti 2011	0	34	0	34		Not estimable
Zupi 2003	12	89	1	92	25.9%	12.40 [1.65, 93.42]
Subtotal (95% CI)		**489**		**441**	**100.0%**	**23.36 [8.30, 65.75]**
Total events	93		2			
Heterogeneity: Chi² = 2.73, df = 4 (P = 0.60); I² = 0%						
Test for overall effect: Z = 5.97 (P < 0.00001)						
1.3.3 At three years after surgery						
O'Connor 1997	23	116	1	56	100.0%	11.10 [1.54, 80.14]
Subtotal (95% CI)		**116**		**56**	**100.0%**	**11.10 [1.54, 80.14]**
Total events	23		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.39 (P = 0.02)						



First generation ablation/resection v second generation ablation

Cochrane Library

Cochrane Database of Systematic Reviews

Endometrial resection and ablation techniques for heavy menstrual bleeding

New search | Review | Intervention

Anne Lethaby, Josien Penninx, Martha Hickey, Ray Garry, Jane Marjoribanks

First published: 30 August 2013 Full publication history

Assessed as up-to-date: 12 June 2013

Editorial Group: Cochrane Menstrual Disorders and Subfertility Group

DOI: 10.1002/14651858.CD001501.pub4

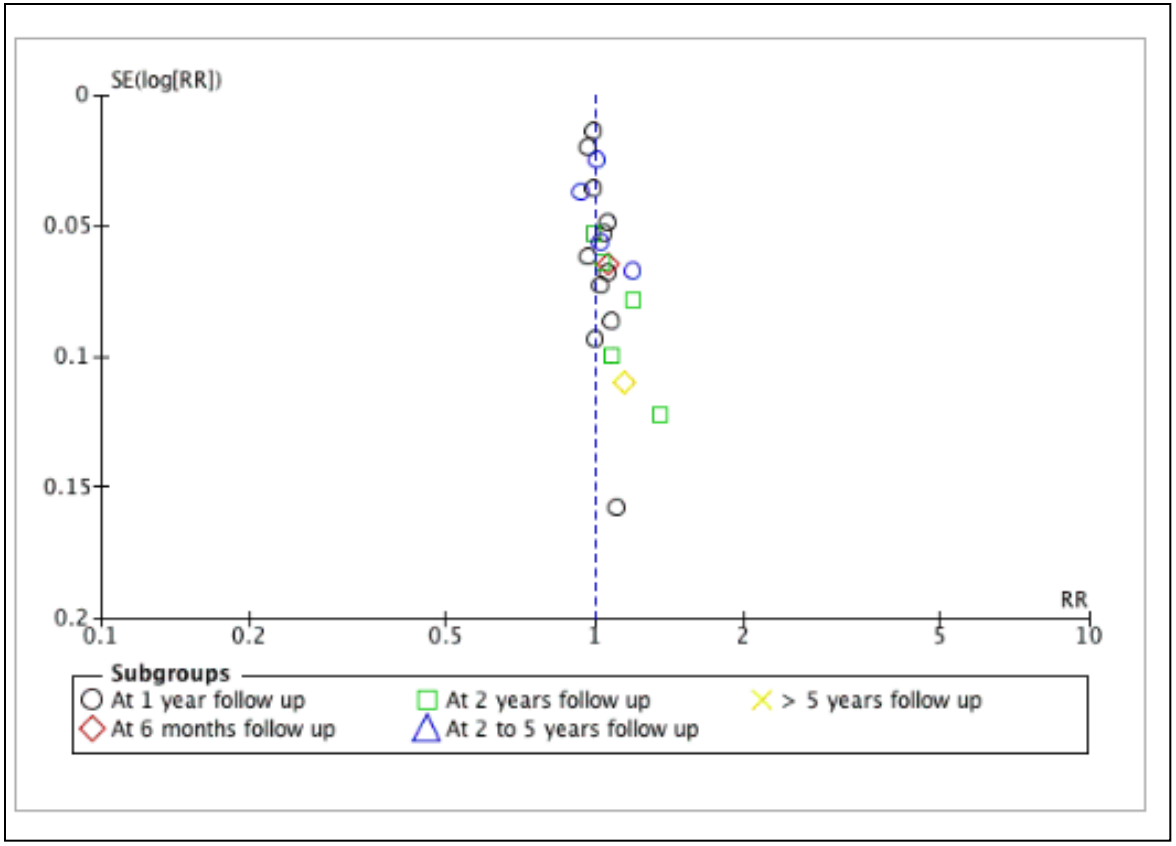
Cited by: 2 articles Refresh Citing literature

- Twenty five trials (4040 women) with sample sizes ranging from 20 to 372 comparing different endometrial resection and ablation techniques:
  - The rapid development of a number of new methods of endometrial destruction has made systematic comparisons between individual methods and with the 'gold standard' first-generation techniques difficult
  - Most of the newer techniques are technically easier to perform than traditional hysteroscopy-based methods but technical difficulties with the new equipment need to be addressed
  - Overall, the existing evidence suggests that success, satisfaction rates and complication profiles of newer techniques of ablation compare favourably with hysteroscopic techniques.
    - There is sufficient evidence to confirm that, on average, second-generation techniques are technically more simple and quicker to perform than first-generation techniques, while satisfaction rates and reduction in heavy menstrual bleeding are similar
    - The potential for second-generation methods to be performed under local anaesthesia is a considerable advantage and should be considered in cases a where general anaesthetic may confer particular risk.

First generation endometrial ablation/resection vs. second generation endometrial ablation

Funnel plots: Publication bia

- Selective reporting of satisfaction rates



For all time points except long-term follow up (10 years) there was no evidence of asymmetry. However, the addition of the single trial assessing satisfaction at 10 years suggested that there was a degree of asymmetry. Thus, long-term results should be considered with caution, until other long-term studies are published.

Cochrane Library

Cochrane Database of Systematic Reviews

Endometrial resection and ablation techniques for heavy menstrual bleeding

New search | Review | Intervention

Anne Lethaby, Josien Penninx, Martha Hickey, Ray Garry, Jane Marjoribanks

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‘Network’ meta-analysis

BMJ

BMJ 2013;346:f2914 doi: 10.1136/bmj.f2914 (Published 14 May 2013)

RESEARCH METHODS & REPORTING

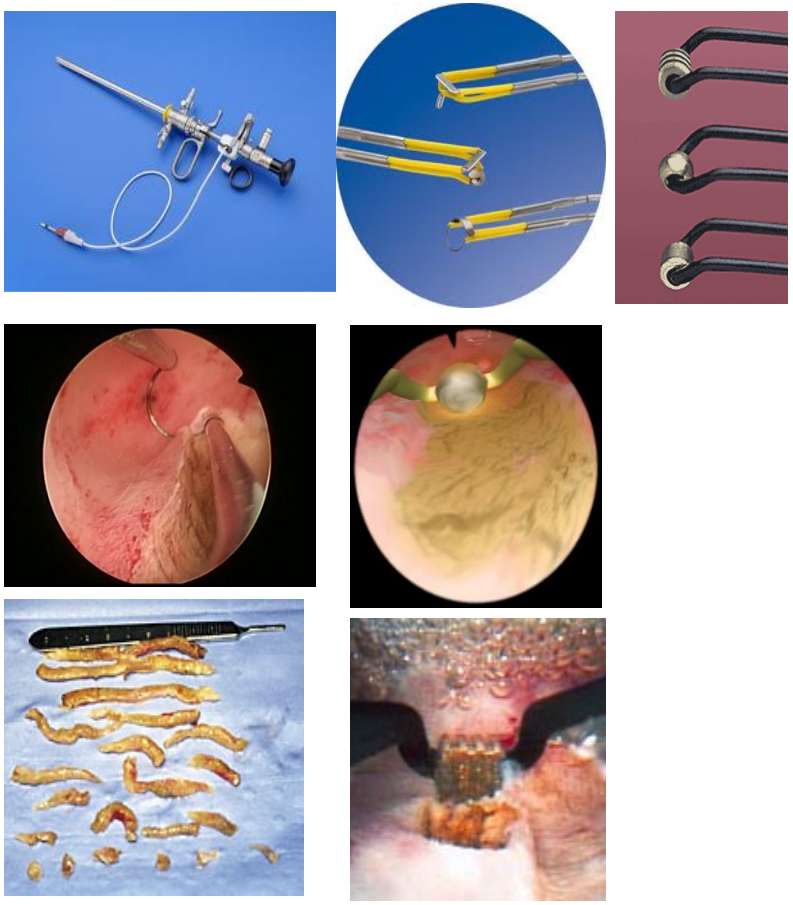
Demystifying trial networks and network meta-analysis

Networks of randomized clinical trials can be evaluated in the context of a network meta-analysis, a procedure that permits inferences into the comparative effectiveness of interventions that may or may not have been evaluated directly against each other. This approach is quickly gaining popularity among clinicians and guideline decision makers. However, certain methodological aspects are poorly understood. Here, we explain the geometry of a network, statistical and conceptual heterogeneity and incoherence, and challenges in the application and interpretation of data synthesis. These concepts are essential to make sense of a network meta-analysis.

Edward J Mills *associate professor*[1 2], Kristian Thorlund *associate professor*[2 3], John P A Ioannidis *professor*[2 4]

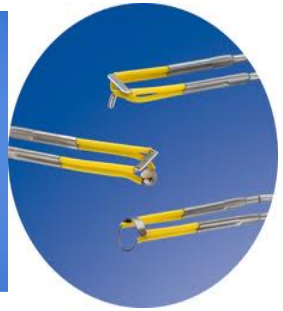
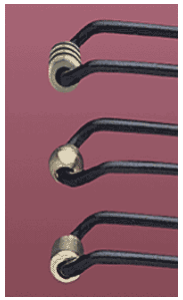
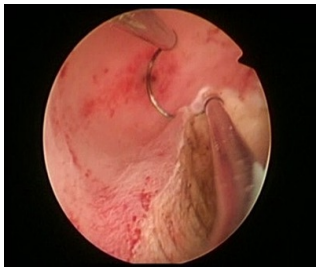
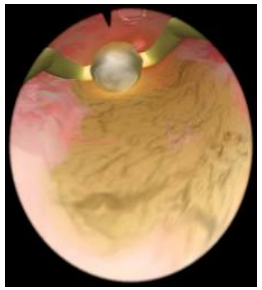
First generation ablation/resection vs. second generation ablation

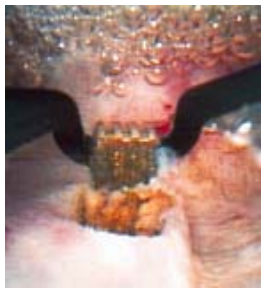
1st generation



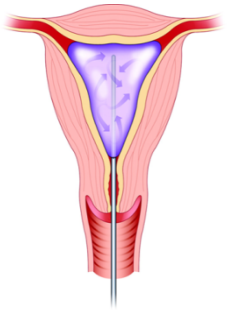
First generation ablation/resection vs. second generation ablation

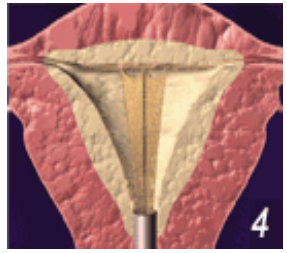
1st generation

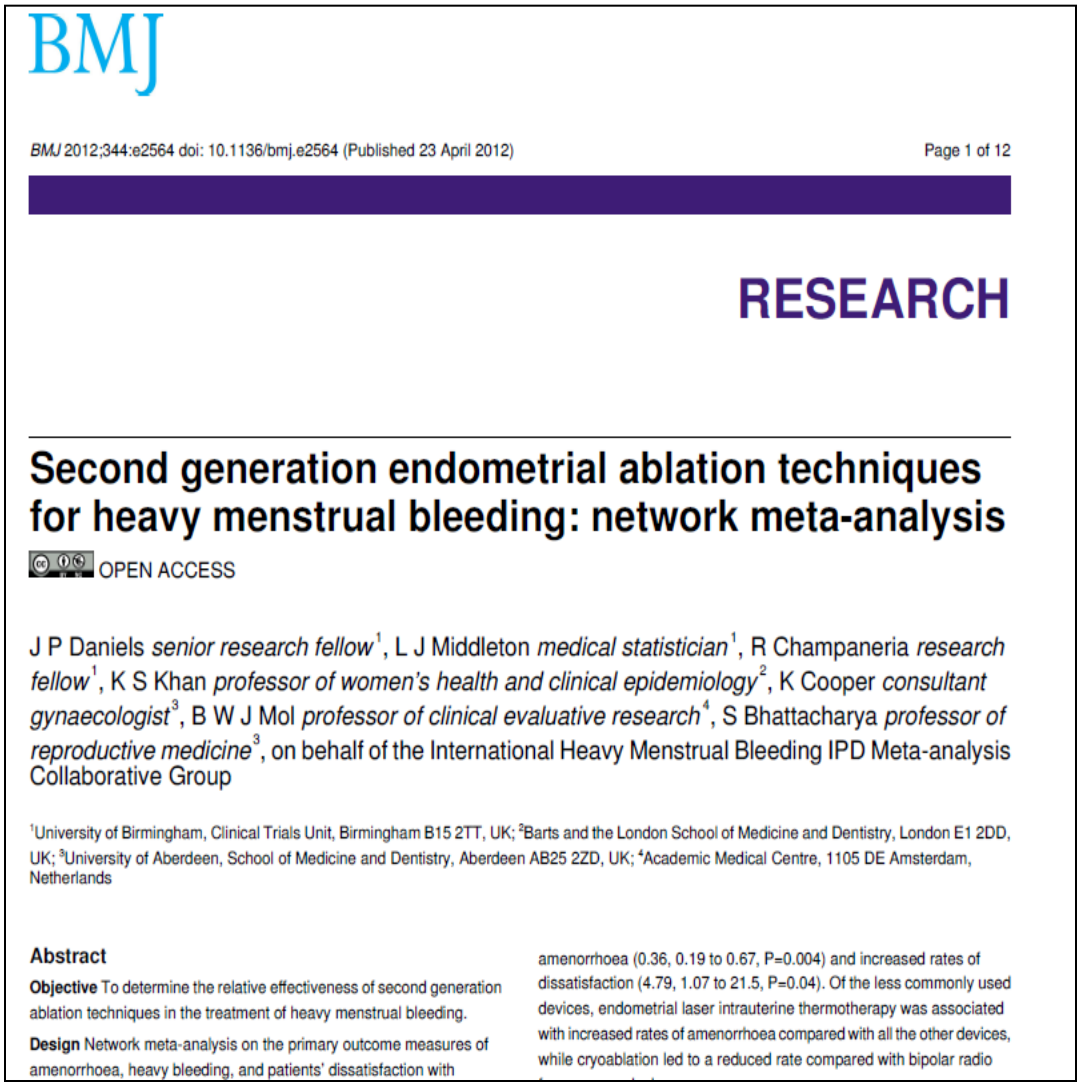


2nd generation





Which ablative device: network meta-analysis?



BMJ

BMJ 2012;344:e2564 doi: 10.1136/bmj.e2564 (Published 23 April 2012)

RESEARCH

Second generation endometrial ablation techniques for heavy menstrual bleeding: network meta-analysis

OPEN ACCESS

J P Daniels *senior research fellow*[1], L J Middleton *medical statistician*[1], R Champaneria *research fellow*[1], K S Khan *professor of women's health and clinical epidemiology*[2], K Cooper *consultant gynaecologist*[3], B W J Mol *professor of clinical evaluative research*[4], S Bhattacharya *professor of reproductive medicine*[3], on behalf of the International Heavy Menstrual Bleeding IPD Meta-analysis Collaborative Group

[1]University of Birmingham, Clinical Trials Unit, Birmingham B15 2TT, UK; [2]Barts and the London School of Medicine and Dentistry, London E1 2DD, UK; [3]University of Aberdeen, School of Medicine and Dentistry, Aberdeen AB25 2ZD, UK; [4]Academic Medical Centre, 1105 DE Amsterdam, Netherlands

Abstract

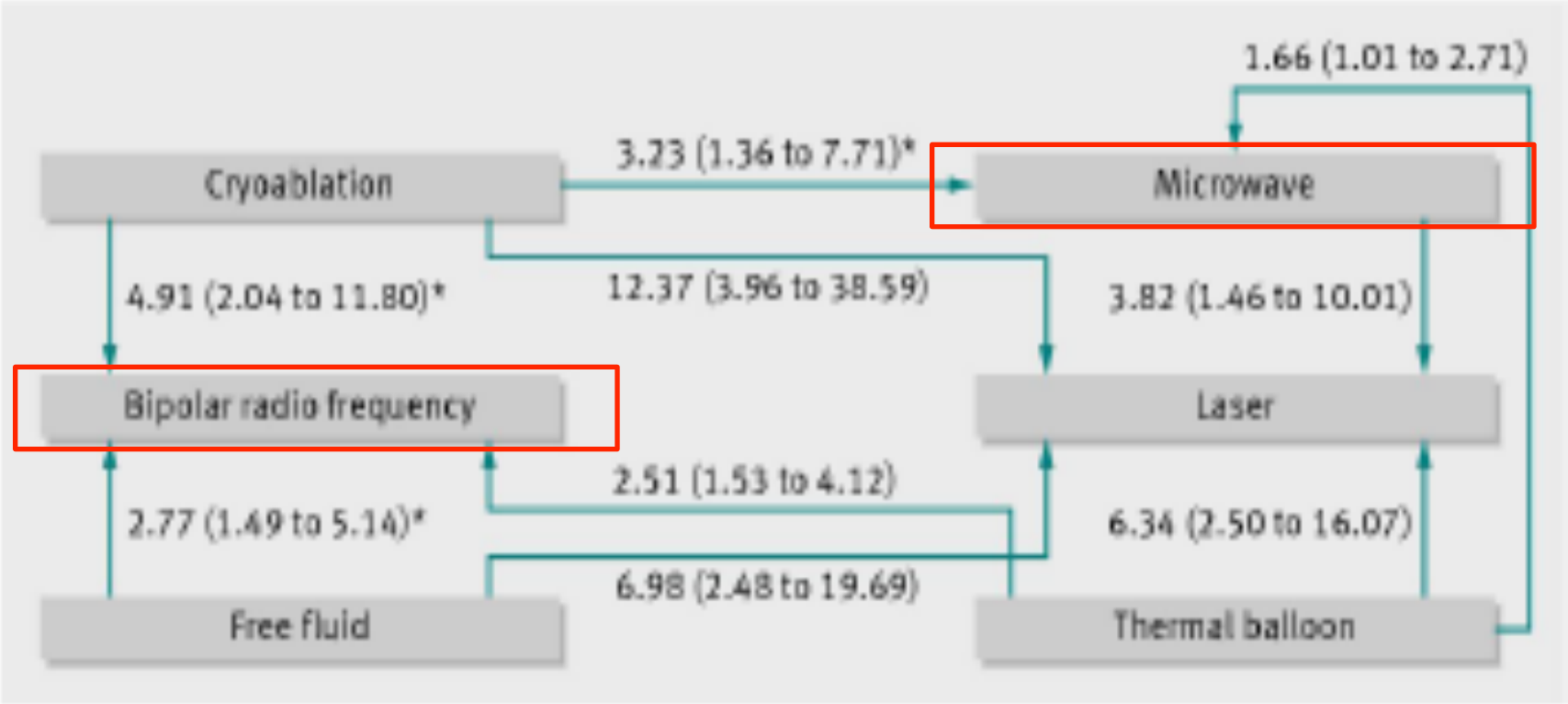
Objective To determine the relative effectiveness of second generation ablation techniques in the treatment of heavy menstrual bleeding.

Design Network meta-analysis on the primary outcome measures of amenorrhoea, heavy bleeding, and patients' dissatisfaction with

amenorrhoea (0.36, 0.19 to 0.67, P=0.004) and increased rates of dissatisfaction (4.79, 1.07 to 21.5, P=0.04). Of the less commonly used devices, endometrial laser intrauterine thermotherapy was associated with increased rates of amenorrhoea compared with all the other devices, while cryoablation led to a reduced rate compared with bipolar radio

Which ablative device?:

Amenorrhoea at 12 months - odds ratio (95% CI)



BMJ

BMJ 2012;344:e2564 doi: 10.1136/bmj.e2564 (Published 23 April 2012)

RESEARCH

Second generation endometrial ablation techniques for heavy menstrual bleeding: network meta-analysis

OPEN ACCESS

J P Daniels *senior research fellow*[1], L J *fellow*[1], K S Khan *professor of women's gynaecologist*[3], B W J Mol *professor of reproductive medicine*[3], on behalf of the Collaborative Group

[1]University of Birmingham, Clinical Trials Unit, Birmingham B UK; [3]University of Aberdeen, School of Medicine and Dentis Netherlands

Abstract

Objective To determine the relative effectiveness of second generation ablation techniques in the treatment of heavy menstrual bleeding.

Design Network meta-analysis on the primary outcome measures of amenorrhoea, heavy bleeding, and patients' dissatisfaction with treatment.

Data sources Nineteen randomised controlled trials (involving 3287 women) were identified through electronic searches of the Cochrane Library, Medline, Embase and PsycINFO databases from inception to April 2011. The reference lists of known relevant articles were searched for further articles. Two reviewers independently selected articles without language restrictions.

Eligibility criteria for selecting studies Randomised controlled trials involving second generation endometrial destruction techniques for women with heavy menstrual bleeding unresponsive to medical treatment.

Results Of the three most commonly used techniques, network meta-analysis showed that bipolar radiofrequency and microwave ablation resulted in higher rates of amenorrhoea than thermal balloon ablation at around 12 months (odds ratio 2.51, 95% confidence interval 1.53 to 4.12, P<0.001; and 1.66, 1.01 to 2.71, P=0.05, respectively), but there was no evidence of a convincing difference between the three techniques in the number of women dissatisfied with treatment or still experiencing heavy bleeding. Compared with bipolar radio frequency and microwave devices, an increased number of women still experienced heavy bleeding after free fluid ablation (2.19, 1.07 to 4.50, P=0.03; and 2.91, 1.23 to 6.88, P=0.02, respectively). Compared with radio frequency ablation, free fluid ablation was associated with reduced rates of amenorrhoea (0.58, 0.19 to 0.87, P=0.004) and increased rates of dissatisfaction (4.79, 1.07 to 21.5, P=0.04). Of the less commonly used devices, endometrial laser intrauterine thermotherapy was associated with increased rates of amenorrhoea compared with all the other devices, while cryoablation led to a reduced rate compared with bipolar radio frequency and microwave.

Conclusions Bipolar radio frequency and microwave ablative devices are more effective than thermal balloon and free fluid ablation in the treatment of heavy menstrual bleeding with second generation endometrial ablation devices.

Introduction

Heavy menstrual bleeding is a common incapacitating problem in women of reproductive age,[1] which can severely affect their quality of life.[2 3] When medical treatments fail to provide adequate relief, surgical interventions, including hysterectomy or destruction of the endometrium, can be considered.[4] Initially, rollerball ablation, transcervical resection, and laser ablation were the predominant endometrial destruction techniques performed under direct hysteroscopic vision. These led to a rapid decrease in the number of hysterectomies performed.[5]

Over the past decade, a second generation of non-hysteroscopic techniques, which are safer, technically easier to perform, involve shorter hospital stays, and can be performed under local anaesthesia, have become dominant.[6 7] These involve devices that are sited and activated to treat the whole endometrial cavity. Destruction is achieved through various methods, the most commonly used[8] being high temperature fluids within a balloon

Conclusions Bipolar radio frequency and microwave ablative devices are more effective than thermal balloon and free fluid ablation in the treatment of heavy menstrual bleeding with second generation endometrial ablation devices.

AUB management: How do systematic reviews & meta-analyses help us?

FIBROIDS & HMB

SEUD 2015

TJ Clark, Birmingham Women's Hospital & University of Birmingham

Laparoscopic versus open myomectomy

Cochrane Library

Cochrane Database of Systematic Reviews

Minimally invasive surgical techniques versus open myomectomy for uterine fibroids

Review | Intervention

Priya Bhave Chittawar, Sebastian Franik, Annefloor W Pouwer, Cindy Farquhar

First published: 21 October 2014 Full publication history

Assessed as up-to-date: 9 July 2014

Editorial Group: Cochrane Menstrual Disorders and Subfertility Group

DOI: 10.1002/14651858.CD004638.pub3

Cited by: 1 article Refresh Citing literature

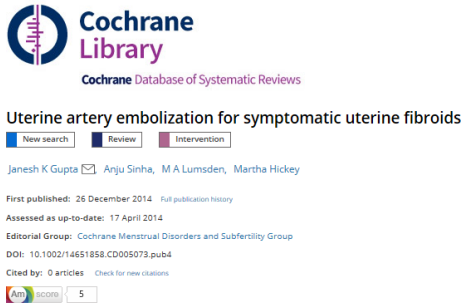
Am score 3

- 9 trials, 808 women compared laparoscopic with open myomectomy; laparoscopic myomectomy was associated with:
  - Less subjectively reported postoperative pain
  - Lower postoperative fever
  - Shorter hospital stay compared
  - No difference in recurrence risk

- Future research
  - More studies are needed to assess rates of uterine rupture, occurrence of thromboembolism, need for repeat myomectomy and hysterectomy at a later stage.

TJ Clark, Birmingham Women's Hospital & University of Birmingham

Uterine artery embolizatic fibroids


Cochrane Library
Cochrane Database of Systematic Reviews

Uterine artery embolization for symptomatic uterine fibroids

New search | Review | Intervention

Janesh K Gupta, Anju Sinha, M A Lumsden, Martha Hickey

First published: 26 December 2014 Full publication history
Assessed as up-to-date: 17 April 2014
Editorial Group: Cochrane Menstrual Disorders and Subfertility Group
DOI: 10.1002/14651858.CD005073.pub4
Cited by: 0 articles Check for new citations

- Conclusions - UAE versus surgery (myomectomy or hysterectomy):
  - No evidence of a difference between the interventions at one and five years
  - Very low quality evidence to suggest that myomectomy may be associated with better fertility outcomes than UAE, but this information was only available from a selected subgroup in one small trial.
  - UAE is a safe, minimally invasive alternative to surgery, patient selection and counselling are paramount due to the much higher risk of requiring further

Implications for research

Although we have some long term follow-up studies comparing UAE with hysterectomy, there is a continued need for further larger randomised controlled trials assessing fertility outcomes of UAE in women with symptomatic fibroids, that is by comparing UAE with myomectomy. The FEMME study (UK) is currently ongoing and we await the results.

AUB management: How do systematic reviews & meta-analyses help us?

MEDICAL TREATMENT OF HEAVY MENSTRUAL BLEEDING (HMB)

SEUD 2015

TJ Clark, Birmingham Women's Hospital & University of Birmingham

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- Protocol (3)
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27 items matching Excessive menstrual bleeding

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Sort by: Date: Newest First

Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding
Anne Lethaby, Munawar Hussain, Josephine R Rishworth, Margaret C Rees
Online Publication Date: April 2015
New search | Conclusions changed | Review | Intervention

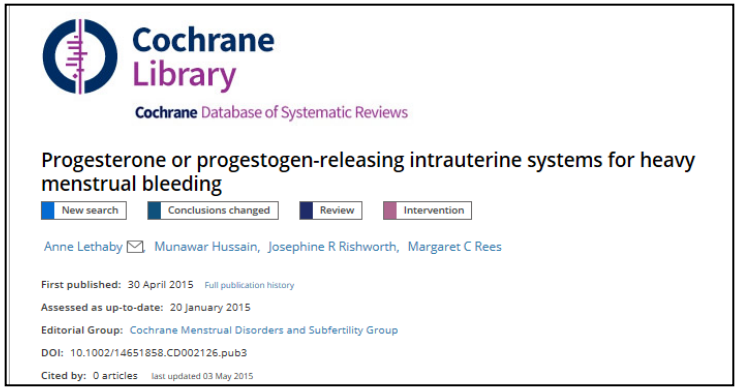
Add-back therapy with GnRH analogues for uterine fibroids
Rafael M Moroni, Wellington P Martins, Rui A Ferriani, Carolina S Vieira, Carolina O Nastri, Francisco José Candido Dos Reis, Luiz Gustavo Brito
Online Publication Date: March 2015
Review | Intervention

Uterine artery embolization for symptomatic uterine fibroids
Janesh K Gupta, Anju Sinha, M A Lumsden, Martha Hickey
Online Publication Date: December 2014
New search | Review | Intervention

Non-surgical interventions for treating heavy menstrual bleeding (menorrhagia) in women with bleeding disorders
Sujoy Ray, Amita Ray
Online Publication Date: November 2014
Review | Intervention

Hormonal treatment for uterine adenomyosis
Kavitha Nagandla, Nazimah Idris, Sivalingam Nalliah, Chandrashekhar T Sreeramareddy, Sheila RK George, Sachchithanantham Kanagasabai
Online Publication Date: November 2014

LNG-IUS for HMB



Cochrane Library

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Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding

New search | Conclusions changed | Review | Intervention

Anne Lethaby, Munawar Hussain, Josephine R Rishworth, Margaret C Rees

First published: 30 April 2015 Full publication history

Assessed as up-to-date: 20 January 2015

Editorial Group: Cochrane Menstrual Disorders and Subfertility Group

DOI: 10.1002/14651858.CD002126.pub3

Cited by: 0 articles last updated 03 May 2015

Abstract

Background

Heavy menstrual bleeding (HMB) is an important cause of ill health in women and it accounts for 12% of all gynaecology referrals in the UK. Heavy menstrual bleeding is clinically defined as greater than or equal to 80 mL of blood loss per menstrual cycle. However, women may complain of excessive bleeding when their blood loss is less than 80 mL. Hysterectomy is often used to treat women with this complaint but medical therapy may be a successful alternative.

The intrauterine device was originally developed as a contraceptive but the addition of progestogens to these devices resulted in a large reduction in menstrual blood loss. Case studies of two types of progesterone or progestogen-releasing systems, Progestasert and Mirena, reported reductions of up to 90% and improvements in dysmenorrhoea (pain or cramps during menstruation). Insertion, however, may be regarded as invasive by some women, which affects its acceptability as a treatment. Frequent intermenstrual bleeding and spotting is also likely during the first few months after commencing treatment.

Objectives

To determine the effectiveness, acceptability and safety of progesterone or progestogen-releasing intrauterine devices in achieving a reduction in heavy menstrual bleeding.

Search methods

All randomised controlled trials of progesterone or progestogen-releasing intrauterine devices for the treatment of heavy menstrual bleeding were obtained by electronic searches of *The Cochrane Library*, the specialised register of MDSG, MEDLINE (1966 to January 2015), EMBASE (1980 to January 2015), CINAHL (inception to December 2014) and PsycINFO (inception to January 2015). Additional searches were undertaken for grey literature and for unpublished trials in trial registers. Companies producing progestogen-releasing intrauterine devices and experts in the field were contacted for information on published and unpublished trials.

Selection criteria

Randomised controlled trials in women of reproductive age treated with progesterone or progestogen-releasing intrauterine devices versus no treatment, placebo, or other medical or surgical therapy for heavy menstrual bleeding within primary care, family planning or specialist clinic settings were eligible for inclusion. Women with postmenopausal bleeding, intermenstrual or irregular bleeding, or pathological causes of heavy menstrual bleeding were excluded.

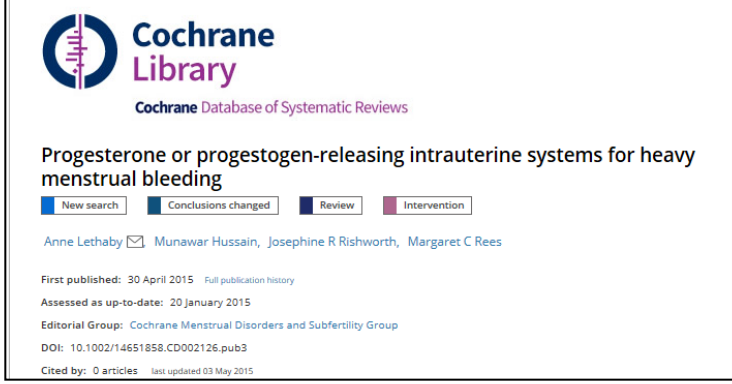
Data collection and analysis

Potential trials were independently assessed by at least two review authors. The review authors extracted the data independently and data were pooled where appropriate. Risk ratios (RRs) were estimated from the data for dichotomous outcomes and mean differences (MD) for continuous outcomes. The primary outcomes were reduction in menstrual blood loss and satisfaction; in addition, rate of adverse effects, changes in quality of life, failure of treatment and withdrawal from treatment were also assessed.

Main results

We included 21 RCTs (2082 women). The included trials mostly assessed the levonorgestrel-releasing intrauterine device (LNG IUS) (no conclusions could be reached from one small study assessing Progestasert which was discontinued in 2001) and so conclusions are based only on LNG IUS. Comparisons were made with placebo, oral medical treatment, endometrial destruction techniques and hysterectomy. Ratings for the overall quality of the evidence for each comparison ranged from very low to high. Limitations in the evidence included inadequate reporting of study

LNG-IUS and HMB



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Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding

New search | Conclusions changed | Review | Intervention

Anne Lethaby, Munawar Hussain, Josephine R Rishworth, Margaret C Rees

First published: 30 April 2015 Full publication history

Assessed as up-to-date: 20 January 2015

Editorial Group: Cochrane Menstrual Disorders and Subfertility Group

DOI: 10.1002/14651858.CD002126.pub3

Cited by: 0 articles last updated 03 May 2015

- Versus oral medications:
  - More effective than oral medication as a treatment for HMB
    - Associated with a greater reduction in HMB, improved quality of life and appears to be more acceptable long term but is associated with more minor adverse effects than oral therapy.
- Versus endometrial ablation
  - No clear benefits over endometrial ablation
    - Some minor adverse effects were more common with the LNG IUS but it appeared to be more cost effective than endometrial ablation techniques.
- Versus hysterectomy
  - Less effective than hysterectomy in reducing HMB
    - Both treatments improved quality of life but the LNG IUS appeared more cost effective than hysterectomy for up to 10 years after treatment (although many women treated with LNG IUS eventually had hysterectomy (up to 46% within 10 years), the LNG IUS remained cost effective.

Implications for research

Further research is required to compare specific types of endometrial destruction techniques with the LNG IUS. Trials should plan for long-term follow-up (at least five years which is the licensed life span of LNG IUS for contraception) and should focus on measuring satisfaction, and acceptability of the treatment options and quality of life of women with HMB.

AUB management: How do systematic reviews & meta-analyses help us?

INDIVIDUAL PATIENT DATA (IPD)

SEUD 2015

TJ Clark, Birmingham Women's Hospital & University of Birmingham

‘IPD’ individual patient data meta-analysis

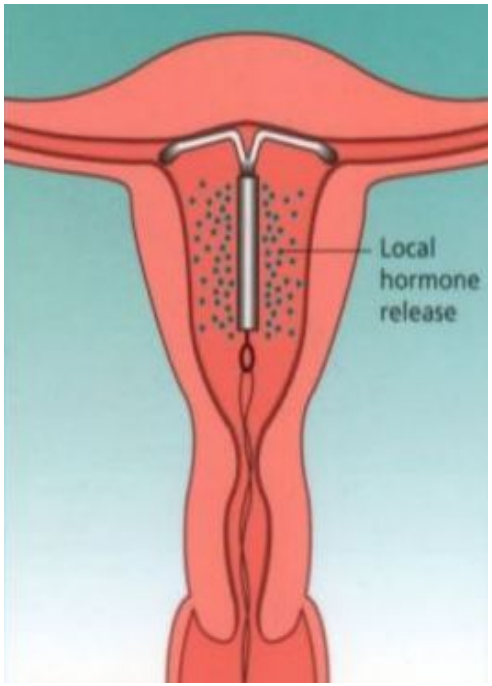
- Primary research data are sought directly from the authors as opposed to extracting summary (aggregate) data from study publications
  - IPD can then be re-analysed centrally and combined, if appropriate, in meta-analyses.

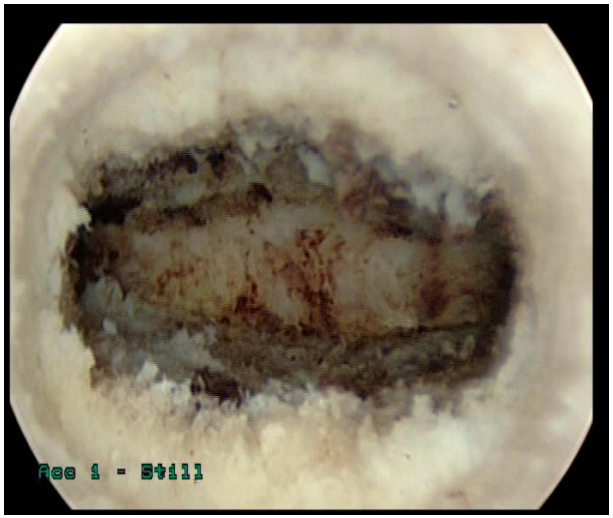
- They take longer, are more resource intensive and cost more than a conventional systematic reviews of published or other summary data.

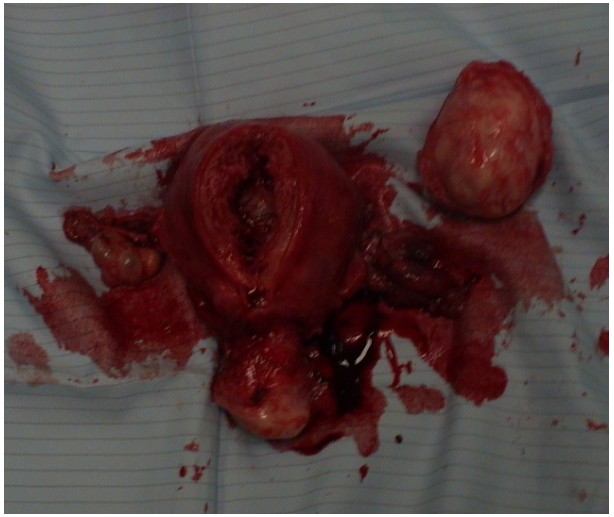
- Why do IPD meta-analysis?
  - May improve the quality of data and the type of analyses that can be done and produce more reliable results
  - Considered to be the gold standard systematic review

LNG-IUS or ablation or hysterectomy for HMB??

- Recent seminal IPD meta-analysis…….







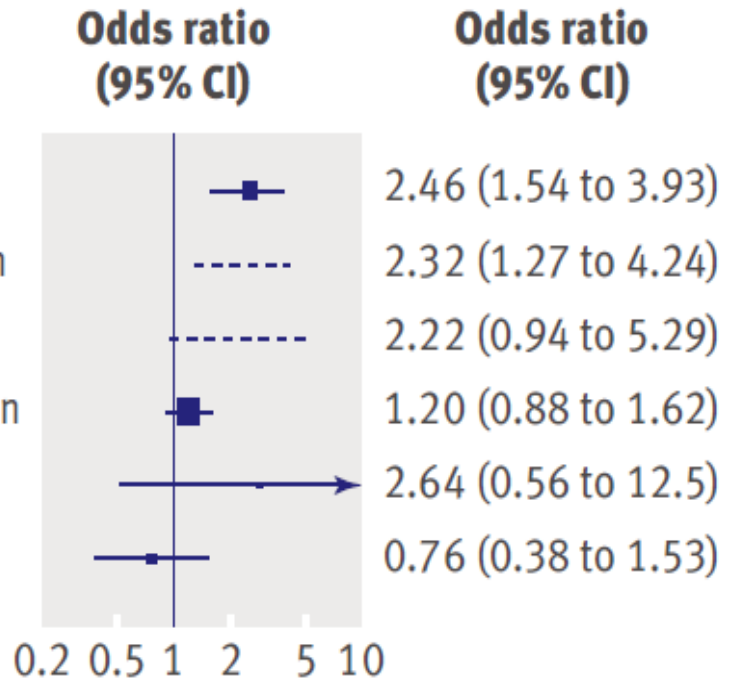


Fig 6 | Summary of dissatisfaction at 12 months. Odds ratios >1 indicate increased dissatisfaction for second treatment listed. Dashed lines represent indirect estima ratios

Conclusions More women are dissatisfied after endometrial destruction than after hysterectomy. Dissatisfaction rates are low after all treatments, and hysterectomy is associated with increased length of stay in hospital and a longer recovery period. Definitive evidence on effectiveness of Mirena compared with more invasive procedures is lacking.

AUB management: How do systematic reviews & meta-analyses help us?

INFORMING ECONOMIC ANALYSES

SEUD 2015

TJ Clark, Birmingham Women's Hospital & University of Birmingham

BMJ

RESEARCH

Hysterectomy, endometrial ablation, and levonorgestrel releasing intrauterine system (Mirena) for treatment of heavy menstrual bleeding: cost effectiveness analysis

T E Roberts, professor of health economics,[1] A Tsourapas, research fellow,[1] L J Middleton, statistician,[2] R Champaneria, research associate,[2] J P Daniels, senior research fellow,[2] K G Cooper, consultant gynaecologist,[3] S Bhattacharya, professor of obstetrics and gynaecology,[4] P M Barton, senior lecturer in mathematical modelling[1]

[1]Health Economics Unit, School of Health and Population Sciences, Public Health Building, University of Birmingham, Birmingham B15 2TT, UK

[2]Birmingham Clinical Trials Unit, University of Birmingham, Birmingham

[3]Department of Obstetrics and Gynaecology, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN

[4]Section of Applied Clinical Sciences, Division of Applied Health Sciences, School of Medicine and Dentistry, University of Aberdeen, Aberdeen Maternity Hospital, Foresterhill, Aberdeen

Correspondence to: T E Roberts
T.E.Roberts@bham.ac.uk

Cite this as: *BMJ* 2011;342:d2202
doi:10.1136/bmj.d2202

ABSTRACT

Objective To undertake a cost effectiveness analysis comparing first and second generation endometrial ablative techniques, hysterectomy, and the levonorgestrel releasing intrauterine system (Mirena) for treating heavy menstrual bleeding.

Design Model based economic evaluation with data from an individual patient data meta-analysis supplemented with cost and outcome data from published sources taking an NHS (National Health Service) perspective. A state transition (Markov) model was developed, the structure being informed by the reviews of the trials and clinical input. A subgroup analysis, one way sensitivity analysis, and probabilistic sensitivity analysis were also carried out.

Population Four hypothetical cohorts of women with heavy menstrual bleeding.

Interventions One of four alternative strategies: Mirena, first or second generation endometrial ablation techniques, or hysterectomy.

Main outcome measures Cost effectiveness based on incremental cost per quality adjusted life year (QALY).

Results Hysterectomy is the preferred strategy for the first intervention for heavy menstrual bleeding. Although hysterectomy is more expensive, it produces more QALYs relative to other remaining strategies and is likely to be considered cost effective. The incremental cost effectiveness ratio for hysterectomy compared with Mirena is £1440 (€1633, $2350) per additional QALY. The incremental cost effectiveness ratio for hysterectomy compared with second generation ablation is £970 per additional QALY.

Conclusion In light of the acceptable thresholds used by the National Institute for Health and Clinical Excellence, hysterectomy would be considered the preferred strategy for the treatment of heavy menstrual bleeding. The results concur with those of other studies but are highly sensitive to utility values used in the analysis.

Wales.[2] The condition prompts one in 20 women of reproductive age to consult her general practitioner and accounts for 20% of all referrals to gynaecology outpatients.[2] Heavy menstrual bleeding can cause considerable distress to women by affecting their performance at work as well as social activities and leads to a measurable reduction in quality of life.[3] Traditionally, the definitive treatment was surgery: in the past, by the age of 55 one in five women in the United Kingdom had had a hysterectomy,[4] over half of which were for heavy menstrual bleeding.[5]

First line treatments for heavy menstrual bleeding include oral drug regimens such as tranexamic acid, mefenamic acid, and the combined contraceptive pill. More recently an alternative medical option is available in the levonorgestrel intrauterine system (Mirena). This intrauterine contraceptive device works to reduce menstrual loss by local release of progestogen and can be fitted in primary or secondary care.[6] Surgical treatments include first and second generation endometrial ablation, which destroys the lining of the cavity of the uterus (endometrium).[6] First generation techniques typically required direct hysteroscopic vision and include endometrial laser ablation, transcervical resection of the endometrium, and rollerball ablation. Second generation techniques are typically non-hysteroscopic, vision control is not required, and they tend to be easier to perform. These latter techniques include fluid filled thermal balloon endometrial ablation, radiofrequency (thermoregulated) balloon endometrial ablation, and microwave endometrial ablation (MEA). Hysterectomy, surgical removal of the uterus, was the only surgical solution until the advent of ablation techniques and is still used when other treatments fail.[6]

Between 2000 and 2005 the number of hysterectomies performed for heavy menstrual bleeding fell from over 20 000 to just over 7000. Instead, 9701

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Infirmary,
AB25 2ZN
[4]Section o
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Cite this a
doi:10.1136

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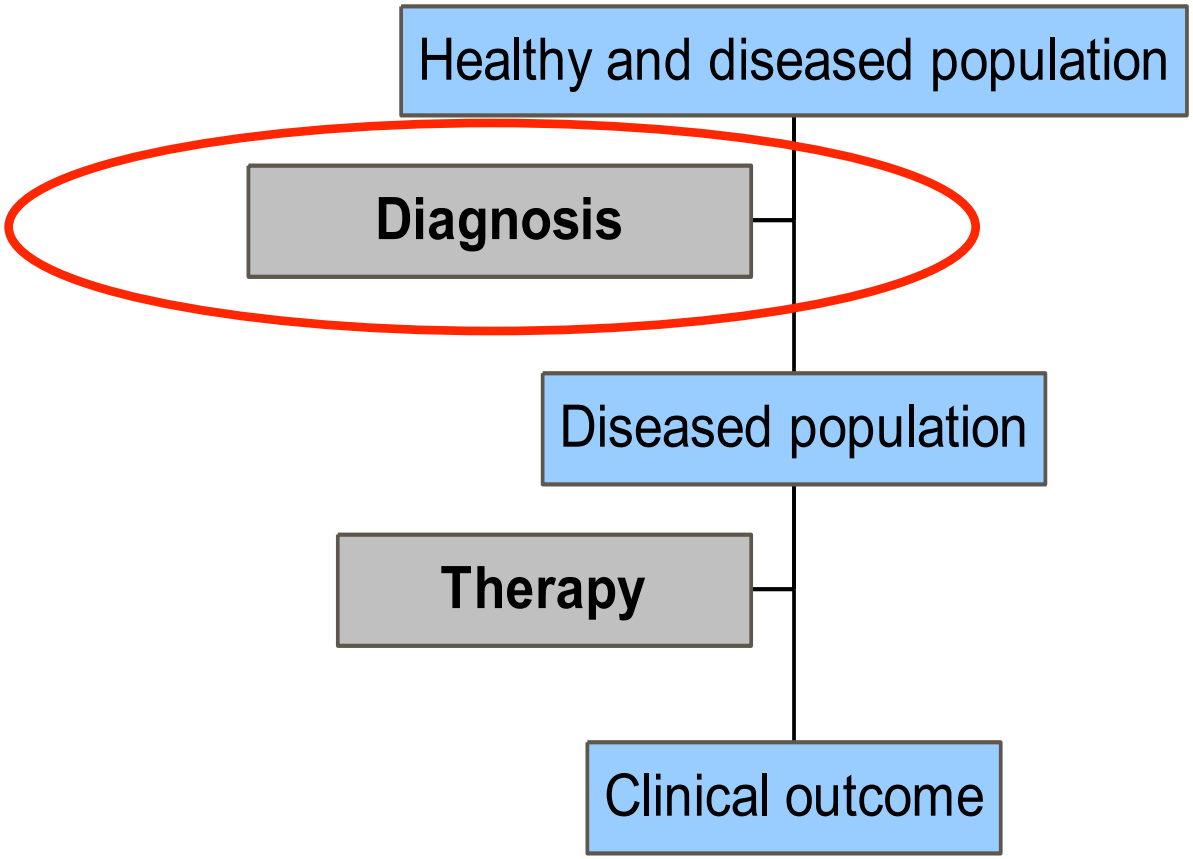
AUB management: How do systematic reviews & meta-analyses help us?

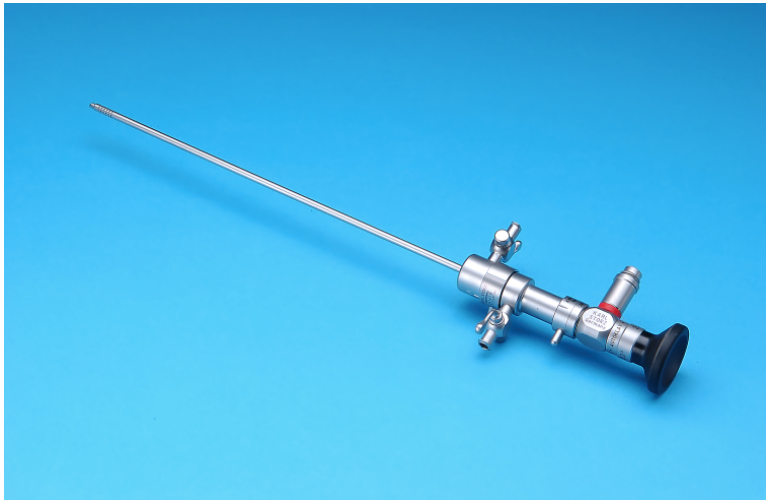
INFORMING GUIDELINES

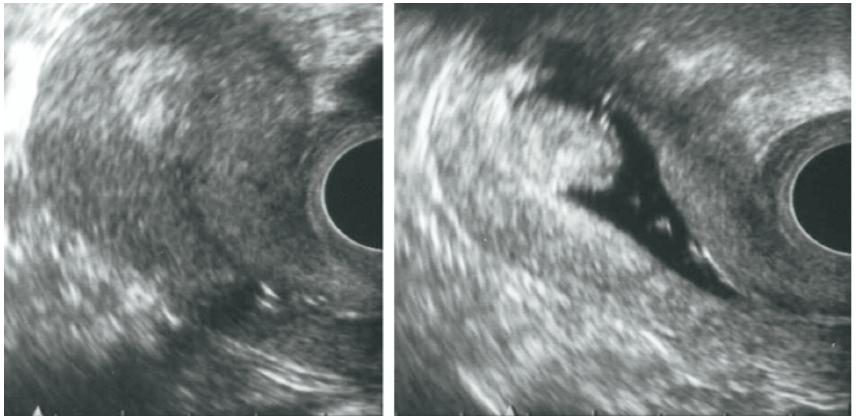
TJ Clark, Birmingham Women's Hospital & University of Birmingham

Diagnosis: Clinical Process

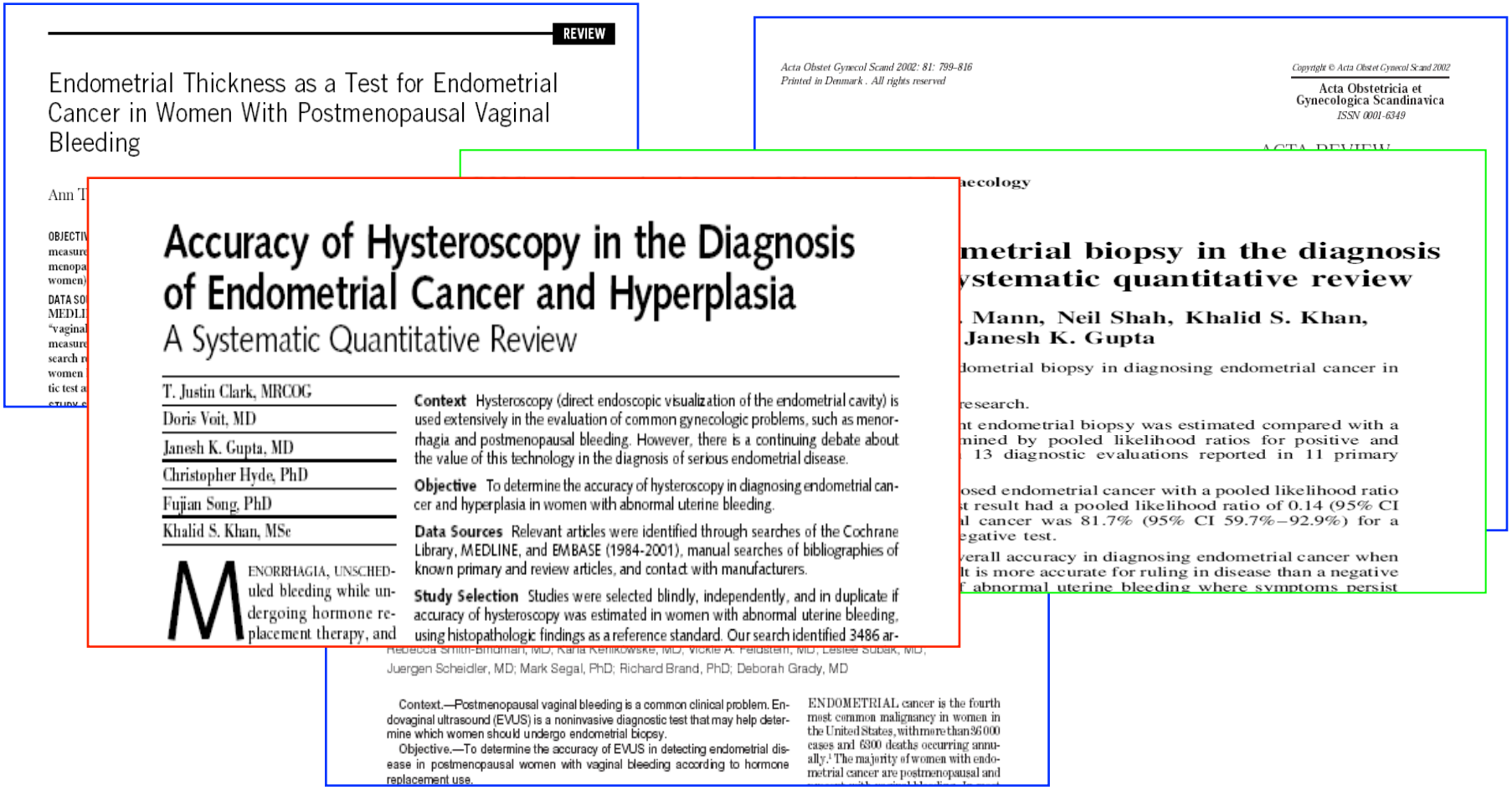


Which test for investigating PMB?





Diagnostic systematic reviews: Investigation for PMB



REVIEW

Endometrial Thickness as a Test for Endometrial Cancer in Women With Postmenopausal Vaginal Bleeding

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Acta Obstet Gynecol Scand 2002: 81: 799–816
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Acta Obstetricia et Gynecologica Scandinavica
ISSN 0001-6349

necology

metrial biopsy in the diagnosis
ystematic quantitative review

. Mann, Neil Shah, Khalid S. Khan,
Janesh K. Gupta

dometrial biopsy in diagnosing endometrial cancer in

research.
nt endometrial biopsy was estimated compared with a
mined by pooled likelihood ratios for positive and
13 diagnostic evaluations reported in 11 primary

osed endometrial cancer with a pooled likelihood ratio
t result had a pooled likelihood ratio of 0.14 (95% CI
l cancer was 81.7% (95% CI 59.7%–92.9%) for a
egative test.
verall accuracy in diagnosing endometrial cancer when
It is more accurate for ruling in disease than a negative
f abnormal uterine bleeding where symptoms persist

Accuracy of Hysteroscopy in the Diagnosis of Endometrial Cancer and Hyperplasia

A Systematic Quantitative Review

T. Justin Clark, MRCOG
Doris Voit, MD
Janesh K. Gupta, MD
Christopher Hyde, PhD
Fujian Song, PhD
Khalid S. Khan, MSc

Context Hysteroscopy (direct endoscopic visualization of the endometrial cavity) is used extensively in the evaluation of common gynecologic problems, such as menorrhagia and postmenopausal bleeding. However, there is a continuing debate about the value of this technology in the diagnosis of serious endometrial disease.

Objective To determine the accuracy of hysteroscopy in diagnosing endometrial cancer and hyperplasia in women with abnormal uterine bleeding.

Data Sources Relevant articles were identified through searches of the Cochrane Library, MEDLINE, and EMBASE (1984-2001), manual searches of bibliographies of known primary and review articles, and contact with manufacturers.

Study Selection Studies were selected blindly, independently, and in duplicate if accuracy of hysteroscopy was estimated in women with abnormal uterine bleeding, using histopathologic findings as a reference standard. Our search identified 3486 ar-

MENORRHAGIA, UNSCHEDuled bleeding while undergoing hormone replacement therapy, and

Rebecca Smith-Bindman, MD; Karla Kerlikowske, MD; Vickie A. Feldstein, MD; Leslee Subak, MD; Juergen Scheidler, MD; Mark Segal, PhD; Richard Brand, PhD; Deborah Grady, MD

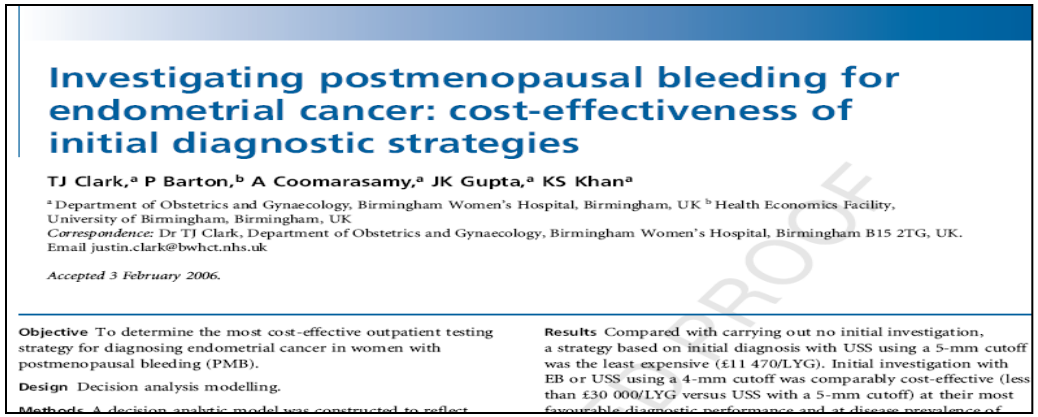
Context.—Postmenopausal vaginal bleeding is a common clinical problem. Endovaginal ultrasound (EVUS) is a noninvasive diagnostic test that may help determine which women should undergo endometrial biopsy.

Objective.—To determine the accuracy of EVUS in detecting endometrial disease in postmenopausal women with vaginal bleeding according to hormone replacement use.

ENDOMETRIAL cancer is the fourth most common malignancy in women in the United States, with more than 36 000 cases and 6800 deaths occurring annually.[1] The majority of women with endometrial cancer are postmenopausal and

Investigation of postmenopausal bleeding:

Evidence - Cost-effectiveness



Investigating postmenopausal bleeding for endometrial cancer: cost-effectiveness of initial diagnostic strategies

TJ Clark,[a] P Barton,[b] A Coomarasamy,[a] JK Gupta,[a] KS Khan[a]

[a] Department of Obstetrics and Gynaecology, Birmingham Women's Hospital, Birmingham, UK [b] Health Economics Facility, University of Birmingham, Birmingham, UK

Correspondence: Dr TJ Clark, Department of Obstetrics and Gynaecology, Birmingham Women's Hospital, Birmingham B15 2TG, UK. Email justin.clark@bwhct.nhs.uk

Accepted 3 February 2006.

UNCORRECTED PROOF

Objective To determine the most cost-effective outpatient testing strategy for diagnosing endometrial cancer in women with postmenopausal bleeding (PMB).

Design Decision analysis modelling.

Methods A decision analytic model was constructed to reflect

Results Compared with carrying out no initial investigation, a strategy based on initial diagnosis with USS using a 5-mm cutoff was the least expensive (£11 470/LYG). Initial investigation with EB or USS using a 4-mm cutoff was comparably cost-effective (less than £30 000/LYG versus USS with a 5-mm cutoff) at their most favourable diagnostic performance and at disease prevalence of

HEALTH TECHNOLOGY ASSESSMENT

VOLUME 18 ISSUE 24 APRIL 2014
ISSN 1366-5278

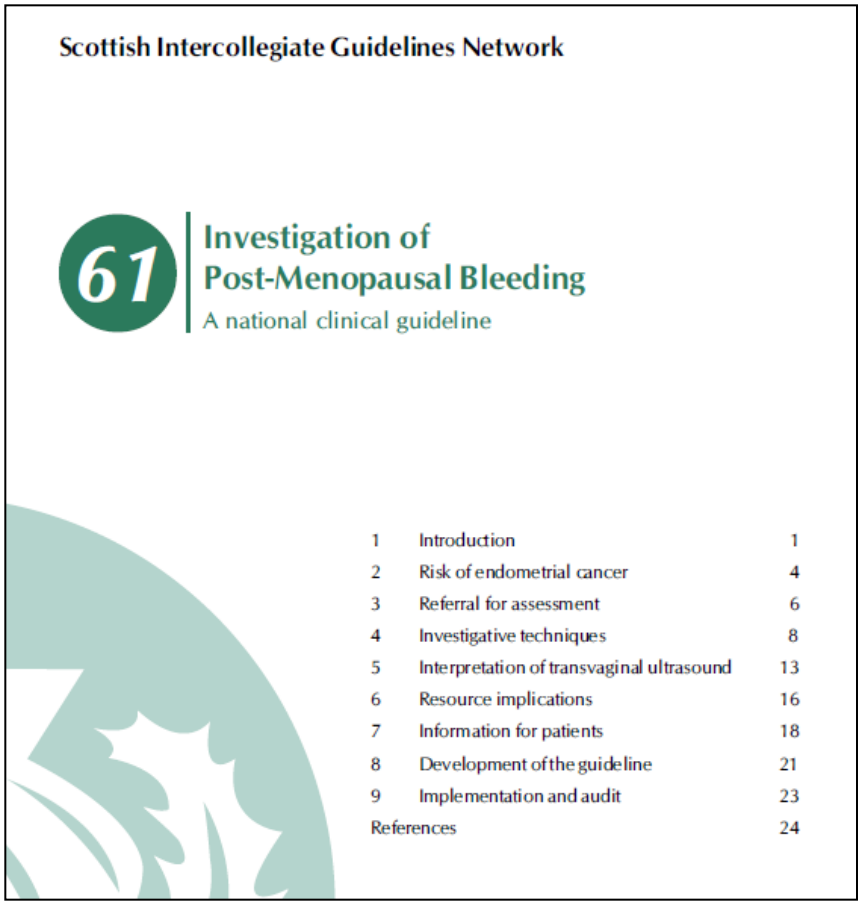
Cost-effectiveness of diagnostic strategies for the management of abnormal uterine bleeding (heavy menstrual bleeding and post-menopausal bleeding): a decision analysis

Natalie A M Cooper, Pelham M Barton, Maria Breijer, Orla Caffrey, Brent C Opmeer, Anne Timmermans, Ben W J Mol, Khalid S Khan and T Justin Clark

DOI 10.3310/hta18240

NHS National Institute for Health Research

Investigation of postmenopausal bleeding: Guidelines



Scottish Intercollegiate Guidelines Network

61 Investigation of Post-Menopausal Bleeding

A national clinical guideline

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4	Investigative techniques	8
5	Interpretation of transvaginal ultrasound	13
6	Resource implications	16
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9	Implementation and audit	23
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INVESTIGATION OF PMB

D In patients on sequential HRT, TVUS measurements should take place during the first half of the cycle where possible.

D D&C should no longer be used as the primary method of investigating PMB.

ENDOMETRIAL BIOPSY

C Histological specimens may be obtained either at the same time as inpatient or outpatient hysteroscopy with curettage or using an endometrium sampling device e.g. Pipelle®.

HYSTEROSCOPY

B Outpatient techniques for hysteroscopy and suction sampling of the endometrium should be available in all diagnostic units.

B Facilities to perform hysteroscopy and curettage under general anaesthetic should be available for when the outpatient procedure is not possible or the patient has a strong preference for a general anaesthetic.

RECURRENT PMB

D Re-investigation of recurrent post-menopausal bleeding should be considered after six months.

RESOURCES FOR PATIENTS

FAMILY PLANNING ASSOCIATION SCOTLAND
FPA Scotland, Unit 10, Fithill Business Centre, 76 Fithill Road, Glasgow G20 7BA
Tel: 0141 576 5015 Fax: 0141 576 5006
Email: fpascotland@dial.pipex.com
http://www.fpa.org.uk

THE BRITISH MENOPAUSE SOCIETY
36 Wird Street, Marlow, Bucks, England SL7 2NB
Tel: 01628 890199 Fax: 01628 474 042
Email: britishmenopausesociety@compuserve.com
http://www.the-bms.org/

NHS24: http://www.nhs24.com/
Scheduled to be available throughout Scotland in 2004.

NHS Helpline (Scotland): 0800 22 44 88

Investigation of Post-Menopausal Bleeding 61

The Scottish Intercollegiate Guidelines Network (SIGN) support improvement in the quality of health care for patients in Scotland by developing national clinical guidelines containing recommendations for effective practice based on current evidence.

The recommendations are graded A B C D to indicate the strength of the supporting evidence.

Good practice points ✓ are provided where the guideline development group wish to highlight specific aspects of accepted clinical practice.

Details of the evidence supporting these recommendations and their application in practice can be found in the full guideline, available on the SIGN website: www.sign.ac.uk.

This guideline was issued in 2002 and will be considered for review in 2005.

For more information about the SIGN programme, contact the SIGN Executive or see the website.

Scottish Intercollegiate Guidelines Network
Royal College of Physicians
9 Queen Street
Edinburgh EH2 1JQ

www.sign.ac.uk

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Quick Reference Guide

This Quick Reference Guide provides a summary of the main recommendations in the SIGN guideline on investigation of post-menopausal bleeding.

The menopause is the permanent cessation of menstruation resulting from the loss of ovarian follicular activity. From a symptomatic perspective post-menopausal bleeding describes the occurrence of vaginal bleeding following a woman's last menstrual cycle. For the purposes of this guideline, an episode of bleeding 12 months or more after the last period is accepted as post-menopausal bleeding.

PMB AND HRT

Older HRT regimens that utilise unopposed oestrogen increase the relative risk of endometrial carcinoma by around six times after five years of use. Progestogens are added to HRT regimens to prevent endometrial hyperplasia and cancer; their inclusion reduces the relative risk of endometrial cancer to around 1.5.

Unscheduled bleeding is the term used for breakthrough bleeding occurring in women on cyclical HRT or any bleeding in women on tibolone (Livial) or continuous combined HRT, although it can take up to six months for amenorrhoea to develop in the latter treatments.

For sequential regimens, abnormal bleeding may:

- be heavy or prolonged at the end of or after the progestogen phase, or
- occur at any time (breakthrough bleeding).

For continuous combined regimens, bleeding should be considered abnormal (requiring endometrial assessment) if:

- it occurs after the first six months of treatment, or
- it occurs after amenorrhoea has been established.

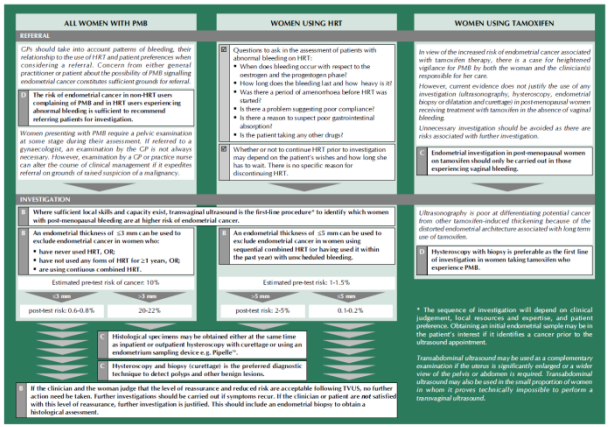
Clinicians should be aware of the background incidence of endometrial cancer among users and non-users of HRT and in those who present with post-menopausal bleeding.

PMB AND TAMOXIFEN

Women receiving tamoxifen in the treatment or prevention of breast cancer experience a three to sixfold greater incidence of endometrial cancer.

Clinicians should be aware that post-menopausal women receiving tamoxifen therapy, particularly for longer than 5 years, are at increased risk of endometrial cancer.

Investigation of Post-Menopausal Bleeding



ALL WOMEN WITH PMB | WOMEN USING HRT | WOMEN USING TAMOXIFEN

REFERRAL

GPs should take into account patterns of bleeding, their relationship to the use of HRT and patient preferences when considering a referral. Concern from either general practitioner or patient about the possibility of PMB signalling endometrial cancer constitutes sufficient grounds for referral.

D The risk of endometrial cancer in non-HRT users complaining of PMB and in HRT users experiencing abnormal bleeding is sufficient to recommend referring patients for investigation.

Women presenting with PMB require a pelvic examination at some stage during their assessment. If referred to a gynaecologist, an examination by the GP is not always necessary. However, examination by a GP or practice nurse can alter the course of clinical management if it expedites referral on grounds of raised suspicion of a malignancy.

✓ Questions to ask in the assessment of patients with abnormal bleeding on HRT:
- When does bleeding occur with respect to the oestrogen and the progestogen phase?
- How long does the bleeding last and how heavy is it?
- Was there a period of amenorrhoea before HRT was started?
- Is there a problem suggesting poor compliance?
- Is there a reason to suspect poor gastrointestinal absorption?
- Is the patient taking any other drugs?

B Whether or not to continue HRT prior to investigation may depend on the patient's wishes and how long she has to wait. There is no specific reason for discontinuing HRT.

In view of the increased risk of endometrial cancer associated with tamoxifen therapy, there is a case for heightened vigilance for PMB by both the woman and the clinician(s) responsible for her care.

However, current evidence does not justify the use of any investigation (ultrasonography, hysteroscopy, endometrial biopsy or dilatation and curettage) in post-menopausal women receiving treatment with tamoxifen in the absence of vaginal bleeding.

Unnecessary investigation should be avoided as there are risks associated with further investigation.

B Endometrial investigation in post-menopausal women on tamoxifen should only be carried out in those experiencing vaginal bleeding.

INVESTIGATION

B Where sufficient local skills and capacity exist, transvaginal ultrasound is the first-line procedure* to identify which women with post-menopausal bleeding are at higher risk of endometrial cancer.

B An endometrial thickness of ≤3 mm can be used to exclude endometrial cancer in women who:
- have never used HRT, OR;
- have not used any form of HRT for ≥1 years, OR;
- are using continuous combined HRT.

Estimated pre-test risk of cancer: 10%

≤3 mm	>3 mm
post-test risk: 0.6-0.8%	20-22%

B An endometrial thickness of ≤5 mm can be used to exclude endometrial cancer in women using sequential combined HRT (or having used it within the past year) with unscheduled bleeding.

Estimated pre-test risk: 1-1.5%

≤5 mm	>5 mm
post-test risk: 2-5%	0.14-0.2%

Ultrasonography is poor at differentiating potential cancer from other tamoxifen-induced thickening because of the distorted endometrial architecture associated with long-term use of tamoxifen.

B Hysteroscopy with biopsy is preferable as the first line of investigation in women taking tamoxifen who experience PMB.

C Histological specimens may be obtained either at the same time as inpatient or outpatient hysteroscopy with curettage or using an endometrium sampling device e.g. Pipelle®.

C Hysteroscopy and biopsy (curettage) is the preferred diagnostic technique to detect polyps and other benign lesions.

B If the clinician and the woman judge that the level of reassurance and reduced risk are acceptable following TVUS, no further action need be taken. Further investigations should be carried out if symptoms recur. If the clinician or patient are not satisfied with this level of reassurance, further investigation is justified. This should include an endometrial biopsy to obtain a histological assessment.

* The sequence of investigation will depend on clinical judgement, local resources and expertise, and patient preference. Obtaining an initial endometrial sample may be in the patient's interest if it identifies a cancer prior to the ultrasound appointment.

Transabdominal ultrasound may be used as a complementary examination if the uterus is significantly enlarged or a wider view of the pelvis or abdomen is required. Transabdominal ultrasound may also be used in the small proportion of women in whom it proves technically impossible to perform a transvaginal ultrasound.

TJ Clark, Birmingham Women's Hospital & University of Birmingham

AUB management: How do systematic reviews & meta-analyses help us?

CONCLUSIONS

TJ Clark, Birmingham Women's Hospital & University of Birmingham

Conclusions

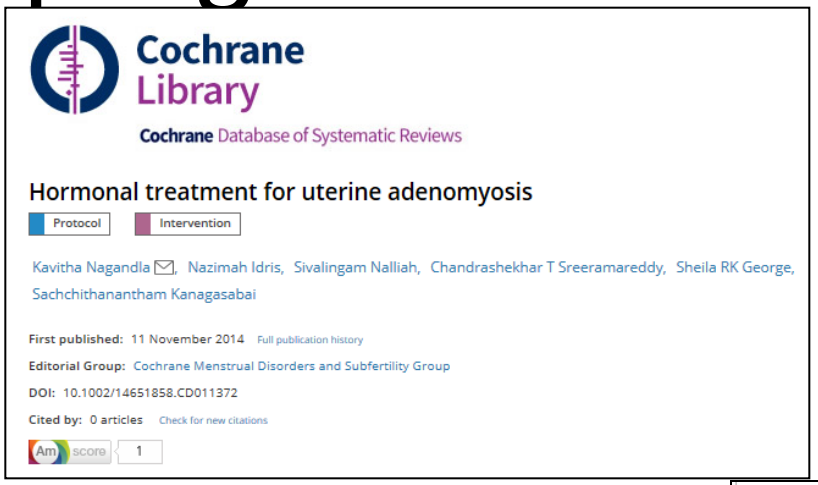
- Abnormal uterine bleeding is highly prevalent and the commonest reason for referral to a gynaecologist
- Questions of diagnosis and therapy need to be answered to inform best practice
- Clinicians are frequently:
  - too busy to identify and keep abreast of relevant data
  - lack the necessary skills to critically appraise the literature to direct their practice
- Systematic reviews can summarise the best data to inform best practice, economic analyses and form the basis of evidence based clinical guidelines and rationalise allocation of scarce health care resources

Conclusions:

HMB & impact of systematic quantitative reviews:

- Diagnosis
  - PMB
    - Accuracy of TVS vs. hysteroscopy vs. ablation
    - Cost-effectiveness analyses
- Therapy
  - HMB
    - Hysterectomy vs. first generation endometrial resection / ablation
    - First vs. second generation ablation
    - Hysterectomy vs. endometrial ablation vs. LNG-IUS
    - Cost-effectiveness analyses

Protocols – reviews in progress…



Cochrane Library

Cochrane Database of Systematic Reviews

Hormonal treatment for uterine adenomyosis

Protocol | Intervention

Kavitha Nagandla, Nazimah Idris, Sivalingam Nalliah, Chandrashekhar T Sreeramareddy, Sheila RK George, Sachchithanantham Kanagasabai

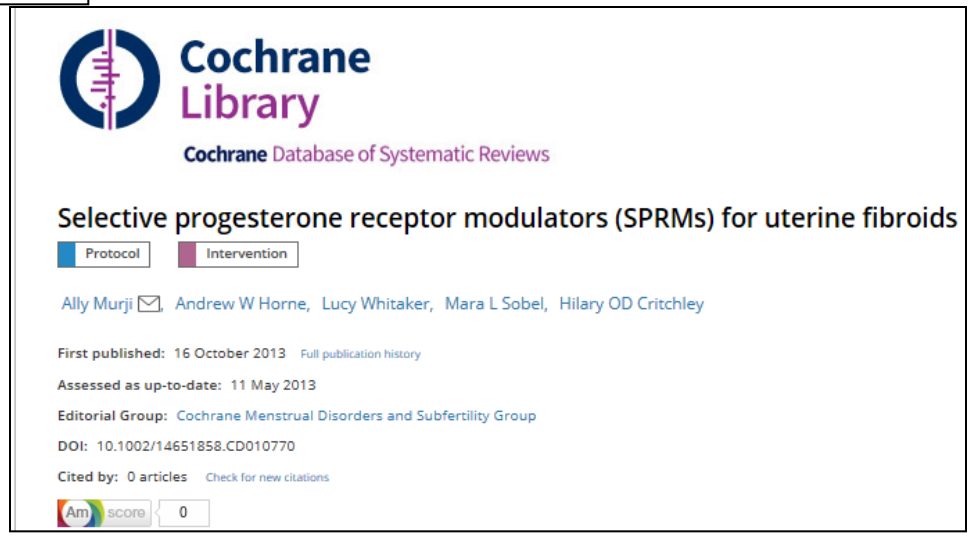
First published: 11 November 2014 Full publication history

Editorial Group: Cochrane Menstrual Disorders and Subfertility Group

DOI: 10.1002/14651858.CD011372

Cited by: 0 articles Check for new citations

Am score 1



Cochrane Library

Cochrane Database of Systematic Reviews

Selective progesterone receptor modulators (SPRMs) for uterine fibroids

Protocol | Intervention

Ally Murji, Andrew W Horne, Lucy Whitaker, Mara L Sobel, Hilary OD Critchley

First published: 16 October 2013 Full publication history

Assessed as up-to-date: 11 May 2013

Editorial Group: Cochrane Menstrual Disorders and Subfertility Group

DOI: 10.1002/14651858.CD010770

Cited by: 0 articles Check for new citations

Am score 0

Conclusions:

HMB & impact of systematic quantitative reviews:

- Impact on research agenda
  - Identify research questions / direct research
  - Influence funders
    - Future research directions in AUB????
      - SPRMs vs alternative medical treatments
      - MIS / enhanced recovery vs. conventional surgery
        - » Hysterectomy / endometrial ablation
        - » Fibroids
      - Radiological interventions vs. surgical therapy
        - » UAE, Vizablate etc.
      - Treatment setting
        - » Office vs. ambulatory vs. inpatient
        - » Hospital vs. community

Thank you for your attention