

# Deutsche Gesellschaft für Gynäkologie und Geburtshilfe



## Leitlinienprogramm

**Indikation und Methodik der Hysterektomie  
bei benignen Erkrankungen –  
Evidenzbericht**

**AWMF-Registernummer**

**015/070**

**Leitlinienklasse**

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**1.1**

In Kooperation mit der Arbeitsgemeinschaft der  
Wissenschaftlichen Medizinischen Fachgesellschaften e.V.  
(AWMF)



## Inhaltsverzeichnis

<b>I. IMPRESSUM.....</b>	<b>5</b>
<b>II. LEITLINIENINFORMATIONEN.....</b>	<b>6</b>
Template-Version.....	6
Herausgeber.....	6
Ansprechpartner .....	7
Leitliniengruppe .....	8
Leitlinienkommission der DGGG.....	10
<b>III. HINTERGRUND UND AUFTRAG .....</b>	<b>11</b>
<b>IV. FRAGESTELLUNGEN .....</b>	<b>11</b>
<b>V. METHODIK.....</b>	<b>13</b>
Evidenztabellen .....	13
<b>1. VERGLEICH VON INTERVENTIONEN ZUR BEHANDLUNG DES SYMPTOMATISCHEN UTERUS MYOMATOSUS .....</b>	<b>15</b>
1.1. Hysterektomie versus Myomenukleation .....	15
1.2. Hysterektomie versus Embolisation der Arteriae uterinae .....	16
1.3. Hysterektomie versus medikamentöse Therapie .....	21
1.3.1. Hysterektomie versus GnRH-Analoga .....	22
1.3.2. Hysterektomie versus Östrogen/Progesteron oder Östrogen/ Progesteronrezeptormodulatoren .....	23
1.3.2.1. Hysterektomie versus Östrogen/Östrogenrezeptormodulatoren .....	23
1.3.2.2. Hysterektomie versus Progesteron/Progesteronrezeptormodulatoren .....	23
1.3.3. Hysterektomie versus lokale Hormongabe .....	25
1.4. Vergleich der Hysterektomieverfahren bei Uterus myomatosus .....	26
<b>2. VERGLEICH VON INTERVENTIONEN ZUR THERAPIE VON DYSFUNKTIONELLEN BLUTUNGSSTÖRUNGEN.....</b>	<b>27</b>
Literaturrecherche: .....	27
Ergebnisse: .....	28
2.1. Hysterektomie versus Endometriumablation .....	28
2.2. Hysterektomie versus lokale (intrauterine) Hormongabe (Intrauterinsystem mit Levonorgestrel) .....	29
2.3. Hysterektomie versus systemische Hormontherapie .....	31
<b>3. VERGLEICH VON INTERVENTIONEN ZUR THERAPIE DER ADENOMYOSIS UTERI .....</b>	<b>31</b>
<b>4. VERGLEICH VON OPERATIVEN VERFAHREN DER HYSTEREKTOMIE.....</b>	<b>33</b>
4.1. Vergleich von abdominaler, vaginaler und laparoskopischer Hysterektomie .....	33
4.1.1. Vaginale Hysterektomie versus abdominale Hysterektomie .....	35
4.1.2. Laparoskopisch assistierte vaginale Hysterektomie versus abdominale Hysterektomie ..	35
4.1.3. Vaginale Hysterektomie versus Laparoskopisch assistierte vaginale Hysterektomie .....	36
4.1.4. Vaginale Hysterektomie versus Laparoskopische Hysterektomie (LoE2a) .....	37
4.1.5. Laparoskopische Hysterektomie versus Abdominale Hysterektomie .....	37
4.1.6. Suprazervikale Hysterektomie versus Totale Hysterektomie .....	38
4.1.7. Spezifische Komplikationen bei Hysterektomieverfahren .....	38
4.1.7.1. urodynamisch erhobene Inkontinenz.....	38
4.1.7.2. Scheidenabschlussdehiszenz .....	39



4.1.7.3.	chronischer Schmerz nach Hysterektomie .....	39
4.1.7.4.	Effekte der Entfernung der Eierstöcke bei prämenopausalen Patientinnen.....	39
4.2.	<b>Vergleich roboterassistierter (RAH) und laparoskopischer Hysterektomie (LAH) .....</b>	<b>40</b>
5.	<b>EVIDENZTABELLEN.....</b>	<b>42</b>
5.1.	<b>Evidenztabelle zu Hysterektomie versus Myomenukleation bei Uterus myomatosus .....</b>	<b>42</b>
5.2.	<b>Evidenztabelle zu Hysterektomie versus Embolisation der Arteriae uterinae bei Uterus myomatosus .....</b>	<b>44</b>
5.3.	<b>Evidenztabelle zu Hysterektomie versus medikamentöser Therapie und Hysterektomie plus additive präoperative medikamentöse Therapie bei Uterus myomatosus.....</b>	<b>63</b>
5.4.	<b>Evidenztabelle zu Hysterektomie versus Endometriumablation bei dysfunktionellen Blutungsstörungen .....</b>	<b>99</b>
5.5.	<b>Evidenztabelle zu Hysterektomie versus lokale (intrauterine) Hormontherapie bei dysfunktionellen Blutungsstörungen.....</b>	<b>120</b>
5.6.	<b>Evidenztabelle zu Hysterektomie versus systemische Hormontherapie bei dysfunktionellen Blutungsstörungen.....</b>	<b>131</b>
5.7.	<b>Nicht eingeschlossene Publikationen zu Interventionen bei dysfunktionellen Blutungsstörungen (nach Volltextscreening, aufgeführt ab 2000).....</b>	<b>134</b>
5.8.	<b>Evidenztabelle zu Hysterektomie versus lokale oder systemische Hormontherapie bei Adenomyosis uteri .....</b>	<b>137</b>
5.9.	<b>Nicht eingeschlossene Publikationen zu Interventionen bei Adenomyosis (nach Volltextscreening).....</b>	<b>139</b>
5.10.	<b>Evidenztabelle zum Vergleich der Hysterektomieverfahren.....</b>	<b>140</b>
5.11.	<b>Nicht eingeschlossene Publikationen zum Vergleich der Hysterektomieverfahren.....</b>	<b>224</b>
5.12.	<b>Kosten-Effektivität von Hysterektomieverfahren: Systematischer Review.....</b>	<b>229</b>
6.	<b>LITERATUR .....</b>	<b>265</b>

## I. Impressum

Evidenzbericht 2014 zur Leitlinie „Indikationen und Methoden der Hysterektomie“, - Vergleich von Interventionen zur Therapie des symptomatischen Uterus myomatosus, von dysfunktionellen Blutungsstörungen und der symptomatischen Adenomyosis uteri;- Methodenvergleich der Hysterektomietechniken. Berlin, Dezember 2014

Autoren: Dr. med. M. Nothacker, MPH, Dr. med. F. Neis, Prof. Dr. med. K. Schwerdtfeger

Auftraggeber: Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG)

Leitlinienkoordinator: Prof. Dr. med. K. Neis

Methodischer Berater (AWMF-zertifizierter Leitlinienberater): Prof. Dr. med. K. Schwerdtfeger



## II. Leitlinieninformationen

### Template-Version

Version E 2015-5-1

### Herausgeber

#### Federführende Fachgesellschaft

**Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG) e.V.**

Repräsentanz der DGGG und Fachgesellschaften

Hausvogteiplatz 12

10117 Berlin

Telefon: +49 (0) 30-5148 83340

Telefax: +49 (0) 30-5148 83344

*info@dggg.de*

<http://www.dggg.de/>

#### Präsident der DGGG

**Prof. Dr. med. Diethelm Wallwiener**

Universitätsfrauenklinik Tübingen

Calwerstraße 7

72076 Tübingen



## Ansprechpartner

Die hier genannten Personen, aber maßgeblich an der Erstellung des Evidenzberichtes beigetragen.

Inhaltliche Fachanfragen zu den im Evidenzbericht abgehandelten Themen sind zunächst ausschließlich an diese Personen zu richten.

**Dr. Monika Nothacker, MPH** (Recherche, Extraktion, Bewertung, Koordination, Redaktion)

**Dr. Felix Neis** (Unterstützung Extraktion)

**Prof. Dr. Karsten Schwertfeger** (Unterstützung Extraktion und Bewertung)

Journalistische Anfragen sind an den Herausgeber oder alternativ an die Leitlinienkommission dieser Leitlinie zu richten.



## Leitliniengruppe

Tabelle 1: Federführende und koordinierende Leitlinienautoren:

Autor	Fachgesellschaft
Prof. Dr. med. K. J. Neis <sup>1,2</sup>	Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG)
Prof. Dr. med. K. Schwerdtfeger <sup>1</sup>	AWMF-Leitlinienberater

<sup>1</sup> methodische Begleitung, Erstellung des Leitlinienberichts

<sup>2</sup> stimmberechtigte Teilnehmer am nominalen Gruppenprozess

Tabelle 2: Weitere beteiligte Leitlinienautoren/innen:

Autor/in Mandatsträger/in	DGGG-Arbeitsgemeinschaft (AG)/ AWMF/Nicht-AWMF-Fachgesellschaft/ Organisation/Verein
Dr. med. W. Zubke <sup>1, 2</sup>	Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG)
Prof. Dr. med. K. Tamussino <sup>1, 2</sup>	Österreich Gesellschaft für Gynäkologie und Geburtshilfe (ÖGGG)
Prim. Dr. med. W. Stummvoll (†)	Österreich Gesellschaft für Gynäkologie und Geburtshilfe (ÖGGG)
PD Dr. med. M. Fehr <sup>1</sup>	Schweizer Gesellschaft für Gynäkologie und Geburtshilfe (SGGG)
Prof. Dr. med. A. Kuhn <sup>2</sup>	Schweizer Gesellschaft für Gynäkologie und Geburtshilfe (SGGG)
Prof. Dr. med. M. Müller	Schweizer Gesellschaft für Gynäkologie und Geburtshilfe (SGGG)
Prof. Dr. med. B. Bojahr	Arbeitsgemeinschaft Gynäkologische Endoskopie (AGE)
PD Dr. med. S. Rimbach	Arbeitsgemeinschaft Gynäkologische Endoskopie (AGE)
Prof. Dr. med. T. Römer <sup>1, 2</sup>	Arbeitsgemeinschaft Gynäkologische Endoskopie (AGE)
Prof. Dr. med. E. Solomayer <sup>2</sup>	Arbeitsgemeinschaft Gynäkologische Endoskopie (AGE)
Dr. med. T. Schollmeyer (†)	Arbeitsgemeinschaft Gynäkologische Endoskopie (AGE)
Dr. med. B. Holthaus	Arbeitsgemeinschaft Gynäkologische Endoskopie (AGE)
Dr. med. F. Neis <sup>2</sup>	Arbeitsgemeinschaft Gynäkologische Endoskopie (AGE)
Prof. Dr. med. B. Gabriel	Arbeitsgemeinschaft für Urogynäkologie und plastische Beckenbodenrekonstruktion (AGUB)
Prof. Dr. med. C. Reisenauer <sup>2</sup>	Arbeitsgemeinschaft für Urogynäkologie und plastische Beckenbodenrekonstruktion (AGUB)
Dr. med. H. Dieterich	Arbeitsgemeinschaft für ästhetische, plastische und wiederherstellende Operationsverfahren in der Gynäkologie (AWOGyn)
Prof. Dr. med. I. B. Runnenbaum <sup>2</sup>	Arbeitsgemeinschaft Gynäkologische Onkologie (AGO)





Autor/in Mandatsträger/in	DGGG-Arbeitsgemeinschaft (AG)/ AWMF/Nicht-AWMF-Fachgesellschaft/ Organisation/Verein
Prof. Dr. med. W. Kleine	Arbeitsgemeinschaft Gynäkologische Onkologie (AGO)
Prof. Dr. med. A. Strauss <sup>2</sup>	Arbeitsgemeinschaft für Ultraschalldiagnostik in Gynäkologie und Geburtshilfe (ARGUS)
Prof. Dr. med. M. Menton <sup>2</sup>	Arbeitsgemeinschaft für Zytopathologie und Kolposkopie (AG CPC)
Prof. Dr. med. I. Mylonas <sup>2</sup>	Arbeitsgemeinschaft Infektiologie und Infektionsimmunologie (AGII)
Prof. Dr. M. David <sup>2</sup>	Deutsche Gesellschaft für Psychosomatische Frauenheilkunde und Geburtshilfe (DGPFPG)
Prof. Dr. med. L-C. Horn	Deutsche Gesellschaft für Pathologie (DGP) Berufsverband Deutsche Pathologen (BDP)
Prof. Dr. med. D. Schmidt	Deutsche Gesellschaft für Pathologie (DGP) Berufsverband Deutsche Pathologen (BDP)
Prof. Dr. med. A. T. Teichmann	Berufsverband der leitenden Ärzte (BLFG ev.)
Dr. med. P. Brandner <sup>2</sup>	Berufsverband der Frauenärzte (BVF)
Dr. M. Nothacker <sup>3</sup>	AWMF-Leitlinienberater

<sup>1</sup> Mitglied der Steuerungsgruppe

<sup>2</sup> stimmberechtigte Teilnehmer am nominalen Gruppenprozess

<sup>3</sup> Erstellung des Evidenzberichtes

Die Deutsche Gesellschaft für Chirurgie (DGCH) und die Arbeitsgemeinschaft Medizinrecht (AG MedRecht) wurde angeschrieben und benannte einen Vertreter, eine aktive Beteiligung erfolgte jedoch nicht.

Ein zweiter Vertreter war beim Berufsverband der Frauenärzte (BVF) benannt, konnte aber nicht teilnehmen.



## Leitlinienkommission der DGGG

Grafische Darstellung der Leitlinienkommission (Stand: Oktober 2014)

<b>Präsident und Vorstand der DGGG</b> Prof. Dr. Diethelm Wallwiener et al.		
<b>Leitlinienbeauftragter</b> Prof. Dr. Matthias W. Beckmann	<b>Leitliniensekretariat</b>	
<b>Stellv. Leitlinienbeauftragter</b> <b>AWMF-Leitlinienbeauftragter</b> Prof. Dr. Erich-Franz Solomayer	<b>Ehrenvorsitzender</b> Prof. Dr. Dietrich Berg	
<b>Delegierte der DGGG Leitlinienkommission</b>		
<b>Gynäkologische Onkologie</b> Prof. Dr. Olaf Ortmann Prof. Dr. Anton Scharl	<b>Wiederherstellende und plastische Gynäkologie</b> Dr. Volker Heyl	<b>Operative Gynäkologie</b> Prof. Dr. Uwe Ulrich Prof. Dr. Erich-Franz Solomayer
<b>Reproduktionsmedizin</b> Prof. Dr. Bettina Toth Prof. Dr. Wolfgang Würfel	<b>Gynäkologische Endokrinologie</b> Prof. Dr. Ludwig Kiesel PD Dr. med. Petra Stute	<b>Urogynäkologie</b> Prof. Dr. Werner Bader PD Dr. Kaven Baessler
<b>Pränatalmedizin</b> Prof. Dr. Franz Kainer Prof. Dr. Ulrich Gembruch	<b>Konservative Gynäkologie (Psychosomatik)</b> PD Dr. Friederike Siedentopf	<b>Geburtsmedizin</b> Prof. Dr. Holger Stepan Prof. Dr. Frank Louwen
<b>Junges Forum</b> Dr. Sarah Schott Dr. Johannes Lermann	<b>Konservative Gynäkologie (Infektiologie)</b> Prof. Dr. Ioannis Mylonas	<b>AG MedRecht</b> Prof. Dr. Alexander Teichmann Dr. Hamann
<b>BLFG</b> Prof. Dr. Michael Untch Dr. Hermann Zoche	<b>Justitiarin des BVF</b> Claudia Halstrick	<b>Präsident des BVF</b> Dr. Christian Albring
<b>Österreichische Vertretung</b> Prof. Dr. Karl Tamussino		<b>Schweizerische Vertretung</b> Prof. Dr. Daniel Surbek

### DGGG-Leitlinienbeauftragter

**Prof. Dr. med. Matthias W. Beckmann**

Universitätsklinikum Erlangen-Nürnberg

Frauenklinik

Universitätsstrasse 21-23

91054 Erlangen

<http://www.frauenklinik.uk-erlangen.de>

### DGGG-Leitliniensekretariat

**Dr. med. Paul Gaß, Tobias Brodkorb, Marion Gebhardt**

Universitätsklinikum Erlangen-Nürnberg

Frauenklinik

Universitätsstrasse 21-23

91054 Erlangen

Telefon: +49 (0) 9131-85/44063 oder +49 (0) 9131-85/33507

Telefax: +49 (0) 9131-85/33951

[fk-dggg-leitlinien@uk-erlangen.de](mailto:fk-dggg-leitlinien@uk-erlangen.de)

<http://www.dggg.de/leitlinienstellungennahmen/>



### III. Hintergrund und Auftrag

Die Hysterektomie ist eine der häufigsten gynäkologischen Operationen. Für die Indikationen zur Hysterektomie wurde 2012 eine S2k Leitlinie fertiggestellt. Die durchgeführte Literaturrecherche und –darstellung wurde im Auftrag der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe (DGGG) und der Leitliniengruppe um eine erneute und damit aktualisierte systematische Recherche und kritische Bewertung für definierte Fragestellungen ergänzt inklusive der Extraktion in Evidenztabelle.

### IV. Fragestellungen

Mit dem Koordinator der Leitlinie und dem Leitlinienbeauftragten der DGGG wurde die Bearbeitung folgender Fragestellungen vereinbart:

1. Welche Ergebnisse liegen für Patientinnen mit Uterus myomatosus zu Nutzen und Schaden einer Hysterektomie (HE) im Vergleich zu den Methoden

- a) Myomenuklation
- b) Embolisation der Arteriae uterinae
- c) medikamentöse Therapie?

2. Welche Ergebnisse liegen für Patientinnen mit Blutungsstörungen zu Nutzen und Schaden einer Hysterektomie vor im Vergleich zu

- a) Endometriumablation
- b) lokaler (intrauteriner) Hormontherapie (IUS mit Levonorgestrel) und
- c) systemischer Hormontherapie?

3. Welche Ergebnisse liegen für Patientinnen mit Adenomyosis uteri zu Nutzen und Schaden einer Hysterektomie vor im Vergleich zu

- a) systemischer Hormontherapie
- b) lokaler Hormontherapie (IUS mit Levonorgestrel) und
- c) Endometriumablation?

4. Welche Ergebnisse liegen zum Vergleich der Hysterektomiemethoden zu Nutzen und Schaden der verschiedenen operativen Verfahren vor?

Als zu untersuchende Endpunkte wurden vereinbart:

Symptomverbesserung/Beschwerdefreiheit



Lebensqualität

Unerwünschte Wirkungen/peri- und postoperative Komplikationen

Ergebnisse zur Wirtschaftlichkeit der Verfahren sollten ggf. dargestellt werden, jedoch nur, soweit sie durch die Recherchen ohne zusätzliche spezifische Suche identifiziert wurden. Eine Bewertung erfolgte nicht. Die Übertragbarkeit von internationalen Daten auf das wurde kritisch gesehen.

Weitere in den Studien untersuchte Endpunkte wie Länge des Krankenhausaufenthalts oder Operationsdauer werden jeweils mit aufgeführt.



## V. Methodik

Es erfolgten systematische Recherchen in Medline via PubMed. Die Suche erfolgte auf Ebene aggregierter Evidenz in Form von systematischen Übersichtsarbeiten und Metaanalysen von randomisierten kontrollierten Studien sowie, falls aggregierte Evidenz nicht oder nicht ausreichend aktuell vorlag, auf Ebene von randomisierten kontrollierten Studien. In der aggregierten Evidenz berücksichtigten Primärstudien wurden im Volltext eingesehen, wenn nicht alle relevanten klinischen oder methodischen Aspekte in den Übersichtsarbeiten aufgeführt waren.

Anhand prospektiv definierter Ein- und Ausschlusskriterien wurde ein Titel-Abstract-Screening durchgeführt. Die ausgewählten Volltexte wurden im Volltext-Screening erneut anhand der Ein- und Ausschlusskriterien überprüft. Eingeschlossene Volltexte wurden in Evidenztabelle extrahiert und methodisch bewertet.

Details wie Datum der Suche, Suchstrategie, Treffer und eingeschlossene Arbeiten sind zu den einzelnen Fragestellungen angegeben.

## Evidenztabelle

Zur Beurteilung der Evidenz (Level 1-5) wurde in dieser Leitlinie das Klassifikationssystem des **Oxford Centre for Evidence-based Medicine** in der letzten aktuellen Version aus dem Jahr 2009 benutzt.

Graduierung der Evidenz nach Oxford (März 2009)

Level	Therapy / Prevention, Aetiology / Harm	Prognosis	Diagnosis	Differential diagnosis / symptom prevalence study	Economic and decision analyses
<b>1a</b>	SYSTEMATIC REVIEWS (with homogeneity*) of RANDOMIZED CONTROLLED TRIALSs	SYSTEMATIC REVIEWS (with homogeneity*) of inception cohort studies; CLINICAL DECISION RULE" validated in different populations	SYSTEMATIC REVIEWS (with homogeneity*) of Level 1 diagnostic studies; CLINICAL DECISION RULE" with 1b studies from different clinical centres	SYSTEMATIC REVIEWS (with homogeneity*) of prospective cohort studies	SYSTEMATIC REVIEWS (with homogeneity*) of Level 1 economic studies
<b>1b</b>	Individual RANDOMIZED CONTROLLED TRIALS (with narrow Confidence Interval"i)	Individual inception cohort study with > 80% follow-up; CLINICAL DECISION RULE" validated in a single population	Validating** cohort study with good" " " reference standards; or CLINICAL DECISION RULE" tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
<b>1c</b>	All or none§	All or none case-series	Absolute SpPins and SnNouts" "	All or none case-series	Absolute better-value or worse-value analyses " " " "
<b>2a</b>	SYSTEMATIC REVIEWS (with homogeneity*) of	SYSTEMATIC REVIEWS (with homogeneity*) of	SYSTEMATIC REVIEWS (with homogeneity*) of Level	SYSTEMATIC REVIEWS (with homogeneity*) of	SYSTEMATIC REVIEWS (with homogeneity*) of



# Indikation und Methodik der Hysterektomie bei benignen Erkrankungen - Evidenzbericht

Level	Therapy / Prevention, Aetiology / Harm	Prognosis	Diagnosis	Differential diagnosis / symptom prevalence study	Economic and decision analyses
	cohort studies	either retrospective cohort studies or untreated control groups in RANDOMIZED CONTROLLED TRIALSs	>2 diagnostic studies	2b and better studies	Level >2 economic studies
<b>2b</b>	Individual cohort study (including low quality RANDOMIZED CONTROLLED TRIALS; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RANDOMIZED CONTROLLED TRIALS; Derivation of CLINICAL DECISION RULE" or validated on split-sample\$\$\$ only	Exploratory** cohort study with good" " " reference standards; CLINICAL DECISION RULE" after derivation, or validated only on split-sample\$\$\$ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
<b>2c</b>	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
<b>3a</b>	SYSTEMATIC REVIEWS (with homogeneity*) of case-control studies		SYSTEMATIC REVIEWS (with homogeneity*) of 3b and better studies		
<b>3b</b>	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
<b>4</b>	Case-series (and poor quality cohort and case-control studies\$\$)	Case-series (and poor quality prognostic cohort studies***)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
<b>5</b>	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"				Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

Quelle (Inhalt, Abkürzungen, Notes): <http://www.cebm.net/?o=1025>



# 1. Vergleich von Interventionen zur Behandlung des symptomatischen Uterus myomatosus

## 1.1. Hysterektomie versus Myomenukleation

Fragestellung/Ein- und Ausschlusskriterien:

Welche Ergebnisse liegen für Patientinnen mit symptomatischem Uterus myomatosus zu Nutzen und Schaden einer Hysterektomie (HE) im Vergleich zu einer Myomenukleation vor?

### Einschlusskriterien:

Patientinnen mit Uterus myomatosus (symptomatisch)

Intervention: Hysterektomie

Comparison (Vergleichsintervention): Myomenukleation

Outcome/Endpunkte: Symptomatik, Lebensqualität, Komplikationen,

**Publikationstyp:** Einschränkung RCT und Quellen aggregierter Evidenz: systematische Reviews, Metaanalysen, Health Technology Assessments

### Ausschlusskriterien:

- Publikationen, die aufgrund der Patientinnencharakteristika, Intervention, Vergleichsintervention, Endpunkte oder aufgrund des Studien- bzw. Publikationstyps nicht den Einschlusskriterien entsprechen
- Doppelpublikationen
- Aggregierte Evidenz (systematische Review, Metaanalysen HTA), für die aktuellere Publikationen zum gleichen Thema vorliegen mit Einschluss der entsprechenden Studien

### Literaturrecherche:

Medline via PubMed: Suche am 27.10.2013 (ab 1990)

("Hysterectomy"[Mesh] OR hysterectomy OR hysterectomies) AND ("Myoma"[Mesh: NoExp] OR myoma OR myomas OR leiomyoma OR leiomyomas OR fibromyoma OR fibromyomas OR fibroma OR fibromas OR fibroid OR fibroids)

Filters: Clinical Trial; Randomized Controlled Trial; Systematic Reviews; Review; Meta-Analysis; Publication date from 1990/01/01 to 2013/10/27

### Ergebnisse

Treffer: n= 641, nach Titel-/Abstractscreening eingeschlossen: 6 systematische Reviews/Übersichtsarbeiten, nach Volltextscreening eingeschlossen: 2 Systematische Übersichtsarbeiten(1, 2) (siehe Tabelle 1).

### Methodische Beurteilung

Es wurde eine systematische Übersichtsarbeit zum Vergleich abdominale Hysterektomie versus abdominale Myomenukleation bei stark vergrößertem Uterus myomatosus -bis ca. 16. SSW - identifiziert (Pundir et al, Oktober 2013(1)). Diese schloss 6 Beobachtungsstudien mit insgesamt 1520 Patientinnen ein. Die Beobachtungsstudien waren von mäßiger methodischer Qualität (LoE 2a). Es wurden keine RCT zum



Thema identifiziert (Recherche in Medline und EMBASE). Eine zweite systematische Übersichtsarbeit (Lethaby et al, November 2011(2)) hatte ebenfalls keine RCT zum Vergleich HE versus Myomenukleation identifiziert. Diese Übersichtsarbeit widmet sich auch der Fragestellung des Vergleichs verschiedener Zugangswege zur Myomenukleation, für diesen Vergleich liegen RCT vor.

#### Inhaltliche Ergebnisse

Die identifizierten Beobachtungsstudien abdominale HE versus abdominale Myomenukleation zeigten bei unterschiedlichen Definitionen der Komplikationen keine signifikanten Unterschiede in Bezug auf „major“ Komplikationen. Diese Ergebnisse wurden an Patientinnen mit Uteri einer Größe bis ca. 16 SSW erzielt. Die Autoren fordern Studien mit Patientinnen, deren Uteri noch stärker vergrößert sind. In Deutschland stellt die laparoskopische Myomenukleation das Verfahren der Wahl da. Der Vergleich abdominale HE versus abdominale Myomenukleation entspricht insofern nicht einer aktuellen Fragestellung. Die Myomenukleation hat gegenüber der Hysterektomie grundsätzlich den Vorteil des potentiellen Fertilitätserhalts.

## 1.2. Hysterektomie versus Embolisation der Arteriae uterinae

Fragestellung/Ein- und Ausschlusskriterien:

Welche Ergebnisse liegen für Patientinnen mit symptomatischem Uterus myomatosus zu Nutzen und Schaden einer Hysterektomie (HE) im Vergleich zu einer Embolisation der Arteriae uterinae (UAE) vor?

#### Einschlusskriterien:

Patientinnen mit Uterus myomatosus (symptomatisch)

Intervention: Operative Intervention (Hysterektomie/Myomenukleation)

Comparison (Vergleichsintervention): Embolisation der Arteriae uterinae Arterienembolisation

Outcome/Endpunkte: Symptomatik, Lebensqualität, Komplikationen,

**Publikationstyp:** Einschränkung auf Quellen aggregierter Evidenz: systematische Reviews, Metaanalysen, Health Technology Assessments

#### Ausschlusskriterien:

- Publikationen, die aufgrund der Patientinnencharakteristika, Intervention, Vergleichsintervention, Endpunkte oder aufgrund des Studien- bzw. Publikationstyps nicht den Einschlusskriterien entsprechen
- Doppelpublikationen
- Aggregierte Evidenz (systematische Review, Metaanalysen HTA), für die aktuellere Publikationen zum gleichen Thema vorliegen mit Einschluss der entsprechenden Studien

#### Literaturrecherche:

Medline via PubMed: Suche am 27.10.2013 (ab 1990)

("Hysterectomy"[Mesh] OR hysterectomy OR hysterectomies) AND ("Myoma"[Mesh:NoExp] OR myoma OR myomas OR leiomyoma OR leiomyomas OR fibromyoma OR fibromyomas OR fibroma OR fibromas OR fibroid OR fibroids)

Filters: Clinical Trial; Randomized Controlled Trial; Systematic Reviews; Review; Meta-Analysis; Publication date from 1990/01/01 to 2013/10/27





#### Ergebnisse

Treffer: n= 641, nach Titel-/Abstractscreening eingeschlossen: 10 Reviews/Metaanalysen, nach Volltextscreening eingeschlossen: 3 systematische Reviews (siehe Tabelle 2). Ausgeschlossen: 7 Reviews, z.T. aktuellere Reviews verfügbar, z.T. mangelhafte Methodik

#### Methodische Beurteilung

Eingeschlossen wurden drei systematische Reviews mit Metaanalysen, jeweils 2012 publiziert(3-5) (siehe Tabelle 1). Ein weiterer systematischer Review von 2013 erbrachte keine zusätzlichen RCT(6) (Rechercheschlussdatum nicht angegeben, eingereicht Juni 2012) und wird deshalb nicht detailliert dargestellt.

Die berücksichtigten Übersichtsarbeiten wiesen unterschiedliche Einschlusskriterien auf. Toor et al.(3) suchten nach jeglichen prospektiven Vergleichsstudien mit mindestens 20 Fällen, Gupta et al.(4) und Jun et al.(5) berücksichtigten nur randomisierte kontrollierte Studien. Es liegen 7 RCT bis 2012 vor, in denen der operativer Eingriff Hysterektomie und/oder Myomenukleation mit der Embolisation der Arteriae uterinae verglichen wird(5, 7-12) (LoE 1a). RCT zum Vergleich der UAE mit laparoskopischer Arterienokklusion wurden in dieser Arbeit nicht berücksichtigt. Die 7 RCT wurden aus der aggregierten Evidenz identifiziert und im Volltext eingesehen. 5 davon vergleichen UAE und HE. Methodisch sind die RCT von moderater bis guter (Van der Kooij) Qualität im Hinblick auf ein Verzerrungsrisiko, jeweils allerdings ohne Verblindung. Auch eine verblindete Auswertung ist nicht beschrieben, dies kann als methodische Einschränkung gewertet werden. Eine Schwäche hinsichtlich einer gemeinsamen Auswertung der Studien liegt in den unterschiedlich definierten Komplikationen. Die Fallzahlberechnung der RCT erfolgte für unterschiedliche Endpunkte (Pinto: Liegezeitverkürzung, Ruuskanen und van der Kooij: Symptomverbesserung, Moss: Lebensqualität, June: keine Fallzahlberechnung). Zusätzlich weisen die Studien unterschiedliche Nachbeobachtungszeiten von 6 Monaten bis zu 5 Jahren auf. Bei der Beschreibung der Endpunkte fehlen zum Teil Angaben für die hysterektomierten Patientinnen.

Die Erhebung zur Zufriedenheit/Lebensqualität kann nicht als valide betrachtet werden, da sie sich auf die Frage beschränkte, ob das gleiche Verfahren wieder gewählt werden würde.

#### Inhaltliche Ergebnisse

##### Vergleich UAE mit HE oder HE/Myomenukleation

Die aggregierten Ergebnisse sind der Evidenztabelle zu entnehmen (Tabelle 2). Die inhaltliche Darstellung fokussiert im Folgenden auf die einzelnen RCT, lediglich für den Endpunkt „Tod“ wird auf die systematische Übersichtsarbeit von Toor et al. verwiesen. In den RCT sind keine Todesfälle beschrieben. Toor et al führen einleitend die von ihnen identifizierten Fallberichte zu Embolisation der Arteriae uterinae mit tödlichen Komplikationen auf (insgesamt 9 Fälle). Todesursachen, soweit angegeben, waren Sepsis und Lungenembolie (siehe Tabelle 2: Toor et al, Rubrik Literaturbelege).

Zum Vergleich UAE mit HE oder HE/Myomenukleation liegen 5 RCT vor. (Pinto et al, Spanien, 2003, n=57(7), Ruuskanen et al, Finnland, 2010, n=55(10), van der Kooij et al, Niederlande, 2010 « Emmy –Trial » , n=155(11), Moss et al, 2011 „REST-trial(9) und Jun et al, 2012(5) ).



### Studiencharakteristika in Bezug auf primäre Endpunkte, Konversionsraten und Nachbeobachtungszeit

1. Pinto et al(7). berechneten die erforderliche Fallzahl anhand einer geschätzten Liegezeitverkürzung für UAE von 3 Tagen. Lediglich dieser Endpunkt wird als „intention to treat“ berichtet, die Endpunkte „bleeding cessation“ and „complications“ werden wegen Cross over von 3 Patientinnen zu UAE (und bei 2:1 Randomisierung zugunsten UAE) „per protocol“ berichtet. Die Patientinnen hatten in der UAE Gruppe ein mittleres Myomvolumen von 72+/-86cm<sup>3</sup> und in der abdominalen HE Gruppe von 113 +/- 138cm<sup>3</sup> mit maximaler Myomgröße von 10cm. Die HE wurde als abdominale HE durchgeführt. Die Nachbeobachtungszeit betrug 6 Monate - dann erfolgte eine Patientinnenbefragung zur Zufriedenheit mit dem jeweiligen Behandlungsverfahren.
2. Ruuskanen et al(10). wählten als primären Endpunkt Symptomverbesserung (1:1 Randomisierung, keine Fallzahlberechnung), berichtet wird zusätzlich über Komplikationen, Reinterventionen und Zufriedenheit. Mittl. Uterusvolumen: 422 cm<sup>3</sup> UAE/438cm<sup>3</sup> HE, im Mittel jew. 8 Myome. HE 61% abdominal (16) 27% vaginal (7), 12% lap. ass. HE). Nachbeobachtungszeit: 2 Jahre.
3. Van der Kooij et al(11). publizierten 2010 die Fünf-Jahresergebnisse der einzigen Multicenterstudie (1:1 Randomisierung, Fallzahlberechnung anhand Symptomverbesserung – Menorrhagie bei mind. 75% der Patientinnen nach UAE ohne HE, dafür 120 Pat. erforderlich). Mittl. Uterusvolumen 321cm<sup>3</sup> UAE, 313cm<sup>3</sup> HE, keine Begrenzung nach oben, (HE abdominal n=63, vaginal n=10, lap.ass. n=1). Primäre Endpunkte: Menorrhagie, Reinterventionsrate und gesundheitsbezogene Lebensqualität.
4. Moss et al,2011 (9) („REST Trial“, n=157) berechneten eine erforderliche Fallzahl von 150 Patientinnen, um für den primären Endpunkt Lebensqualität (gemessen mit SF36) mit 80% Power einen 10%igen Unterschied zu entdecken. Randomisierung 2:1 zugunsten UAE. Bei der Durchführung der UAE musste aufgrund technischen Versagens 3x eine Operation durchgeführt werden. In der operativen Gruppe wurden 42 Hysterektomien und 9 Myomenukleationen durchgeführt, alle von abdominal. Eine MM musste in HE umgewandelt werden). Eine Nachbeobachtung liegt bis 5 Jahre vor.
5. Jun e al. 2012(5) (n=127) weisen keine Fallzahlberechnung aus. Als primäre Endpunkte werden Lebensqualität und Komplikationen genannt, die Randomisierung erfolgte 1:1. Es wurden 10 HE und 54 MM durchgeführt. Technisches Versagen wird nicht berichtet. Die Erhebung der Lebensqualität erfolgte nur nach 6 Mo, die Nachbeobachtung insgesamt erstreckte sich über 42Monate

### Ergebnisse zur Symptomverbesserung:

1. Pinto et al. (nach 6 Mo) erhoben die Veränderung der Blutungsstärke mittels eines standardisierten Fragebogens der durch die Patientinnen ausgefüllt wurde. **86%** der Patientinnen mit UAE zeigten eine Verbesserung der Blutung ( „20 (56%) of 36 patients had a full recovery; five (14%), a partial recovery; and six (17%), amenorrhea), **14%** keine Verbesserung oder Verschlechterung. Bei abdominaler, vermutlich totaler HE keine Angaben zu HE.
2. Ruuskanen et al. (nach 2 J) fanden bei



**82%** der Patientinnen mit UAE eine Symptomverbesserung und in **93%** nach HE (p 0,173 nicht signifikant). Es wurde bei Aufnahme, nach 6 Monaten und zwei Jahren jeweils der gleiche Fragebogen von den Patientinnen ausgefüllt mit den Aspekten: Symptomverbesserung insgesamt, Veränderung der Menstruationsblutung und Veränderung der Drucksymptome.

3. Van der Kooij et al (nach 5 J) erhoben

75,9% Besserung mit UAE in Bezug auf Blutungsstörungen und Inkontinenz- bzw. Defäkationsbeschwerden, keine Angaben zu HE.

4. Moss et al. (nach 5 Jahre) Symptom-Score UAE + HE beide verbessert, nicht signifikant

5. Jun et al. nach 6 Monaten: nicht angegeben.

#### Ergebnisse zur Lebensqualität:

Zufriedenheit/gesundheitsbezogene Lebensqualität:

1. nach 6 Mo bei Pinto et al. 78% mit UAE und 88% mit HE, die gleiches Verfahren wieder wählen würden.
2. Nach 2 Jahren bei Ruuskanen et al. 89% mit UAE und 97% mit HE, die gleiches Verfahren wählen würden.
3. Nach 5 Jahren bei van der Kooij et al. SF 36, 85,3% zufrieden mit UAE, 88,6% mit HE
4. Nach 5 Jahren bei Moss et al.: UAE: +4,5, HE+4,8 n.s mit EuroQol-5D, nahe Werte gesunde Frauen Würden Behandlung weiterempfehlen: 90%UAE; 87% OP
5. Nach 6 Mo bei Jun et al.: SF36 sign. besser bei UAE p<0,05

Es zeigten sich in keiner Studie signifikante Unterschiede, bis auf SF36 nach 6 Monaten bei Jun et al, dort beträgt der Anteil der Hysterektomien im Verhältnis zur Myomenukleation etwa 1/6 (10/54), insofern ist die Aussagesicherheit zu HE begrenzt.

#### Ergebnisse zur Anzahl der Reinterventionen/Komplikationen

Reintervention:

nach 6 Monaten bei Pinto et al. 9% (3/40), HE: n.a.,

nach 2 Jahren bei Ruuskanen et al. UAE: 19% (5/19, 3x HE) ; HE: 10% (2x Laparotomie),

nach 42 Monaten bei Jun et al: UAE : n=12 (19%), Surgery: n= 9 (15%) p=0,02

nach 5 Jahren bei van der Kooij UAE: 28,4% (23/88, alle HE); HE: 10% 9/89 (1x vesicovaginale Fistel-OP, sonst v.a. pers. abd.Schmerz)

nach 5 Jahren bei Moss et al: 32% UAE, 4% HE; 0% MM (cave: 60% mit neuen Myomen)

Es zeigte sich zu jedem Zeitpunkt eine signifikant erhöhte Reinterventionsrate nach UAE

**Primäres Versagen der UAE** bei arteriellen Spasmen oder Gefäßdissektion (cave: abweichende Gefäßverläufe): Pinto: 5 (3x HE), Ruuskanen: 1 (1xHE), van der Kooij: 4 (4xHE), Moss 3 (2xHE)

**Primäres Versagen der operativen Methode** 1. der vaginalen oder lap.ass. vag. HE: Ruuskanen 5x Konversion zu abdominaler HE, 2. Der Myomenukleation Moss: 1x (konvertiert in HE)



**Perioperative Komplikationen:** In Einzelstudien: mehr „Minor complications“ bei UAE (auch Arteriendissektion als „minor“ gewertet bei Pinto), mehr „major complications“ bei HE (Blutverlust/Transfusion, Blasenverletzung, Inkontinenz, mehr Probleme mit Defäkation). Moss et al: 19% Komplikationen bei UAE; 25% bei HE (SIR-Klassifikation), nicht signifikant. Jun et al: Minor complication: UAE: 31 (50%), Surgery : 14 (23%)  $p=0,03$ , Major complication: UAE group : 0, Surgery group 4 (6%)  $p=0,005$

Insgesamt bei aggregierter Auswertung kein signifikanter Unterschied, cave: unterschiedliche Definition der Komplikationen.

#### Weitere Endpunkte:

1. Pinto et al: Länge des Krankenhausaufenthalts: HE > 5 die, UAE 1,7die im Mittel, Unterschied: 4.14 die (95% CI: 3.06, 5.22.,  $p<0,001$ ). Differenz in der Aufnahme der Alltagsaktivität: HE 36.18 die +/- 20.47; UAE: 9.50 die +/- 7.21 Differenz 26.68 die zugunsten der UAE (95% CI: 18.85, 34.50) ( $P<0,001$ ).

#### 2.Vergleich UAE mit HE oder Myomenukleation (MM):

2 RCT: Mara et al, Tschechien, 2008 (n=121)(8), Manyonda et al, 2012 „Fume-Trial“, n=163(12)

Mara et al. 2008, keine Powerberechnung. Einzige Studie mit Endpunkten Fertilität, Schwangerschaft siehe aggregierte Evidenz – Cochrane Review Gupta et al. (4)

Manyonda et al, 2012, primärer Endpunkt Lebensqualität, 80%ige Power, einen 10% Unterschied zu entdecken mit  $p=0,05$ , n=150. UAE versus MM (alle abdominal), weitere Endpunkte: Nachbeobachtung mind. 12 Monate,

#### Symptomverbesserung:

Manyonda nach 12 Mo: Score UAE: 29,5 MM: 18,3  $p<0,002$  zugunsten MM

Mara et al nach ca. 24 Mo . UAE 88,5%, MM 87,9%

#### Reinterventionen:

Mara et al nach ca. 24 Mo: UAE 32,8% (n=19), MM= 3,2%

Manyonda et al: UAE: 1xHE, 6 Mal Cross over zu MM, MM: 6x HE, 4x vorher gewünscht, 2x intraoperativ, Reintervention nach 2 Jahre UAE: 14% (8/57), MM 2,7% (1/37)

#### Komplikationen:

Mara et al. UAE: 8 (13,8%), MM 5(8,1%) nicht signifikant.

Manyonda et al: Major complications UAE: 2 (2,9%) , MM. 6(8%), nicht signifikant,

#### Lebensqualität/Zufriedenheit:

Mara et al: n.a.

Manyonda et al. : Health related Quality of Life: MM 86,3%, UAE 72,9%  $p<0,001$  zugunsten MM

#### Zusammenfassung/Fazit:

RCT, die Hysterektomie und uterine Arterienembolisation bei symptomatischen Uterus myomatosus vergleichen, zeigen langfristig einen vergleichbaren Anstieg der Lebensqualität (bei geringer



Ergebnissicherheit, da nur Daten aus einer Studie). In Bezug auf die Zufriedenheit mit der Intervention ergaben sich keine Unterschiede. In Bezug auf perioperative Komplikationen führt die Hysterektomie zu mehr „major“ Komplikationen und die uterine Arterienembolisation zu mehr „minor“ Komplikationen bei insgesamt nicht signifikant unterschiedlichen Komplikationsraten.

Bei uteriner Arterienembolisation war der Krankenhausaufenthalt signifikant kürzer (im Mittel um ca. 4 Tage) und die Wiederaufnahme der Alltagsaktivitäten signifikant rascher (im Mittel um ca. 26 Tage).

Die uterine Arterienembolisation weist im Vergleich zur Hysterektomie eine mehrfach erhöhte Reinterventionsrate auf (nach 5 Jahren UAE 28,4% versus HE 10% sowie UAE 32% versus HE 4%).

### 1.3. Hysterektomie versus medikamentöse Therapie

#### Einschlusskriterien:

Patientinnen mit Uterus myomatosus (symptomatisch) und geeignet für operativen Eingriff

Intervention: medikamentöse Therapie

Comparison (Vergleichsintervention): Placebo , andere medikamentöse Therapie oder unmittelbare operative Therapie

**Anmerkung:** Als Vergleichsintervention wurde entweder „keine medikamentöse antihormonelle Therapie“ oder Hysterektomie gewählt, da sich in Vorabrecherchen zeigte, überwiegend Studien zur präoperativen Therapie des Uterus myomatosus vorliegen, d.h. zum additiven Nutzen der Therapie

Outcome/Endpunkte: Symptomatik, Lebensqualität , Komplikationen,

Studien/Publicationstyp: RCT, systematische Übersichtsarbeiten, Metaanalysen, Health Technology Assessments

#### Ausschlusskriterien:

- Publikationen, die aufgrund der Patientinnencharakteristika, Intervention, Vergleichsintervention, Endpunkte oder aufgrund des Studien- bzw. Publikationstyps nicht den Einschlusskriterien entsprechen

- Doppelpublikationen

- Aggregierte Evidenz (systematische Review, Metaanalysen HTA), für die aktuellere Publikationen zum gleichen Thema vorliegen mit Einschluss der entsprechenden Studien

#### Literaturrecherche:

Medline via PubMed: Suche am 30.06.2014 (ab 1990)  
(gnrh OR progesterone OR estrogen OR progestin OR aromatase) AND ("Myoma"[Mesh:NoExp] OR myoma OR myomas OR leiomyoma OR leiomyomas OR fibromyoma OR fibromyomas OR fibroma OR fibromas OR fibroid OR fibroids)

Filters: Clinical Trial; Randomized Controlled Trial; Systematic Reviews; Meta-Analysis; Publication date  
from 1990/01/01 to 2014/06/30



#### Ergebnisse:

Treffer: n= 305, nach Abstractsichtung eingeschlossen: 6 systematische Reviews(13-18), 1 RCT (Elzaher et al, 2013)(19) (siehe Tabelle 3 und Tabelle 4, ausgeschlossene Publikationen siehe Tabelle 5) .

#### 1.3.1. Hysterektomie versus GnRH-Analoga

Zum Nutzen einer präoperativen Therapie mit GnRH-Analoga wurden 2 systematische Reviews mit Metaanalysen identifiziert ( Zhang et al. 2014(13) und Lethaby et al. 2001(14)).

#### Methodische Beurteilung

Lethaby et al. schlossen 21 RCT ein, davon 6, die GnRH Analoga versus Placebo testeten. 5 dieser 6 Studien wurden doppel-blind durchgeführt. Die weiteren Studien verglichen eine sofortige Intervention mit der zusätzlichen Gabe von GnRH Analoga, hier kann nicht entsprechend verblindet werden. 3 Operateure und 1 Sonographeur waren verblindet. In 8/21 Studien wird eine adäquate verdeckte Zuteilung beschrieben. Nur in 4 Studien lag eine Powerkalkulation vor und 8 Studien wiesen eine Intention to treat –Auswertung auf. Zhang et. al schlossen im Vergleich zu Lethaby 5 zusätzliche, aktuellere RCT ein, die jedoch nicht als Intervention die Hysterektomie beinhalteten, sondern Myomenukleation und hysteroskopische Abtragung von Myomen. Damit bleibt das methodische Niveau der Studien zur Intervention Hysterektomie überwiegend schlecht-mäßig. (Eine Studie zum Vergleich von GnRH-Analoga und Ulipristal vor Intervention wird unter 1.3.2 besprochen). In Bezug auf die Durchführung der Metaanalysen kritisierten Zhang et al, 2014, dass Lethaby et al, 2001 nur das Fixed –Effects-Modell zur Berechnung der Effekte einsetzten, obwohl die Studienergebnisse für viele Endpunkte eine signifikante Heterogenität zeigten. Sie benutzten deshalb das Random-Effects-Modell, das nicht von „einem wahren Wert“, sondern von einer gewissen inhärenten Varianz der Effekte der Primärstudien ausgeht. Dennoch bleiben sie eine Erklärung der Heterogenität schuldig. Die Ergebnisse weisen deshalb insgesamt keine hohe Aussagesicherheit auf.

#### Inhaltliche Ergebnisse

Zhang et al. führen als Ergebnis der GnRH-Analoga-Behandlung an:

- Eine signifikante Verkleinerung der Myome
- Ein signifikanter Anstieg von Hb und Hämatokrit
- Eine signifikante Verminderung der präoperativ erhobenen Symptome
- Ein signifikant höherer Anteil an vaginalen Hysterektomien
- Eine signifikante Verringerung an Längsschnittlaparotomien

Diese Ergebnisse berichteten Lethaby et al, 2001 ebenfalls. Elzaher et al, 2013(19) publizierten einen RCT zu präoperativen GnRH-Analog und erhoben als primären Endpunkt die Rate an vaginalen Hysterektomien. Gegenüber Placebo konnten ebenfalls signifikant mehr vaginale Hysterektomien durchgeführt werden.

Der Behandlungserfolg nahm in der Auswertung von Zhang et al, 2014, v.a. bei älteren Frauen bei einer Dauer von 3 Monaten im Vergleich zu 8 Wochen zu.

Die Rate perioperativer Komplikationen nach GnRH-Gabe war im Vergleich zu keiner GnRH- Behandlung nicht signifikant unterschiedlich. Dieses Ergebnis unterscheidet sich von Lethaby et al. 2001, die bei Anwenden des Fixed Effects Modell (dort werden schmalere Konfidenzintervalle erreicht) einen signifikante





Abnahme des Blutverlusts und der Gesamtkomplikationsraten fanden – bei hoher Heterogenität der Ergebnisse.

In beiden Reviews wird angemerkt, dass die Nebenwirkungen der GnRH – Analoga ungenügend berichtet sind.

### 1.3.2. Hysterektomie versus Östrogen/Progesteron oder Östrogen/Progesteronrezeptormodulatoren

#### 1.3.2.1. Hysterektomie versus Östrogen/Östrogenrezeptormodulatoren

Deng et al. 2012(18) erstellten eine systematische Übersichtsarbeit zu den Effekten von selektiven Östrogenrezeptormodulatoren zur Behandlung von symptomatischen Myomen. Sie schlossen 3 Studien ein(20-22), alle mit Raloxifen als selektivem Östrogenrezeptormodulator. Eine Studie untersuchte verschiedene Dosierungen von Raloxifen mit einem Placeboarm, eine Raloxifen versus Placebo und eine dritte Raloxifen und GnRH-Analoga versus Placebo. Alle drei Studien sind klein, mit deshalb unsicheren Effekten, d.h. geringer Güte der Evidenz.

Unter Raloxifen (60mg) zeigte sich weniger Wachstumsvergrößerung der Myome als unter Placebo, mit 180mg wurde ein Wachstumsstillstand, aber keine Myomverkleinerung erreicht. Symptome waren gegenüber Placebo nicht signifikant verändert und besserten sich nach 6 Monaten in beiden Gruppen.

Ein Vergleich zu Hysterektomie oder die Angabe von Raten sekundärer Hysterektomien war nicht Bestandteil der Studien oder des Reviews.

Song et al. 2012(17) analysierten den Effekt von Aromatasehemmern auf Myome. Sie identifizierten eine randomisierte kontrollierte Studie mit 70 Teilnehmerinnen und einer Beobachtungszeit von 3 Monaten, in der Aromatasehemmer im Vergleich zu GnRH-Analoga eingesetzt wurden(23). Die Qualität der Evidenz wird als niedrig beschrieben.

Sowohl unter GnRH-Analoga als auch unter Aromatasehemmer verringerte sich die Myomgröße nach 3 Monaten signifikant. An unerwünschten Wirkungen berichteten fast alle Patientinnen unter GnRH-Analoga von Hitzewallungen („hot flashes“), diese wurden unter Aromatasehemmer nicht berichtet. Andere Endpunkte wurden nicht berichtet.

#### 1.3.2.2. Hysterektomie versus Progesteron/Progesteronrezeptormodulatoren

##### Progesteronantagonist Mifepriston

Es wurde ein systematischer Review zur Therapie von Myomen mittels Mifepriston identifiziert, Tristan et al, 2012(16), drei Studien mit Mifepriston bei Myomen konnten eingeschlossen werden ((24), (25), (26)) Vergleichsintervention waren: - unterschiedliche Dosierungen, Placebo und Vitamin-B- Tabletten. Hysterektomie als Vergleichsintervention wurde nicht identifiziert. Die 3 Studien wurden methodisch als von niedriger Qualität eingestuft (nach GRADE) aufgrund vermutlich keiner verblindeten Auswertung und niedrigen Fallzahlen (imprecision).

Inhaltlich zeigte sich unter der Therapie mit Mifepriston eine signifikante Abnahme der Blutungsstärke nach 3 und 6 Monaten (OR ca. 18 mit weiten Konfidenzintervallen) und in einer Studie eine Verbesserung der Dysmenorrhoe (OR ca. 11 mit sehr weiten Konfidenzintervallen). Ein Effekt auf Größe der Myome oder des Uterus konnte in der zusammenfassenden Auswertung nicht nachgewiesen werden. Unter Mifepriston



wurde weitaus häufiger eine Endometriumhyperplasie (ohne auffällige Endometriumhistologie) gefunden (OR ca. 30 bei sehr weiten Konfidenzintervallen).

In einer Studie wurde unter Mifepriston im Vergleich zu Placebo eine in Teilen verbesserte Lebensqualität ermittelt (Uterine Fibroid Symptoms Quality of Life Questionnaire).

#### **Selektiver Progesteronrezeptormodulator Ulipristalacetat**

Zu Ulipristalacetat wurde eine zusätzliche Recherche durchgeführt

#### **Einschlusskriterien:**

- Patientinnen mit Uterus myomatosus (symptomatisch)
- Intervention/Vergleichsintervention: medikamentöse Therapie mit Ulipristal versus Placebo oder andere medikamentöse Therapie  
Outcome/Endpunkte: Lebensqualität, Symptomatik, Komplikationen,
- Publikationstyp: RCT, systematische Übersichtsarbeiten, Metaanalysen, Health Technology Assessments

#### **Ausschlusskriterien :**

- Nicht den Einschlusskriterien entsprechend.
- Für RCT : bereits in Systematischer Übersichtsarbeit/Metaanalyse/HTA erfasst
- Aktuellere Publikation liegt vor, keine Zusatzinformation
- Dubletten

#### **Literaturrecherche:**

1. Medline via PubMed: Suche am 30.06.2014 (ab 1990)  
("ulipristal" AND ("Myoma"[Mesh:NoExp] OR myoma OR myomas OR leiomyoma OR leiomyomas OR fibromyoma OR fibromyomas OR fibroma OR fibromas OR fibroid OR fibroids))

Filters: Clinical Trial; Randomized Controlled Trial; Systematic Reviews; Meta-Analysis; Publication date from 1990/01/01 to 2014/06/30

#### **Ergebnisse**

Treffer: n= 10, Nach Volltextdurchsicht eingeschlossen: 1 systematischer Review(27) mit 2 Primärstudien und 1 zusätzliche Primärstudie(28) (siehe Tabelle 3 und Tabelle 4)  
Ausgeschlossene Studien auf Abstract- und Volltextebene siehe Tabelle 5.

#### **Zusammenfassende Beurteilung und inhaltliche Darstellung**

Zu Ulipristalacetat zur Behandlung von Myomen liegen drei aktuelle Studien vor(28-30). Der selektive Progesteronrezeptormodulator wurde in einem methodisch korrekten RCT gegenüber Placebo in Bezug auf Blutungsstärke/Amenorrhoe und Verringerung des Uterusvolumens getestet. patientinnenberichtete Endpunkte (PRO) waren nicht unterschiedlich bis auf die Ergebnisse eines nicht validierten Fragebogen zu „Measurement of Discomfort Due to Uterine Fibroids“ zugunsten von Ulipristal (kein klinisch relevanter Mindestunterschied bekannt). In einem zweiten, ebenfalls methodisch guten RCT (Nicht-Unterlegenheits-Studie!) wurde in Bezug auf die Gabe von 3,75mg Leuprolidacetat i.m. versus 5mg Ulipristalacetat in Bezug





auf die Verringerung der Blutungsstärke eine Nichtunterlegenheit erreicht (Studiendauer 3 Mo). Leuprolid verringerte die Uterusgröße signifikant mehr als 5, oder 10mg UA täglich über 3 Monate. Allerdings traten unter Leuprolid i.m. signifikant mehr moderate bis starke Hitzewallungen auf. Eine Mehrfachgabe von Ulipristalacetat (bis zu 4Mal je 12 Wochen), die in einer dritten offenen Studie ohne Vergleichsgruppe untersucht wurde, erhöht die Rate an Amenorrhoe und verringerten starken Blutungen weiter. Randomisiert (doppel-blind) wurde in dieser Studie die Gabe von Norethisteronacetat als Add-back Therapie. Diese zeigte gegenüber Placebo einen signifikanten Effekt in Bezug auf geringere Blutungsstärke und schnelleres Wiedereintreten der Menstruation.

Die drei Studien sind vom Hersteller von Ulipristal finanziell gefördert, Mitarbeiter der Firma hatten Anteil an der Konzept und Auswertung.

### 1.3.3. Hysterektomie versus lokale Hormongabe

Zur Applikation von Progesteronen bei Uterus myomatosus liegt ein systematischer Review vor, Sangkomkamhang et al, 2013<sup>(15)</sup>.

Die Autoren identifizierten drei Studien mit unterschiedlichen Vergleichsgruppen : Hysterektomie versus Levonogestrel-IUS (Inki et al, 2002(31)), Levonorgestrel –IUS versus Kontrazeptiva (Sayed et al, 2011(32)) und Lynestrenol versus Leuprolin (Verspyck et al, 2000(33)).

#### Methodische Beurteilung

Aufgrund mangelnder Verblindungsmöglichkeit und nicht verblindeter Auswertung, unklarer verdeckter Zuteilung und selektiver Berichterstattung sowie in 2 Studien zusätzlich einem hohen Loss to Follow up Rate, wurden die Studien als überwiegend mit einem unklaren Verzerrungsrisiko behaftet eingestuft. Die Qualität der Evidenz wurde (nach GRADE) als niedrig eingestuft.

#### Inhaltliche Ergebnisse

##### Symptomverbesserung

Inki et al. machen zur klinischen Symptomatik keine Angaben. Eine Oligo- oder Amenorrhoe wurde nach 12 Monaten bei 51% der Patientinnen mit dann noch liegendem LNG-IUS erreicht, 32% berichteten über Zwischenblutungen. 46% der Patientinnen mit LNG-IUS hatten sich nach 12 Monaten für eine Hysterektomie entschieden.

Sayed et al geben eine signifikant höhere Rate an verbesserten Blutungsparametern untern LNG-IUS im Vergleich zu einem oralen Kontrazeptivum (Kombinationspräparat) nach 12 Monaten an (88% vs 54%). Der Hb-Wert war unter LNG-IUS signifikant höher als unter oraler Kontrazeption. Die Größe der Myome war nach 12 Monaten nicht unterschiedlich.

Verspyck et al. konnten nach 16 Wochen zwar eine signifikante Reduktion der Myomgröße unter Leuprolin im Vergleich zu Lynestrenol feststellen, jedoch keinen signifikanten Unterschied in der klinischen Beschwerdesymptomatik (pelvic pain) bei insgesamt kleiner Fallzahl und Loss to Follow up >20%. Der Hb-Wert war nicht unterschiedlich zwischen den Gruppen.

Sayed und Verspyck enthalten keine Angaben darüber, ob sich Patientinnen in der Folge für eine Hysterektomie entschieden.

##### Lebensqualität



Angaben zur Lebensqualität waren keiner der 3 Studien zu entnehmen

### Komplikationen

Inki et al geben mehr Ovarialzysten in der LNG-IUS-Gruppe an als in der HE – Gruppe. Weitere Angaben zu Komplikationen liegen nicht vor.

Verspyck et al geben keine signifikanten Unterschiede in therapiebedingten Komplikationen an (Kopfschmerz, Schwindel und Gewichtszunahme waren jeweils nicht signifikant, cave: kleine Fallzahl).

## 1.4. Vergleich der Hysterektomieverfahren bei Uterus myomatosus

Es konnten sechs Studien in dem systematischen Review von Nieboer et al. 2009(34) identifiziert werden, bei denen Op-Dauer, Blutverlust, Komplikationen, Morbidität und Hospitalisationsdauer verglichen wurden, d. h. in 6 RCT war das Vorliegen eines symptomatischen Uterus myomatosus explizit angegeben:

1. Benassi 2002, n=119, Uterusgewicht 200-1300g, VH versus AH (35);
  2. Ferrari 2000, n= 62, mittleres Uterusgewicht 400g in beiden Gruppen, LAVH vs TAH (36);
  3. Hwang 2002, n=90, Myome mindestens 6cm oder Uterusgewicht 450g, VH versus VALH versus AH (37);
  4. Long 2002, n=167, Uterusgewicht >280g und Kontraindikationen für VH, LAVH versus TLH(38);
  5. Ribeiro, 2003:n=60, Uterusgewicht bis 400ml, VH versus TAH versus LH(39);
  6. Tsai 2003, n= 125, vergrößerte Uteri bis Mitte Symphyse-Nabel, LAVH versus TAH (40).
- Mit späterem Publikationsdatum, d.h. bei Nieboer et al, 2009 nicht eingeschlossen, wurden zwei randomisierte Studien zum Vergleich der Hysterektomieverfahren bei symptomatischem Uterus myomatosus (ohne Berücksichtigung der roboterassistierten Hysterektomie) identifiziert (Sesti 2008, n= 150, mittleres Uterusgewicht 325g, VH versus LAVH versus Minilaparotomie(41); Drahonovsky 2010, n= 125, VH versus LAVH versus TH(42)). In 6 Studienarmen wurde vaginal operiert, in jeweils 5 laparoskopisch assistiert vaginal sowie abdominal und in 3 Studienarmen total laparoskopisch.

Die vaginale Hysterektomie hatte (bei unterschiedlichen eingeschlossenen Größen der Uteri) generell die kürzesten Operationszeiten. Bezüglich postoperativer Schmerzen und Rückkehr zur Alltagsaktivität zeigte sich ebenfalls ein Benefit der vaginalen Hysterektomie. Eine zusammenfassende Auswertung liegt nicht vor.

## 2. Vergleich von Interventionen zur Therapie von dysfunktionellen Blutungsstörungen

### Fragestellung/Ein- und Ausschlusskriterien

Welche Ergebnisse liegen für Patientinnen mit Blutungsstörungen zu Nutzen und Schaden einer Hysterektomie vor im Vergleich zu

- a) Endometriumablation
- b) lokaler (intrauteriner) Hormontherapie (IUS mit Levonorgestrel) und
- c) systemischer Hormontherapie?

### PICO Schema / Einschlusskriterien

Patientinnen: mit dysfunktionellen Blutungsstörungen (nicht aufgrund von bekannten Myomen oder bekannter Adenomyosis uteri)

Intervention: Hysterektomie

Comparison (Vergleichsintervention):

Endometriumablation (unterschiede Verfahren der 1. und der 2. Generation)

Intrauterine Therapie (Intrauterinsystem mit Levonorgestrel)

Systemische medikamentöse Therapie

Outcome: Symptomatik, Lebensqualität, Komplikationen

Publikationstyp: RCT, systematische Übersichtsarbeiten, Metaanalysen, Health Technology Assessments

### Ausschlusskriterien:

- Publikationen, die aufgrund der Patientinnencharakteristika, Intervention, Vergleichsintervention, Endpunkte oder aufgrund des Studien- bzw. Publikationstyps nicht den Einschlusskriterien entsprechen
- Doppelpublikationen
- Primärpublikationen, deren Inhalte bereits in Arbeiten aggregierter Evidenz enthalten sind
- Aggregierte Evidenz (systematische Review, Metaanalysen HTA) bei Vorliegen aktuellerer systematischer Übersichtsarbeiten zum gleichen Thema mit Einschluss der entsprechenden Studien

### Literaturrecherche:

Medline via PubMed: Suche am 05.05.2014 (ab 1990)  
(Menorrhagia[Mesh] OR menorrhagia[tw] OR polymenorrhoea [tw] OR "heavy bleeding" [tw] OR DUB[tw] OR AUB [tw] OR (abnormal AND bleeding)tw)) AND hysterectomy [tw]

Filters: Clinical Trial; Randomized Controlled Trial; Systematic Reviews; Meta-Analysis; Publication date from 1990/01/01 to 2014/05/05



Ergebnisse:

Recherche:

Treffer: n= 236, eingeschlossen nach Abstractscreening n=24, eingeschlossen nach Volltextbeurteilung n=10, davon 4 Publikationen aggregierter Evidenz (systematische Reviews, Metaanalysen, Health Technology Assessment) und 6 Primärstudien, deren Publikationsdatum nach dem Rechercheschlussdatum der Systematischen Reviews lag oder die in diesen nicht berücksichtigt wurden (siehe Tabellen 6-9)

Ausgeschlossene Studien siehe Tabelle 10

## 2.1. Hysterektomie versus Endometriumablation

### Methodische Beurteilung:

In die Auswertung wurden Ergebnisse aus drei systematischen Reviews einbezogen: Fergusson et al, 2013(43), Lethaby et al, 2013(44) und Matteson et al, 2012(45) (übereinstimmende RCT). Die aktuellste Recherche für den Vergleich Hysterektomie versus Endometriumablation (bis 10/2013) wiesen Fergusson et al. auf. Bis zum Recherchedatum am 5.5.2014 wurden keine zusätzlichen Primärstudien identifiziert (siehe Tabelle 6).

Es liegen 8 RCT mit insgesamt 1.280 randomisierten Frauen zur Frage des Vergleichs von Endometriumablation und Hysterektomie vor. Es handelt es sich um Studien mit kleiner Fallzahl, d.h., die Primärstudien sind zum Nachweis klinisch signifikanter Unterschiede oft nicht ausreichend gepowert. Die Art der Randomisierung und des Allocation concealment (verdeckte Zuteilung) ist überwiegend beschrieben und korrekt.

Insgesamt liegt eine moderate Evidenz hinsichtlich der Aussagesicherheit für die meisten Endpunkte /bzw. Ergebnisse vor in Bezug auf das Risiko einer systematischen Verzerrung (Bias). Die Qualität der Evidenz wurde endpunktbezogen in den Übersichtsarbeiten vor allem herabgestuft wegen mangelnder Verblindung. Diese ist nur für die Studienauswertung, nicht für ihre Durchführung möglich.

Teilweise wurde weiterhin eine Herabstufung der Aussagesicherheit vorgenommen bei Vorliegen sehr weiter Konfidenzintervalle, die eine Unsicherheit über das tatsächliche Effektausmaß anzeigen.

Inhaltliche Ergebnisse: Die Endometriumablation erreicht nicht den niedrigen Blutungsscore nach Hysterektomie. In der subjektiven Wahrnehmung der Frauen ist die stärker wahrgenommene Blutung in der Gesamtauswertung allerdings nur nach einem Jahr statistisch signifikant, nicht zu späteren Zeitpunkten, obwohl der PBAC-Score in Jahr 2 für Patientinnen mit Endometriumablation deutlich ansteigt.

Die Endometriumablation weist zeitabhängig mehrfach erhöhte Reinterventionsraten von 11%-36% auf, -je nach Zeitintervall von 1-4 Jahren-, im Gegensatz von nur wenigen Fällen mit einer Reintervention nach Hysterektomie.

Im Hinblick auf die Zufriedenheit der Patientinnen zeigt sich ein leichter Trend zugunsten der Hysterektomie, der im 2. Jahr Erhebungsjahr in der Metaanalyse statistische Signifikanz erreichte, nicht jedoch zu anderen Zeitpunkten. Sowohl nach Hysterektomie als auch nach Endometriumablation wurden hohe Zufriedenheitswerte erreicht.

Ebenso weisen einige Lebensqualitäts-Dimensionen gemessen mit dem validierten Instrument SF-36 signifikante Vorteile nach 1-2Jahren für die Hysterektomie auf (soziale Funktion, Schmerz, Energie, generelle Gesundheitseinschätzung).



Bei Limitationen der emotionalen Rolle fanden sich bei Patientinnen nach Endometriumablation höhere Werte. In Messungen mit anderen Lebensqualitätsinstrumenten wurden keine statistisch signifikanten Unterschiede erreicht.

Keine Unterschiede fanden sich auch - bei geringer methodischer Güte der Evidenz- in Bezug auf sexuelle Gesundheit (Daten aus 5 Studien(46-50), nur eine Studie mit validiertem Fragebogen(48)).

Die Hysterektomie weist im Vergleich zur Endometriumablation mehrfach erhöhte Raten an kurzfristigen, perioperativen Komplikationen auf (siehe Fergusson et al, 2013(43)) wie Fieber, Sepsis, Scheidenstumpf- bzw. -schlusshämatom, Wundhämatom. Dies gilt auch für das Auftreten von Infektionen als Langzeitkomplikation. Hierbei wurde in den Auswertungen nicht nach der Hysterektomietechnik differenziert.

Die einzige signifikant erhöhte Komplikation nach Endometriumablation ist der Overload mit Flüssigkeit.

Ein Cochrane Review (Lethaby et al. 2013(44)) untersuchte Studienergebnisse differenziert nach Endometriumablationstechniken der ersten und der zweiten Generation.

In Bezug auf die Reinterventionsraten bzw. die Anzahl späterer Hysterektomien zeigte sich kein eindeutiger gesicherter Unterschied zwischen Verfahren der 1. und der 2. Generation. Lediglich in einer Studie war die Reinterventionsrate nach 10 Jahren niedriger bei Ablationstechniken der 2. Generation(44).

Die von der Leitliniengruppe nicht primär angefragten Endpunkte Krankenhausaufenthalt, Dauer des Eingriffs, Zeit bis Wiederaufnahme der Alltagsaktivitäten waren im Ergebnis signifikant kürzer für die Endometriumablation.

Fazit: Die Auswertung zeigt - bei insgesamt moderater methodischer Güte der Evidenz - signifikante Vorteile für die Hysterektomie hinsichtlich der Symptomkontrolle sowie Trends zugunsten der Hysterektomie in einigen Bereichen der Lebensqualität für den Fragebogen SF36 bei überwiegend gleichen Lebensqualitätsergebnissen für andere Lebensqualitätsmessungen. Die Hysterektomie weist mehrfach höhere perioperative Kurz- und Langzeitkomplikationsraten auf sowie eine längere Eingriffsdauer, längeren Krankenhausaufenthalt und längere Zeit bis zur Wiederaufnahme der Alltagsaktivität.

## 2.2. Hysterektomie versus lokale (intrauterine) Hormongabe (Intrauterinsystem mit Levonorgestrel)

(51)In die Auswertung gingen die Ergebnisse von zwei systematischen Übersichtsarbeiten ein (Matteson et al, 2012(45), Bhattacharya et al. 2011), die dieselbe randomisierte Studie identifizierten (mit 6 Primärpublikationen bis zum Rechterschlussdatum bei Matteson 1/2011). Weiterhin wurden die Ergebnisse von zusätzlichen 5 Primärstudien berücksichtigt, die in den systematischen Übersichtsarbeiten entweder aufgrund des vor der Publikation liegenden Rechterschlussdatums nicht einbezogen wurden oder deren Inhalte in den systematischen Übersichtsarbeiten nicht abgebildet sind. Bei 4 dieser Studien handelt es sich ebenfalls um Publikationen des primär identifizierten RCT (siehe Tabelle 8).

### Methodische Beurteilung

Methodisch liegt ein guter RCT mit einer 10 Jahres Nachbeobachtung vor. Die Ergebnisse aus diesem multizentrischen RCT (n= 236 Patientinnen aus 5 Krankenhäusern in Finnland) einschließlich der Follow up Untersuchungen sind in 10 Publikationen (zwischen 2001 und 2013) veröffentlicht. Bei der Rekrutierung zu dieser Studie wurde die Ablehnung der Studienteilnahme einer nicht unbeträchtlichen Zahl von Frauen



zugunsten einer sofortigen Operation dokumentiert, weit seltener zugunsten einer Medikation (siehe Matteson et al, 2012). Randomisierung und Allocation Concealment (verdeckte Zuteilung des Randomisierungsergebnisses) waren korrekt. Die Studie ist nicht verblindet, primärer, ausreichend gewogener Endpunkt ist Lebensqualität.

2012 wurde ein zweiter unizentrischer RCT aus Italien mit weit weniger Patientinnen (n=72) publiziert zum dem hinsichtlich der methodischen Durchführung keine näheren Informationen vorliegen. Beide RCT wurden mit dem Evidenzgrad 1b beurteilt, wegen geringer Fallzahl 1b- für den italienischen RCT. Einschränkend muss festgestellt werden, dass aufgrund der multiplen Auswertungen des finnischen RCT zufallsbedingte Ergebnisse nicht auszuschließen sind. Ergebnisse aus nur einer randomisierten Studie sollten grundsätzlich durch eine zweite Studie bestätigt werden, d.h. die Aussagesicherheit ist eingeschränkt.

#### Inhaltliche Ergebnisse

Mehr Patientinnen des finnischen Kollektivs mit Hysterektomie (52% LH, 20% TAH, 28% TVH) wiesen nach 12 Monaten und nach 5 Jahren einen geringeren Blutungsscore auf. Unter LNG-IUS zeigten 51% der Patientinnen Amenorrhoe oder Oligomenorrhoe nach 12 Monaten und 75% nach 5 Jahren. Nach 5 Jahren hatten 42% der Patientinnen mit LNG-IUS diese Therapie wegen intermittierender oder weiterhin starker Blutung beendet. In der italienischen Studie wird als Ergebnis festgestellt, dass in beiden Gruppen nach 12 Monaten eine signifikante Senkung des PBAC-Scores erreicht wurde.

Mehr Patientinnen mit LNG-IUS des finnischen Kollektivs berichteten nach 12 Monaten über Unterbauchschmerzen (statistisch signifikanter Unterschied: 30% LNG-IUS vs. 14% Hysterektomie,  $p=0.02$ ). In beiden Gruppen wurde nach 12 Monaten signifikant weniger Rückenschmerz angegeben. Nach 5 Jahren zeigten sich keine Unterschiede im Hinblick auf Unterbauchschmerz, in dieser Zeit verringerten sich die angegebenen Unterbauch-Beschwerden stärker bei Patientinnen mit LNG-IUS, diese gaben nach 5 Jahren auch signifikant weniger Rückenschmerzen an. Prämenstruelle Symptome verringerten sich in beiden Gruppen. Aus der italienischen Studie liegen zu diesen Endpunkten keine Daten vor.

Erhebungen zur Lebensqualität (SF 36, EuroQol) zeigten keine signifikanten Unterschiede zwischen den beiden Verfahren in der finnischen Studienpopulation. Während sich die Lebensqualität in den ersten 5 Jahren in beiden Gruppen deutlich verbesserte, zeigte sie sich nach 10 Jahren in beiden Gruppen rückläufig ohne signifikante Unterschiede. In der italienischen Studie fanden sich nach 12 Monaten keine signifikanten Unterschiede für die Gesamtauswertung des SF 36. In beiden Gruppen wurde eine signifikante Verbesserung erreicht. Im Hinblick auf die Teilbereiche Rollenfunktion und die mentale Gesundheit wurde ein statistisch signifikanter Vorteil für LNG-IUS festgestellt.

Nach einem und nach 5 Jahren fanden sich in der finnischen Studienpopulation keine Unterschiede in der sexuellen Funktion. Die Zufriedenheit war nach 5 Jahren für beide Verfahren über 90%, es wurden keine Unterschiede festgestellt.

Nebenwirkungen sind für die finnische Studienpopulation beschrieben.

46% der Patientinnen mit LNG-IUS wurden im Verlauf von 10 Jahren hysterektomiert (42% nach 5 Jahren). Nach Hysterektomie traten signifikant mehr „major“ (n=12 versus n=1 unter LNG-IUS) Komplikationen wie Thromboembolie auf sowie signifikant mehr „minor“ Komplikationen (27% versus 0% unter LNG-IUS).





Nach 10 Jahren nahmen signifikant mehr hysterektomierte Patientinnen Medikamente gegen Inkontinenz ein (12%) als unter LNG-IUS (1%), ebenso wiesen hysterektomierte Patientinnen signifikant mehr Harnwegsinfekte auf.

Kosteneffizienz: In der Auswertung nach 10 Jahren aus Finnland wird über geringere Kosten für die primäre Therapie mit LNG-IUS berichtet, trotz der hohen sekundären Hysterektomie rate.

Fazit: Es liegen nur zwei randomisierte Studien vor. Bei vergleichbarer Lebensqualität wurde eine geringere Symptomverbesserung unter LNG-IUS erreicht, was in einer Studie zu hohen Abbruchraten mit sekundärer Hysterektomie führte.

## 2.3. Hysterektomie versus systemische Hormontherapie

### Methodische Beurteilung

Methodisch liegt ein kleiner, methodisch fragwürdiger RCT vor. Die Selektion der Patientinnen erscheint mit einem hohen Verzerrungsrisiko behaftet: Frauen unter Medikation, die damit unzufrieden waren, wurden in eine additive Medikationsarm und einen HE Arm randomisiert. Die kleine Fallzahl erlaubt nur den Nachweis eines sehr großen Unterschieds subjektiv erhobener Parameter (siehe Tabelle 9)

### Inhaltliche Ergebnisse

Bezüglich der Lebensqualität wurde kein Unterschied nachgewiesen (siehe Evidenztabelle, Tabelle 9). Der hohen Rate an Reinterventionen unter Medikation steht eine erhöhte Rate an Komplikationen bei HE entgegen.

## 3. Vergleich von Interventionen zur Therapie der Adenomyosis uteri

### Fragestellung/Ein- und Ausschlusskriterien

Welche Ergebnisse liegen für Patientinnen mit Adenomyosis uteri zu Nutzen und Schaden einer Hysterektomie vor im Vergleich zu

- a) Endometriumablation
- b) lokaler (intrauteriner) Hormontherapie (IUS mit Levonorgestrel) und
- c) systemischer Hormontherapie?

**Outcome:** Symptomatik, Lebensqualität, Komplikationen

**Publikationstyp:** RCT, systematische Übersichtsarbeiten, Metaanalysen, Health Technology Assessments

### Ausschlusskriterien:

- Publikationen, die aufgrund der Patientinnencharakteristika, Intervention, Vergleichsintervention, Endpunkte oder aufgrund des Studien- bzw. Publikationstyps nicht den Einschlusskriterien entsprechen
- Doppelpublikationen
- Primärpublikationen, deren Inhalte bereits in Arbeiten aggregierter Evidenz enthalten sind
- Aggregierte Evidenz (systematische Review, Metaanalysen HTA) bei Vorliegen aktuellerer

systematischer Übersichtsarbeiten zum gleichen Thema mit Einschluss der entsprechenden Studien

#### Literaturrecherche:

Medline via PubMed: Suche am 05.05.2014 (ab 1990)  
(Adenomyosis[MesH] OR adenomyosis OR adenomyos\*) AND hysterectomy  
Filters activated: Meta-Analysis, Systematic Reviews, Randomized Controlled Trial, Publication date from 1990/01/01 to 2014/05/05.  
Treffer: 14, eingeschlossen nach Abstractscreening: 3, eingeschlossen nach Volltextscreening: 1 RCT (siehe Tabelle 11 und Tabelle 12).

#### Methodische Beurteilung

Es liegt ein kleiner RCT vor (n=86, Loss to follow up in einer Gruppe n=11 (25%)). Die Randomisierung erfolgte korrekt, die Durchführung des Allocation concealments (verdeckte Zuteilung) ist nicht beschrieben. Ebenso fehlt bei unverblindeter Durchführung der Studie ein Hinweis auf eine verblindete Auswertung. Als Endpunkte der Studie werden genannt: Symptomverbesserung und Lebensqualität. Die Powerberechnung wird ohne Nennung eines Endpunkts dargestellt. Der RCT wurde aufgrund der kleinen Fallzahl und des Loss to follow von 25% in der HE-Gruppe mit 1b- bewertet (Anzeige von „Imprecision“).

#### Inhaltliche Ergebnisse

Die Diagnosestellung erfolgte bei Menorrhagie mittels Ultraschall und MRT. Es wurden abdominale Hysterektomien durchgeführt. Bei 8 Patientinnen bestätigte sich die Diagnose Adenomyosis nicht (25%, bei 6 Patientinnen lagen ausschließlich Myome vor, bei 2 ein unauffälliger Uterus). Nach 12 Monaten wurde in der LNG-Gruppe eine Oligo- oder Amenorrhoe-Rate von 87% erreicht. In beiden Gruppen stiegen die Hb-Werte an und waren nicht statistisch signifikant unterschiedlich.

Die Lebensqualität (gemessen mit einem auch türkisch validierten Instrument der WHO - WHOQOL-BREF TR) - stieg in beiden Gruppen postinterventionell statistisch signifikant an, in der LNG-IUS Gruppe in allen Domänen, in der Hysterektomie Gruppe in 3 von 5 Domänen.

In Bezug auf Komplikationen trat in der Hysterektomiegruppe eine postoperative Wundinfektion auf, die eine Sekundärnaht erforderte. Weitere Komplikationen wurden nicht berichtet. Folgende Nebenwirkungen wurden berichtet: Kopfschmerzen (12%), Brustspannen (7%), Akne (4%), transiente depressive Episode (2%). Ein IUS wurde spontan ausgestoßen, nach 12 Monaten führten 98% der Patientinnen die LNG-IUS-Therapie fort.

**Fazit:** Es wurde lediglich eine randomisierte Studie zum Vergleich von Hysterektomie mit anderen Interventionen für Adenomyosis bedingte Blutungsstörungen identifiziert. In dieser führten sowohl LNG-IUS als auch die Hysterektomie zu Symptom- und Lebensqualitätsverbesserung bei niedrigen Komplikationsraten soweit für die Hysterektomie beurteilbar. Insbesondere im Vergleich zu den Ergebnissen bei unspezifischen dysfunktionellen Blutungsstörungen zeigte sich in dieser Studie kein Abbruch der LNG-IUS-Therapie nach einem Jahr.



### 4. Vergleich von operativen Verfahren der Hysterektomie

Recherchezeitraum: 01.01.2008 - 15.04.2014

Datenbanken: Medline via PubMed

Recherchestrategie: „hysterectomy“ Limits: Review, systematic Review, Metaanalysis

Einschlusskriterien:

Patientinnen: Nicht-schwangere Patientinnen mit gutartiger Erkrankung der Gebärmutter

Intervention/Vergleichsintervention: abdominale HE versus laparoskopisch assistierte oder laparoskopisch oder vaginale HE bzw. roboterassistierte HE und andere Kombinationen dieser Vergleiche.

Outcome: Morbidität (Blutung, Schmerzen, Verletzungen, Aktivität), Lebensqualität, soweit erfasst: Kosten-Effektivität

Studiendesign/Publicationstyp: Aggregierte Evidenz (systematischer Review/Metaanalyse)

Sprachen: Deutsch, Englisch, Französisch, Spanisch

Ausschlusskriterien:

- schwangere Patientinnen/Patientinnen unter der Geburt/Patientinnen mit Krebserkrankungen/Patientinnen mit anderer Erkrankung
- Intervention oder Vergleichsintervention nicht Hysterektomie bzw. Komplikation von Hysterektomien
- Primärpublikation, Brief, Kommentar, narrativer Review
- andere Sprache
- keine zusätzl. Informationen

Ergebnisse:

Treffer: 935, Eingeschlossene Abstracts: 27 Eingeschlossene Volltexte: 16 (siehe Tabelle 13), Ausgeschlossene Texte: 10 (siehe Tabelle 14), 1 Review in extra Anhang dargestellt (Pynnä et al, 2014 Kosten-Effektivitätsanalyse von HE-Verfahren und Alternativen)

#### 4.1. Vergleich von abdominaler, vaginaler und laparoskopischer Hysterektomie

Zum Vergleich der Hysterektomieverfahren exklusive der roboterassistierten Hysterektomie wurden 12 systematische Reviews bzw. Metaanalysen eingeschlossen (siehe Tabelle 13, ausgeschlossene Studien siehe Tabelle 14). Den umfassendsten Review zum Vergleich von Hysterektomieverfahren bei benigner Indikation (vaginal, abdominal, laparoskopisch) erstellten Nieboer et al, 2009 (Cochrane Review, systematische Suche bis August 2008)(34). Aktuellere Reviews mit Metaanalysen konnten zu folgenden Hysterektomie-Technik-Vergleichen identifiziert werden:

- Suprazervikale Hysterektomie versus Totale Hysterektomie (Lethaby et al, 2012, Suche bis 7/2011)(52),
- vaginale Hysterektomie versus Totale Laparoskopische Hysterektomie (Gendy et al, 2011, Suche bis 6/2010)(53)
- Laparoskopisch assistierte vaginale Hysterektomie versus abdominale Hysterektomie (Yi et al, 2011, Suche bis 6/2010)(54)
- Laparoskopisch assistierte vaginaler Hysterektomie versus vaginale Hysterektomie (Guo et al, 2013)(55)



Zum Abgleich mit Nieboer et al. wurden auch zeitgleich oder bis 1 Jahr früher publizierte Studien berücksichtigt mit folgenden Hysterektomie-Technik-Vergleichen:

- Totale Abdominale Hysterektomie versus Totale Laparoskopische Hysterektomie (Walsh et al, 2009, Suche bis 8/2007)(56)
- Laparoskopische Hysterektomie versus Abdominale Hysterektomie in Bezug auf Lebensqualität (Kluivers et al, 2008, Suche bis 1/2006)(57)
- Weitere eingeschlossenen Reviews thematisieren spezifische Komplikationen nach Hysterektomie: Inkontinenz (Duru et al, 2012(58), Robert et al, 2008(59))
- Scheidenabschlussdehiszenz (Uccella et al, 2011(60), Agdi et al, 2009(61))
- chronische Schmerzen (Brandsborg et al, 2008)(62).

Ein letzter Review vergleicht die Hysterektomie mit und ohne Eierstocksentfernung bei prämenopausalen Frauen (Orozco et al, 2008)(63).

Aufgrund mangelnder Verfügbarkeit des Volltextes konnte der Review von Adelman et al, 2014(64) zu Verletzungen der Harnwege/Blase bei laparoskopischer Hysterektomie nicht umfassend berücksichtigt werden.

Zusätzlich zu den Reviews wurde eine Primärstudie zum Vergleich der Lebensqualität nach laparoskopischer und abdominaler Hysterektomie von 2012 berücksichtigt (Nieboer et al, 2012(65), nicht extrahiert).

### Methodische Beurteilung

Die eingeschlossenen Übersichtsarbeiten/Metaanalysen sind hinsichtlich ihrer Erstellung überwiegend von guter methodischer Qualität, d.h. es erfolgte eine ausreichend beschriebene systematische Recherche und Studienselektion. Die methodische Bewertung der eingeschlossenen Primärstudien erfolgte in 11 Reviews mittels des Cochrane Risk of Bias Tools oder des JADAD Scores. In zwei Reviews (Duru(58), Brandsborg(62)) wird die Studienqualität narrativ beschrieben, ein Review macht keine Ausführungen zur Qualität der Primärstudien (Agdi(61)). Die eingeschlossenen Primärstudien zu Vergleichen von Hysterektomietechniken sind alle randomisiert-kontrollierte Studien. Allerdings fanden sich in Bezug auf die unterschiedlichen Technik-Vergleiche unterschiedlich gute Studien von überwiegend moderater bis überwiegend schlechter Qualität. Eine grundsätzliche Schwäche der meisten Primärstudien liegt in der mangelnden Verblindung von Patientinnen und Behandelnden. Viele Studien weisen keine primären Endpunkte auf bzw. eine Powerberechnung fehlt. Wenngleich die Randomisierung in der Regel adäquat durchgeführt wurde, fehlen in vielen Studien Angaben über die Gewährleistung der verdeckten Zuteilung (allocation concealment).

Hinsichtlich der Erstellung von Metaanalysen berücksichtigen nicht alle Autoren die zugrundeliegende Heterogenität der Primärstudienresultate. Bei hoher Nicht-Zufalls-Bedingter Heterogenität ( $I^2$  über 70%) ist ein metaanalytisches Ergebnis ohne Sensitivitätsanalysen bzw. ohne adäquate Erklärung für die Heterogenität nicht verlässlich, auch wenn der Rechnung ein statistisches Modell zugrunde gelegt wird, dass grundsätzlich nicht von einem wahren Wert ausgeht (Random effects Modell im Unterschied zum Fixed effects Modell).



Übersichtsarbeiten, die sich mit Komplikationen von Hysterektomien befassten, konnten nicht immer auf randomisierte kontrollierte Studien zurückgreifen, was die Ergebnissicherheit grundsätzlich weiter schmälert. Ein weiteres Problem liegt in der oft unterschiedlichen Definition von Komplikationen, deren Aggregation inhaltlich problematisch ist.

Lebensqualität wurde nur in wenigen Studien durch eine ausreichende Anzahl von Patientinnen und mit validierten Instrumenten erfasst. Die Aggregation der Ergebnisse ist bei unterschiedlichen eingesetzten Instrumenten problematisch und zum Teil nicht möglich.

Nieboer et al. 2009, weisen darauf hin, dass Langzeitergebnisse zu den unterschiedlichen OP-Verfahren weitgehend fehlen.

### Inhaltliche Ergebnisse

#### 4.1.1. Vaginale Hysterektomie versus abdominale Hysterektomie (LoE 1a-)

Nieboer et al, 2009(34) schlossen für diesen Vergleich 4 Studien ein. Zu dieser Fragestellung wurde keine aktuellere Arbeit identifiziert. Aufgrund weiter Konfidenzintervalle (siehe Evidenztabelle) wurde ein LoE 1a- vergeben.

Es zeigt sich eine deutliche schnellere Rückkehr zu Alltagsaktivitäten und eine deutlich kürzere Aufenthaltszeit in der Klinik. Alle anderen Endpunkte (Blutverlust, intra- und postoperative Komplikationen, Zufriedenheit, Lebensqualität) sind nicht signifikant unterschiedlich, zum Teil sehr heterogen oder nicht in ausreichendem Maße bzw. uneinheitlich (Zufriedenheit, Lebensqualität) erhoben.

#### 4.1.2. Laparoskopisch assistierte vaginale Hysterektomie versus abdominale Hysterektomie (LoE 1a)

Yi et al., 2011(54), vergleichen die laparoskopisch assistierte vaginale Hysterektomie mit der abdominalen Hysterektomie, sie schließen 23 RCT ein. Die Studien sind mehrheitlich von akzeptabler methodischer Qualität, bis auf die Verblindung (nur eine Studie mit adäquater Verblindung) und fehlende Angaben zum Allocation concealment in etwa der Hälfte der Studien.

Hinsichtlich folgender Morbiditäts-Endpunkte weist die laparoskopisch assistierte vaginale Hysterektomie einen statistisch signifikanten Vorteil auf: Blutverlust (MD 47.92 ml, 95% KI 77.79 bis 18.06 ml;  $p = 0.002$ ), Hb-Abfall (MD 0.52 g/100 ml, 95% KI 0.73 bis 0.31 g/100 ml;  $p < 0.00001$ ), postoperative Schmerzen an Tag 1-3 (Tag 1: MD 1.48, 95% KI 1.95 bis 1.01,  $p < 0.00001$ ; Tag 2: MD 2.07, 95% KI 2.49 bis 1.66,  $p < 0.00001$ ; Tag 3: MD 1.81, 95% KI 2.25 bis 1.37,  $p < 0.00001$ ), Rückkehr zur Alltagsaktivität (MD 13.32 Tage, 95% KI 16.77 bis 9.88 Tage;  $p < 0.00001$ ), „minor“ Komplikationen (OR 0.50, 95% KI 0.36–0.70;  $p = 0.0001$ ) und Gesamtkomplikationen ((OR 0.60, 95% KI 0.44 bis 0.81;  $p = 0.0008$ )). Das Risiko für „major“ Komplikationen ist jedoch für die laparoskopisch assistierte vaginale Hysterektomie etwa zweieinhalbfach so hoch wie für die abdominale Hysterektomie (OR 2.54, 95% KI 1.13–5.70;  $p = 0.02$ ). Die Metaanalysen zu Blutverlust und Rückkehr zur Alltagsaktivität weisen eine hohe Heterogenität auf. Die Ergebnisse der Primärstudien sind zum Teil widersprüchlich (Blutverlust) oder von stark differierender Dauer (Rückkehr zu Alltagsaktivität variiert über mehrere Tage in den Studien).

In Bezug auf Endpunkte, die für das Krankenhaus relevant sind, ist die Operationszeit für die laparoskopisch assistierte vaginale Hysterektomie in der Metaanalyse statistisch signifikant länger als für die



abdominale Hysterektomie, während die Aufenthaltsdauer in der Klinik deutlich kürzer ist – auch für diese beiden Endpunkte liegt allerdings eine starke Heterogenität vor.

Die Autoren thematisieren Lebensqualität als den „key outcome“, legen dazu aber keine Auswertung vor, sondern machen einen Bedarf nach weiterer Forschung geltend, mit Verweis auf die Arbeit von Kluivers et al, 2008(57). Diese hatte anhand einer systematischen Suche verfügbarer Primärstudien 6 Wochen nach laparoskopisch assistierter vaginaler HE eine bessere Lebensqualität der Patientinnen wie nach abdominaler HE gefunden aber keinen Unterschied nach einem Jahr, bei allerdings berichteter schlechter Studienqualität für diesen Endpunkt.

Nieboer et al, 2009 werteten weniger Studien aus als Yi et al, 2011 – mit den gleichen Ergebnissen. Im Hinblick auf die Lebensqualität stellen sie die deskriptiv gleichen Ergebnisse wie Kluivers et al, 2008 dar.

### 4.1.3. Vaginale Hysterektomie versus Laparoskopisch assistierte vaginale Hysterektomie

Zu diesem Vergleich liegt eine Metaanalyse von Guo et al, 2013(55) mit 9 RCT vor (LoE 1a-). Die Primärstudien haben überwiegend kleine Fallzahlen und nur zwei der Studien wurden doppel-blind durchgeführt. Die methodische Studienbewertung anhand des Jadad-Scores ergab im Median drei (von fünf möglichen Punkten). Aufgrund der überwiegend sehr weiten Konfidenzintervalle wurde ein LoE 1a- vergeben.

Im Ergebnis der aggregierten Auswertung waren die beiden Verfahren nicht statistisch unterschiedlich im Hinblick auf Blutverlust, Dauer des postoperativen Ileus, generelle Komplikationsraten sowie Konversionsraten und Länge des Aufenthalts. Die Gesamtkomplikationsraten liegen mit 38/238 für die LAVH und 32/277 sehr nah beieinander (OR 1,18 95%KI 0,71-1,97) bei geringer Heterogenität ( $I^2$  40%). Das Ergebnis bezüglich des Blutverlusts unterliegt einer hohen Heterogenität ( $I^2$  95%). Vier von fünf der Studien, die Angaben zum Blutverlust machen, wiesen einen geringeren Blutverlust bei vaginaler Hysterektomie auf, der in drei der Studien statistisch signifikant war. Nur in einer Studie – Summitt et al, 1992(66)- wurde ein signifikant höherer Blutverlust angegeben. Summitt et al. machen keine Angaben, wie das Ausmass des Blutverlusts erhoben wurde („estimated blood loss“). Der Hämatokrit am 2. postoperativen Tag war in derselben Studie nach vaginaler Hysterektomie signifikant höher als nach LAVH (35,2 versus 32,6%). Im Ergebnis der Metaanalyse aus den Studien zeigte sich kein signifikant unterschiedlicher Blutverlust (+51 ml für die LAVH 95% KI -39 bis 142ml) bei weiten Konfidenzintervallen.

Auch das Ergebnis hinsichtlich der Länge des paralytischen Ileus zeigte eine hohe Heterogenität ( $I^2$  98%): von den drei Studien, die dazu Angaben machen, ergab sich in zwei eine kürzere Ileusdauer, in einer Studie eine längere (Ergebnis: +2,22h für LAVH 95%KI -6,99 bis 11,44; nicht signifikant).

Die Konversionsraten (Angabe aus 6 Studien) zeigten einen Trend zugunsten der vaginalen Hysterektomie (6/217 versus LAVH 15/223), der jedoch nicht signifikant war (OR 2,21 95%KI 0,92 bis 5,32), es lag keine Heterogenität vor.

Für die laparoskopisch assistierte vaginale HE liegt eine signifikant längere mittlere Operationszeit vor (+39.59 für LAVH; 95% KI, 20:00-59.18 Minuten;  $p < 0.001$ ). In allen Studien war die Operationszeit für die vaginale Hysterektomie signifikant kürzer. Allerdings unterliegt auch dieses Ergebnis einer hohen Heterogenität ( $I^2$  97%), da die Zeitunterschiede stark differieren und sich zum Teil nicht überlappen (mittlere



Differenz in den einzelnen Studien zwischen +9 Minuten(67) bis +58 Minuten(68) für die LAVH). Angaben zur Erfahrung der Operateure und zu den Messzeitpunkten fehlen in der Metaanalyse.

Die Länge des Krankenhausaufenthaltes ist in der Metaanalyse nicht signifikant unterschiedlich (+1,17 Tage für LAVH 95%KI -0,1 bis 2,43) bei ebenfalls hoher Heterogenität ( $I^2$  97%), die sich v.a. dadurch erklären lässt, dass in einer Studie ein signifikant abweichender, kürzerer Aufenthalt nach vaginaler HE angegeben wurde(68), während in den anderen Studien keine Unterschiede bestehen.

Nieboer et al. 2009(34) werteten zu diesem Vergleich nur 2 RCT aus. Es ergab sich für keinen Endpunkt ein statistisch signifikanter Unterschied.

#### 4.1.4. Vaginale Hysterektomie versus Laparoskopische Hysterektomie (LoE2a)

Gendy et al. 2011(53) konnten für diese Auswertung 5 RCT schlechter bis mittlerer Qualität nach Jadad einschließen (Median 2 von 5 Punkten). Es fanden sich aus diesen Studien keine Hinweise für einen Unterschied in der Gesamtkomplikationsrate oder in bedeutsamen Komplikationen Grad II und III zwischen den beiden Verfahren. Allerdings machen die Autoren auf die hohe Heterogenität der Ergebnisse aufmerksam sowie auf einen möglichen Publikationsbias in Bezug auf diese Parameter. Aus diesem Grund wurden die Studien von 1a auf 2a abgewertet. Auch die Auswertungen zu Blutverlust und Konversionsrate zeigen keinen Unterschied. Die laparoskopische Hysterektomie war mit einer signifikant längeren Operationszeit (MD 29.31 Minuten; 95% KI, 13.33– 45.30 Minuten;  $p < 0,003$ ), aber signifikant kürzerem Krankenhausaufenthalt von ca. einem halben Tag (MD, 0.62 Tage; 95% KI, 0.89 bis 0.35 Tage;  $p < 0,0001$ ) verbunden. Postoperativ (am 1. Tag, nach 3 Stunden !) wiesen die laparoskopisch operierten Patientinnen in einer Studie signifikant niedrigere Schmerzscores auf(69).

Nieboer et al. 2009(34) werteten die Daten von 4 der 5 RCT aus und fanden keinen signifikant kürzeren Krankenhausaufenthalt und auch nicht signifikant weniger postoperative Schmerzen nach einer laparoskopischen Operation. Dagegen zeigte sich für die vaginale Hysterektomie ein signifikant höherer Blutverlust und eine höhere Transfusionsrate bei nicht signifikant unterschiedlicher Operationszeit.

Lebensqualität als Endpunkt wird bei Gendy et al, 2011 nicht thematisiert und auch Nieboer et al, 2009 berichten nicht über diesen Endpunkt im Vergleich VH vs LH.

#### 4.1.5. Laparoskopische Hysterektomie versus Abdominale Hysterektomie

Walsh et al, 2009(56) konnten zu dem Vergleich total laparoskopische versus abdominale HE nur 3 Studien einschließen (Suche bis Mitte 2007). Sie fanden signifikant weniger Gesamtkomplikationen und « minor » Komplikationen sowie einen signifikant geringeren Blutverlust bei der laparoskopischen Operation bei einem nichtsignifikanten Trend zu mehr « major » Komplikationen. Die Operationszeit dagegen war signifikant länger bei einem nicht signifikanten Trend zu einem kürzeren Klinikaufenthalt. Lebensqualität wird als Endpunkt nicht berichtet.

Nieboer et al, 2009(34) (Suche bis Mitte 2008) fanden bei dem Vergleich « laparoskopische » versus « abdominale » HE eine signifikant kürzere Zeit bis zur Aufnahme der Alltagsaktivität bei laparoskopischer Operation. Andererseits wies die laparoskopische Operation signifikant (OR 2,4) mehr Harnwegs/Blasenverletzungen im Vergleich zur abdominalen Operation auf. Es zeigten sich jedoch signifikant weniger postoperative Wundinfektionen und ein niedrigerer Blutverlust. Die laparoskopischen Operationszeiten waren signifikant länger.



Nieboer et al, 2012(65). publizierten einen Vergleich der erhobenen Lebensqualität nach laparoskopischer und abdominaler Hysterektomie (n=59) Aufgrund der niedrigen Fallzahl und ohne Verblindung ist die Qualität dieser Studie als niedrig einzustufen (LoE 2b-). Mit einer Rücklaufquote von 83% werteten sie den SF-36 4 Jahre nach Hysterektomie aus. Sie fanden einen statistisch signifikanten Vorteil für die laparoskopische Hysterektomie (mittl. Differenz + 50,4 Punkte). Allerdings finden sich extrem weite Konfidenzintervalle (1,0-99,7).

#### 4.1.6. Suprazervikale Hysterektomie versus Totale Hysterektomie

Lethaby et al. 2012(52) publizierten eine Metaanalyse zum Vergleich der totalen versus der suprazervikalen Hysterektomie. Sie konnten 9 RCT mit ca. 1500 Patientinnen einschließen, dabei berücksichtigten sie sowohl abdominale als auch laparoskopische Techniken. Sie fanden keine signifikanten Unterschiede hinsichtlich :

Inkontinenz innerhalb von 2 Jahren postoperativ und nach 2 mehr als 2 Jahren postoperativ (Daten aus einer Studie) für die spezifischen Endpunkte :

Stress (Belastungs-) - und Urgeinkontinenz sowie inkomplette Blasenentleerung  
Diese Ergebnisse stimmen mit denen überein, die Robert et al. 2008(59) in einer ersten Metaanalyse zu diesem Vergleich mit Daten aus 3 Studien erhoben hatten.

Obstipation oder Stuhlinkontinenz innerhalb von 2 Jahren postoperativ und nach mehr als 2 Jahren postoperativ (Daten aus einer Studie). Obstipation wurde nur für die abdominale Hysterektomie erhoben. Die aufgetretene Heterogenität konnte durch unterschiedliche Ausgangswerte in den Studien erklärt werden.

Sexueller Funktion (Zeitraum 2 Jahre, 6 Studien). Die Ergebnisse konnten aufgrund unterschiedlicher Erhebung nicht gepoolt werden. In den eingeschlossenen Primärstudien zeigten sich keine signifikanten Unterschiede

Dyspareunie innerhalb von 2 Jahren (3 Studien) oder nach mehr als 2 Jahren (Daten aus seiner Studie). Auch hier zeigte sich eine substantielle Heterogenität, die durch die unterschiedlichen Erhebungsmethoden erklärt wird.

Lebensqualität (5 Studien). Die Lebensqualität verbesserte sich in den Studien im Verhältnis prä- zu postoperativ unabhängig vom Operationsverfahren.

Im Hinblick auf perioperative Komplikationen zeigten sich signifikante Vorteile für die suprazervikale Hysterektomie (weniger Blutverlust, Fieber und Harnverhalt), in Bezug auf sonstige, intermediäre Endpunkte fand sich nach suprazervikaler Hysterektomie zum Teil eine zyklische Blutung.

Die Operationszeit war für die suprazervikale Hysterektomie signifikant kürzer.

#### 4.1.7. Spezifische Komplikationen bei Hysterektomieverfahren

##### 4.1.7.1. urodynamisch erhobene Inkontinenz

Duru et al. 2012(58) untersuchten die Auswirkungen der Hysterektomie unter Einbeziehung von 21 Studien auf urodynamische Endpunkte und fanden keine Erhöhung urodynamisch gemessener Belastungsinkontinenz bei allerdings erhöhter berichteter Inkontinenz. Die Detrusoraktivität war ebenfalls urodynamisch gemessen signifikant erhöht. Da die Ergebnisse auf z.T. kleinen Beobachtungsstudien im Sinne von Vorher-Nach-Studien beruhen, können sie nicht als sicher gelten (LoE 2-3). Die Autoren fanden





darüber hinaus Hinweise für einen Publikationsbias und merken selbstkritisch an, dass die Einschränkung auf englischsprachige Publikationen ggf. dazu beiträgt, negative Ergebnisse nicht zu finden, die, wie sie vermuten, ggf. eher national publiziert werden.

#### 4.1.7.2. Scheidenabschlussdehiszenz

Agdi et al. 2009(61) veröffentlichten eine systematisch erhobene Zusammenstellung von Scheidennahtdehiszenzen und fanden – bei geringer Inzidenz insgesamt (bis zu 1%) – diese häufiger bei laparoskopischer Technik im Vergleich zu abdominaler und vaginaler Technik (von 58 identifizierten Fällen traten 51% nach laparoskopischer, 33% nach abdominaler und 14% nach vaginaler HE auf). Uccella et al. 2011(60) analysierten laparoskopische und roboterassistierte Hysterektomien in Bezug auf die Durchführung der Scheidenabschlußnaht und erhoben eine signifikant geringere Dehiszenzrate bei von vaginal aus durchgeführter Naht, weshalb sie dieses Vorgehen empfehlen. Diesen Reviews liegen weitgehend keine RCT zugrunde.

#### 4.1.7.3. chronischer Schmerz nach Hysterektomie

Brandsborg et al, 2008(62) untersuchten chronischen Schmerz nach Hysterektomie unter Einschluss von 11 Studien (bei fehlender Angabe der Auswahlkriterien). Sie stellen zunächst fest, dass die Indikationsstellung zur Hysterektomie in 60-100% (auch) aufgrund von Schmerzen gestellt wird, in 3 Studien war dies die Hauptindikation. Die postoperative Prävalenz an Schmerzen nach 1-3 Jahren variierte in den Studien zwischen ca. 5% und 32%, was eine erfolgreiche Minderung von Schmerzen nach Hysterektomie zeigt.

Neu aufgetretener Schmerz fand sich in 3 Studien mit einer Prävalenz zwischen 1 und 14% und postoperativ betrugen die Raten an verstärkten Schmerzen (Angaben aus 2 Studien) 2,9-5%. Nur eine Studie enthielt Angaben zu der Auswirkung der Schmerzen auf den Alltag. 5,6% der Patientinnen gaben eine deutliche bis starke Beeinträchtigung an und etwa 6% nahm opioidhaltige Analgetika ein.

Die Schmerzhäufigkeit korrelierte nicht mit einer spezifischen Operationstechnik (vaginal, abdominal oder laparoskopisch), lediglich in einer Studie war sie mit einer Oophorektomie korreliert.

#### 4.1.7.4. Effekte der Entfernung der Eierstöcke bei prämenopausalen Patientinnen

Orozco et al. 2008(63) suchten Studien mit dem Vergleich Hysterektomie mit und ohne Entfernung der Eierstöcke bei prämenopausalen Patientinnen. Dazu lag eine Studie vor, bei der perimenopausale Patientinnen (45-55J) anlässlich der Hysterektomie eine zusätzliche Entfernung der Eierstöcke wählen konnten. Ein Jahr postoperativ zeigten sich kein negativer Effekt hinsichtlich Sexualität und psychischem Wohlbefinden bei Patientinnen mit Eierstocksentfernung. Die Autoren des systematischen Reviews beschreiben einen unklaren Effekt auf die Lebensqualität bei methodisch sehr geringer Studienqualität und merken an, dass die Ergebnisse Hinweisscharakter haben.

### Zusammenfassung/Fazit

Im Vergleich zur abdominalen Hysterektomie weisen die vaginale Hysterektomie und die laparoskopische Hysterektomie eine deutlich raschere Rückkehr zu Alltagsaktivitäten auf. Nieboer et al. 2009 fanden zusammenfassend keine Vorteile einer laparoskopischen Hysterektomie gegenüber der vaginalen Hysterektomie bei höheren Raten an Harnwegskomplikationen.

Die Ergebnisse der systematischen Reviews berücksichtigen folgende, klinisch relevante Aspekte nicht explizit:



Größe und Mobilität des Uterus

Erfahrung des Operateurs mit der jeweiligen Technik

Komorbidität der Patientin

Diese Aspekte sollten bei der Entscheidungsfindung immer berücksichtigt werden.

## 4.2. Vergleich roboterassistierter (RAH) und laparoskopischer Hysterektomie (LAH)

### Methodische Beurteilung

Es wurden 3 systematische Übersichtsarbeiten zur roboterassistierten Hysterektomie bei benignen gynäkologischen Konditionen eingeschlossen, 2 von diesen behandeln den generellen Vergleich laparoskopischer und roboterassistierter Hysterektomie – bei allen (70) bzw. nur bei benignen Indikationen(71). Eine dritte Arbeit analysiert die Literatur für roboterassistierte single-site port Interventionen(72) (siehe Tabelle 13 unten).

Die beiden erstgenannten Reviews identifizierten jeweils 2 RCT zu roboterassistierter Hysterektomie versus laparoskopischer Hysterektomie bei benignen Konditionen(73, 74). Die Vollpublikation des 2. RCT erfolgte 2013, so dass nur in der aktuellsten systematischen Übersichtsarbeit darauf zurückgegriffen werden konnte. Da einige Angaben fehlten, wurden beide Originalarbeiten eingesehen.

Es handelt sich um zwei RCT mit nicht sehr großer Fallzahl (n=62 und n=100). Bei Paraiso et al, 2013 erfolgte in 85% der Fälle die randomisiert zugeteilte Intervention (53/62), nur diese wurden ausgewertet (per protocol Analyse). Die Patientinnen waren in Bezug auf den Eingriff verblindet. Die Anzahl der Patientinnen erlaubte eine 90%ige Power, um einen Unterschied in der OP-Zeit (Schnitt-Nahtzeit) von 30 Minuten zu entdecken. Sarlos et al randomisierten - unverblindet, da unterschiedliche OP-Anfahrt/Räume je Verfahren- 100 Patientinnen und erzielten damit eine 85%ige Power, einen 15minütigen Unterschied in der OP-Zeit (Schnitt-Nahtzeit) nachzuweisen. In beiden RCT hatten die Operateure mindestens 20 RAH durchgeführt bei jeweils langjähriger laparoskopischer Expertise. Methodisch erscheint der Endpunkt Op-Zeit-Unterschied von 15-30 Minuten fraglich patientinnenrelevant. Die Studien waren nicht dafür ausgelegt, z.B. einen Unterschied bei postoperativen Schmerzen oder bei Lebensqualität zu entdecken. Die Randomisierung und verdeckte Zuteilung sind jeweils korrekt beschrieben. Bei nichtverblindeter Auswertung besteht ein erhöhtes Verzerrungsrisiko insbesondere im Hinblick auf subjektive Endpunkte. Es handelt sich insgesamt um RCT moderater methodischer Qualität

Der Review zur roboterassistierten Hysterektomie mit nur einem Arbeitskanal (single-site port)(72) schließt keine RCT, sondern nur retrospektive Fallserien und Einzelfallberichte ein, deren Berichtsqualität und methodische Aussagesicherheit nicht hoch sind.

### Inhaltliche Ergebnisse:

#### Roboterassistierte Hysterektomie bei benigner Indikation – Ergebnisse der RCT

##### Komplikationen

Paraiso et al berichten nur von „major complications“ – in beiden Gruppen traten keine auf. Auch bei Sarlos et al traten keine „major complications“ auf. „Minor complications“ waren nicht signifikant unterschiedlich (RAH 14, LAH 11).





Der Blutverlust war in beiden RCT nicht signifikant unterschiedlich (Paraiso: RAH 283 ml, LH 294 ml und Sarlos 87ml RAH, 79 ml LAH).

Der Schmerzmittelverbrauch wird bei Sarlos als nicht unterschiedlich in beiden Gruppen angegeben.

Konversionen werden bei Paraiso et al, in zwei Fällen von RAH zu LH aufgrund operativer Komplikationen angegeben, 1 Mal eine Konversion von LAH zu Laparatomie ebenfalls wegen operativer Komplikationen. Bei Sarlos et al wird von 1 Konversion RAH zu LAH berichtet und von 5 Fällen, in denen der Uterus nicht robotergestützt, sondern durch vaginales Morcellement entfernt wurde.

#### Lebensqualität

Paraiso et al, erhoben präoperativ mittels SF 36 die Lebensqualität und in weiteren Fragebogen einen Schmerzscore sowie den Grad an Alltagsaktivität.

Die Lebensqualität war nach 6 Monaten nicht signifikant unterschiedlich in beiden Gruppen. Sarlos et al erzielten dagegen eine signifikant verbesserte Lebensqualität (erhoben mittel EQ-5D in der RAH Gruppe nach 2-3 und 6-8 Wochen (+13) im Verhältnis zu LAH (+4,  $p < 0,001$ ). Daten nach 6 Monaten liegen nicht vor. Die Ergebnisse sind demzufolge uneinheitlich, bei Sarlos ist die mangelnde Verblindung zu bedenken.

#### Operationszeit

In beiden RCT war die Schnitt-Naht-Zeit bei RAH im Vergleich zu LAH statistisch signifikant erhöht. Bei Paraiso benötigte der schnellste Operateur 46 Min. länger für die RAH, durchschnittlich lag die OP-Zeit 70 Min. höher (172 vs 170 Min.  $p < 0,001$ ). Bei Sarlos et al. machte die Differenz 20 Minuten aus (96 +/-28 robot HE, 76 +/-21 LAH diff. 20 (11–29)  $p < 0,001$ ) bei allerdings weitem Konfidenzintervall zwischen 11 und 29 Minuten. Der Aufenthalt im Operationssaal verlängerte sich zusätzlich durch die sogenannte „docking time“ – das Anbringen der Instrumente- bei der RAH.

#### Länge des Krankenhausaufenthalts

Die Länge des Krankenhausaufenthalts war für beide Interventionen in beiden RCT nicht signifikant unterschiedlich: 1, 4 Tage in beiden Gruppen bei Paraiso 3, 3 bzw. 3,1 die bei Sarlos)

Zusammenfassung: Für die roboterassistierte hysterektomie im Vergleich zur laparoskopischen Hysterektomie wurde in randomisierten Studien bislang keine Verbesserung in Bezug auf Komplikationsraten und perioperative Blutungen gezeigt bei deutlich längeren Operationszeiten. Für eine Verbesserung der Lebensqualität liegen heterogene Daten vor. Kostenaspekte werden in den RCT nicht adressiert. Sarlos et al. haben laut mündlicher Auskunft die RAH bei benignen Indikationen inzwischen verlassen (Mündl, Auskunft Prof. Neis 10/14).

#### Roboterassistierte Hysterektomie mit nur einem Arbeitskanal (single-site port intervention)

Iavazzo et al. 2014(72) konnten 6 Publikationen einschließen, 3 Fallserien und 3 Fallberichte, davon 4 bei benigner Indikation mit insgesamt 16 Patientinnen. Es wurde eine mediane Operationszeit von 109 Minuten erreicht mit einer erforderlichen Konversion. Es wurde von keiner Bluttransfusionsgabe berichtet, die Klinikaufenthaltsdauer lag bei 2-6 Tagen. Daten zu Komplikationen oder Follow up liegen nicht vor.

## 5. Evidenztabellen

### 5.1. Evidenztabelle zu Hysterektomie versus Myomenukleation bei Uterus myomatosus

Tabelle 3: Eingeschlossener Systematischer Review zum Vergleich Hysterektomie versus Myomenukleation bei Uterus myomatosus

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (Oxford)
Systematic Review Pundir et al, 2013(1)	Search in Medline and EMBASE, no study design restriction mentioned  Women with uterus myomatosus	perioperative morbidity associated with abdominal myomectomy in comparison with abdominal hysterectomy for uterine fibroids.  primary outcome : major morbidity rate  secondary outcomes : uterine size, estimated blood loss, blood transfusion, operating time, duration of hospital stay.	The results identified six observational studies including 1520 participants.  All studies scored moderately on the N-OQA (Newcastle-Ottawa Quality Assessment for observational studies) scale and were limited to a uterine size of up to 18 weeks.  1. Major morbidity rate :  There was no significant difference in the rate of major morbidity (RR 0.94; 95% CI = 0.31, 2.81; p = 0.91) between the two operations. It was concluded that based on variable quality data from retrospective cohort studies, abdominal myomectomy and hysterectomy appear to have similar major morbidity rates for the uterine size up to 16-18 weeks.	<b>Cave : results extracted from the abstract because full text not available</b>  Conclusion of the authors : well- designed trials with a standardised morbidity outcome and including uterine size greater than 18 weeks are required.	n.a.	4



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (Oxford)
Systematic Review Lethaby A. et al, 2011	<p>Search in Medline 1966 to June 2009, EMBASE 1980 to June 2009, and The Cochrane Database of Systematic Reviews 2009, Issue 2 (1966 to date of issue).</p> <p>An additional search within The Cochrane Library was carried out for the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA). We also searched for retractions of studies included in the review</p> <p>We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA).</p>	Laparoscopic myomectomy (maintains fertility compared with hysterectomy;	No adequate studies found	<b>No RCT identified</b>	-	-



## 5.2. Evidenztabelle zu Hysterektomie versus Embolisation der Arteriae uterinae bei Uterus myomatosus

Tabelle 4: Eingeschlossene Systematische Reviews/Metaanalysen zum Vergleich operative Intervention (Hysterektomie, Myomenukleation) /Embolisation der Arteriae uterinae

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
Martin et al., 2013 Review, Metaanalysen Cardiovasc Intervent Radiol (2013)	Search in PubMed, MEDLINE, Cochrane and CINAHL databases + citations in reviews	Use, efficacy and complications for UAE in symptomatic fibroids	<p>1.) 8 RCT, n=350 UAEs no difference between overall and minor complications, but more severe complications in surgery major complications : Mara: UAE &gt; surgery REST, Pinto : UAE &lt; surgery</p> <p>Reinterventions : significant increase of reinterventionstions for UAE relative to surgery in 3of 4 RCT</p> <p>2.) 76 non RCT, n=11195 Total rate of complications 24,9%</p>	Same RCT comparing HE and UAE as in Toor et al. !	See Toor et al, for RCT : Additionally included : Ambat S et al, 2009 Uterine artery embolization versus laparoscopic occlusion of uterine vessels for management of symptomatic uterine fibroids. Int J Gynecol Obstet 105(2):162–165	1a-3



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p>3.) 41 Case studies, n=83 Total rate of complications 0,55%</p> <p>Major complications in surgery more severe.</p> <p>Major complications :</p> <p>Surgery : urinary and defaction dysfunction, febrile morbidity, systemic and local infection.</p> <p>UAE : fever, postembolisation syndrome, local groin syndroms, artery dissection, contras allergy</p> <p>UAE : 4x death : 1 large embolus, 2x sepsis with multiorgan system failure, 1 nontarget embolisation with pulmonary, cardial and systematic infarction.</p> <p>Reintervention : Great success in short-term</p> <p>REST :</p> <p>UAE : 1year: 13%,</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			5years : 32% surgery : 1year: 2%, 5 year : 2% EMMY : UAE: 2 years : 23,5%, 5years : 28,4% surgery : 5years : 10,7% Repeat UAE in RCT : 2,29% HE rate in RCT : 13,7% Total reintervention rate : 16% Much literature failed to publish reintervention rate. UAE often delayed complications → significant less major complications, but at the cost of increased reinterventions			
Toor S. et al, 2012(3) Systematic Review and Metaanalysi s American	<b>Search period</b> : 1948- 9/2011 (1 RCT 2012 additionally included) <b>Databases</b> : PubMed, Medline, EMBASE, and Cochrane	symptomatic cohort of patients with a diagnosis of uterine leiomyomas treated with	283 full texts, 220 excluded, 54 study populations/ 61 publications : 7 RCT, 37 prospective case series, 10 retrospective case	Studienbeschreibung und –bewertung nach STROBE, 2 zusätzliche Items : prospektives Design, weniger als 10% Lost to Follow up,	<b>Death as consequence                      of UAE :</b> 1.Vashist A. et al, 1999, Lancet (75) (case report : fatal sepsis) 2. De Blok S. et al, 2003, J Vasc Interv	1+ bis 3



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
Journal of Radiology	<p>Databases</p> <p><b>Type of studies included :</b> all but case reports</p> <p>Inclusion and exclusion criteria :</p> <p>Only english publications</p> <p>Symptomatic cohort of patients with a diagnosis of uterine leiomyomas treated with UAE;</p> <p>minimum follow-up duration of 1 month by clinic visit, telephone, or questionnaire; explicit collection and reporting of complications with quantitative data;</p> <p><b>minimum of 20 patients treated;</b></p> <p>original study (not a review article or letter); and study patients who were not a subset of patients from another included</p> <p>Publication. Studies addressing the use of UAE in a two-step</p>	<p>uterine artery embolization (=UAE ) using reporting standards from the Society of Interventional Radiology (SIR)</p> <p><b>1.primary Outcome :</b> Major complications requiring prolongation of inpatient hospital stay (&gt; 48 hours), hospitalization, or permanent adverse sequelae. (permanent amenorrhoe (only unless patient &lt;40y))</p> <p><b>2. secondary Outcome :</b></p>	<p>series</p> <p>Cave : case reports and case series&lt; 20 not included,</p> <p>Single center trials 44, multicenter trials 10, inpatient only 46</p> <p>Publication year 1998-2011, 8.159 Patients</p> <p>Follow up 3-60 months, &gt;6 months for 90% of studies</p> <p>52% PolyvinylAlcohol as embolization particle 20% variable particle use, 13% Tris-Acryl gelatin microspheres</p> <p>Almost half of the studies excluded patients who had a pedunculated subserosal fibroid, a fibroid or uterus larger than a specific predetermined size limit, or concomitant uterine adenomyosis</p> <p><b>Cave :</b> « The I<sup>2</sup> statistic calculated for most complications was</p>	<p>The pooled proportions of all outcomes were calculated using the DerSimonian-Laird weights for the random effects model. Pooled estimates of proportions and their 95% CIs were calculated.</p> <p>I<sup>2</sup> 30-50%= moderate heterogeneity, I<sup>2</sup> substantial = 50-75%, I<sup>2</sup> considerable &gt; 75%)</p> <p>Publication bias was as-sessed</p> <p><b>Cave:</b> RCT mit sehr kleinen Fallzahlen, Gewicht kommt durch prospektive Fallserien, hier keine Vergleichsgruppen, insgesamt nur indirekte Vergleiche möglich</p>	<p>Radiol(76) (case report : fatal sepsis)</p> <p>3. Lefebvre et al, 2004 J Obstet Gynaecol Can(77)</p> <p>5 case reports : Vashihst A et al, 1999, Lanocita R et al, 1999 (78) (pulmonary embolism), de Blok S. et al, 2003, 2 case reports personal communication 2002 by R. Worthington-Kirsch (without cause given)</p> <p>4. [no authors listed], 2009 (79) (case report : pulmonary embolism )</p> <p>5. Hamoda et al, 2009 Cardiovasc Intervent Radiol (case report : pulmonary embolism)(80)</p> <p><b>RCT with UAE :</b></p> <p>1. Hald K et al, 2009 J Vasc Interv Radiol 2009(81) (UAE vs laparoscopic occlusion n=66)</p>	

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
	<p>procedure with surgery were excluded because this might confound the outcomes of UAE alone.</p> <p>Suchbegriffe : "uterine artery embolization," "leiomyoma," "complications," "treatment outcome," and "clinical outcome"</p> <p>Abstracts and full texts screened by 2 reviewers</p>	<p>a. clinical symptom improvement (menorrhagia, bulk symptoms) and dysmenorrhea</p> <p>b. reintervention data (number of repeat UAE procedures, myomectomies and hysterectomies )</p>	<p>substantial »</p> <p><b>1. Major complications :</b> Definition : requiring prolongation of inpatient hospital stay (&gt; 48 hours), hospitalization, or permanent adverse sequelae</p> <p>In Total : 2,9%(2,2-3,8) RCT : 6,6% (2,7-12%) I<sup>2</sup> 71% prosp. Studies : 2,8% (2,1-3,5] I<sup>2</sup> 54%</p> <p><b>1a.Death:</b> not described in included studies but 5 publications with 7 case reports mentioned ;cause : sepsis or pulmonary embolism</p> <p><b>1b. Readmission because of morbidity due to the intervention :</b> In total, 163 of 6223 patients (2.7% [1.9–3.7%]) were readmitted because of</p>		<p>2.Mara M et al, 2008 Cardiovasc Intervent Radiol (UAE vs Myomectomy n=121)(8)</p> <p>3. Moss JG et al, 2011, BJOG (« REST trial », UAE vs Surgery :HE or Myomectomy,n=157)(9)</p> <p>4. Ruuskanen A et al, 2010 Eur Radiol (UAE vs Hysterectomy, n=55)(10)</p> <p>5.van der Kooij et al, 2010 Am J Obstet Gynecol 2010( « Emmy –Trial » UAE vs HE,n=177)(11)</p> <p>6.Pinto I et al, 2003 Radiology(UAE vs HE, n=57)(7)</p> <p>7. Manyonda IT et al, 2012 Cardiovasc Intervent Radiol (« FUME trial », UAE vs Myomectomy N=163)(12)</p> <p>RCT with comparison of</p>	





Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p>morbidity from the procedure</p> <p><b>2 .Specific complications</b></p> <p>- <b>permanent amenorrhea</b> : reported in 40 studies, pooled rate of 3.9% (2.7–5.3%)</p> <p>- <b>Fibroid tissue passage:</b> reported in 20 studies, 4.7% [3.9–5.7%]</p> <p>- Hysterectomy as a result of a complication, such as severe uterine infection or ischemia : no of. Studies not reported, occurred in a total of 26 of 4903 patients= 0.7% (0.5–0.9%)</p> <p>- <b>Angiography related complications:</b> funnel plot indicated risk of publication bias 44 studies, 6953 patients, 2.9% (2.1–3.9%) I<sup>2</sup>=70% kind of complications not</p>		<p>two embolization agents :</p> <p>8.Pisco JM et al, 2008, Vasc Interv Radiol</p> <p>9.Spies JB et al, 2004 Vasc Interv Radiol</p> <p>10. Yu SC et al, 2011, J Vasc Interv Radiol</p> <p>11. Bilhim T et al, 2011 J Vasc Interv Radiol</p>	



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p>reported</p> <p><b>-Deep venous thrombosis or Pulmonary embolism :</b> 54 studies, 7632 patients, 0,2% (0,2-0,4%) I²0%</p> <p><b>-infections :</b> 49 studies, 7149 patients, 2,5%(1,8-3,2%) I²62%</p> <p><b>3. reintervention rate</b> reported in 42 studies representing 4682 patients, follow up 0.25 to 5 years n= 430 reinterventions (9,2%), annual rate of 5.3% (4.2–6.4%); 81 repeat UAE procedures, 81 myomectomies, and 257 hysterectomies</p> <p><b>4. Clinical symptom improvement</b> data available for 2930 patients from 30 studies. Clinical follow-up duration ranged from 0.25 to 2.0 years - Menorrhagia (29</p>			

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p>studies, 2345 patients, 16 studies &lt;1y: 84,7-93,7%</p> <p>- Bulk symptoms (22 studies, 1544patients, 13 studies &lt;1y) 75,4-90.5%</p> <p>-Dysmenorrhoe (14 studies, 1060 patients, 7 studies &lt;1y) 73,8-98.7%</p> <p><b>5.Subgroup analyses comparing the midyear of treatment before 2002 versus 2002 or later</b></p> <p>trends of higher rates of readmission (3.2% [2.2–4.6%] vs 2.2% [0.8–4.1%]) and complication-related hysterectomy (0.9% [0.6–1.3%] vs 0.4% [0.2–0.8%]) in the older studies.</p> <p>6.Subgroup analysis comparing major complications in relation to quality of studies :</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			Low quality score (29 studies, 2299 patients) : 2,4% (1,6-3,5%) I <sup>2</sup> 50% High quality score (25 studies, 5860 patients) : 3,4% (2,3-4,7%), I <sup>2</sup> 70%			
<b>Gupta JK et al, 2012(4)</b> Systematic Review Cochrane Database of Systematic Reviews	Suchzeitraum : 1950-11/2011 Datenbanken : The Cochrane Menstrual Disorders & Subfertility Group Trials register (searched November 2011), the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, 4th Quarter 2011), MEDLINE (1950 to November 2011) and EMBASE (January 1980 to November 2011). We also contacted authors of eligible RCTs for unpublished data. Studientyp : Randomised controlled trials (RCTs) of UAE	UAE versus any medical or surgical therapy for symptomatic uterine fibroids Outcomes : 1. Patient satisfaction at 5 years/Health related Quality of Life at 1 Year 2. Live birth/.Pregnancy rates 3.. Fibroid recurrence 4. Adverse events within 1 month 5. Adverse	6 Rcts with 732 women were included. 3 trials compared UAE with abdominal hysterectomy, 2 trials compared UAE with myomectomy, 1 trial compared UAE with surgery (43 hysterectomies and 8 myomectomies)  Size of fibroids was a limiting factor in two studies (larger than 10 cm in Pinto 2003 and 12 cm in Mara 2008) Indications to treatment were menorrhagia and pressure symptoms due to myomata	Evidenzbewertung nach Endpunkten mit GRADE Qualitätsbewertung der Einzelstudie mit Cochrane Risk of Bias Tool Alle Studien ohne Verblindung FUME und Pinto : incomplete outcome reporting (not intention to treat reporting) REST : selective reporting Ruuskanen : Random sequence generation and allocation concealment not reported	RCT : UAE vs HE 1. Pinto I et al, 2003 Radiology(UAE vs HE, n=57)(7) 2. Ruuskanen A et al, 2010 Eur Radiol (UAE vs Hysterectomy, n=55)(10) 3. van der Kooij et al, 2010 Am J Obstet Gynecol 2010( « Emmy –Trial » UAE vs HE ,n=177)(11) RCT : UAE vs HE or Myomectomy 4. Moss JG et al, 2011,BJOG (« REST trial », UAE vs	1+/1-



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
	versus any medical or surgical therapy for symptomatic uterine fibroids. <b>Ein- &amp; Ausschlusskriterien :</b>	events Major complications	<b>1. Patient satisfaction/QoL</b> Reported in 5 studies. Satisfaction rates measured by asking women whether they would undergo the same treatment again (REST 2011; EMMY 2010; Ruuskanen 2010; Pinto 2003) or whether they obtained symptom relief (Mara 2008) : Moderately good evidence that there is no significant difference between UAE and surgery in patient satisfaction rates at two years (OR 0.69, 0.40 to 1.21, 516 women, 5 trials) or at five years (OR 0.90, 95% CI 0.45 to 1.80, 295 women, 2 trials) without heterogeneity, and very low level evidence suggesting that quality of life at one year improved equally in both		Surgery :HE or Myomectomy,n=157)(9) RCT : UAE vs Myomectomy 5. Mara M et al, 2008 Cardiovasc Intervent Radiol (UAE vs Myomectomy n=121) 6. Manyonda IT et al, 2012 Cardiovasc Intervent Radiol (« FUME trial », UAE vs Myomectomy N=163)(12)  Not included because not comparing sugery with UAE: Hald et al, 2007 (Hald K et al, 2009 J Vasc Interv Radiol 2009(81) (UAE vs laparoscopic occlusion n=66))	



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p>groups (mean difference -7.60, -17.55 to 2.35, 1 trial, 122 women).</p> <p><b>2. Fertility</b> Analysis restricted to the limited cohort of women (n=66) who tried to conceive in one study of UAE versus myomectomy (Mara 2008), 26 women after UAE and 40 after myomectomy.: Very low level evidence suggesting that myomectomy may be associated with better fertility outcomes than UAE,</p> <p><b>2a. Live birth :</b> Analysis restricted to the limited cohort of women (n=66) who tried to conceive in one study of UAE versus myomectomy (Mara 2008) . No significant difference between the groups in live birth rate</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p>(OR 0.33, 95% CI 0.11 to 1.00)</p> <p><b>2b. Pregnancy :</b> Significantly fewer pregnancies in the UAE group (OR 0.29, 95% CI 0.10 to 0.85, 66 women)</p> <p>REST 2011 reported fertility outcomes in a comparison between the UAE arm and a subgroup of eight women in the surgical arm (8/51) who opted for myomectomy rather than hysterectomy. There were 10 pregnancies in the UAE group (10/106) and two in the myomectomy group (2/8). These data have not been included in analysis due to the strong risk of selection bias.</p> <p><b>3. Major complications</b> Reported in all studies (n=627)</p>			





Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p><b>(Definition Ruuskanen :</b> Major complications = result in admission to hospital for therapy, an unplanned increase in the level of care, prolonged hospitalisation &gt;48h, permanent adverse sequelae or death (2 in HE : 1 relaparatomy because of bladder lesion, .1 haematoma with infection) <b>cave :</b> definitions are heterogeneous between studies) - No significant difference between the two interventions in the rate of major complications (UAE : 22/374, HE : 23/297 ; OR 0.54, 95% CI 0.29 to 1.01, I<sup>2</sup>=27%) Compared to surgery, UAE was associated with a significantly reduced length of the procedure, length of</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p>hospital stay and time to resumption of routine activities and UAE decreased the likelihood of needing a blood transfusion.</p> <p>Reported in 5 studies : No significant differences between UAE and surgery in the rate of intra procedural complications (OR 1.01; 95% CI 0.52 to 1.95, 512 women, 5 trials, I<sup>2</sup>=24% or any complications within one month (OR 1.38, 0.55 to 3.50, 1 trial, n=121)</p> <p><b>4. Minor Complications</b></p> <p>UAE was associated with higher rates of minor short term and long term complications, more unscheduled readmissions after discharge and an</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p>increased surgical reintervention rate. This increase in the surgical reintervention rate may balance out the initial cost advantage of UAE (reinterventions within 2 years: OR 5.09, 95% CI 2.82 to 9.18, 608 women, 5 trials; within 5 years: OR 5.79, 95%CI 2.65 to 12.65, 289 women, 2 trials).</p> <p>No significant difference in ovarian failure rates at long term follow-up (Three studies, two studies reported the number of women with FSH levels over 40 IU/L within two years (EMMY 2010; REST 2011), OR 1.01, 95% CI 0.53 to 1.94, 297 women, One study reporting the number of women with FSH over 10 IU/L within six months (Mara 2008) OR 4.80, 95% CI 0.97 to 23.64, 120 women.</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<b>Recurrence rate :</b> Mara 2008 : recurrence rate of fibroids within two years of follow-up : No significant difference between the groups (OR 1.32, 95% CI 0.38 to 4.57, 120 women)			
Jun F. et al, 2012(5) RCT, Systematic Review and Metaanalysi s Arch Gynecol Obstet.	1. RCT: Patients : female, $\geq 18$ y. , all premenopausal, symptomatic fibroids (menorrhagia, pressure symptoms, pelvic pain) at least 4cm visible in MRT , no upper limit in size.  Exclusion criteria : contraindication MRT, surgery, pelvic inflammatory disease, pregnancy  2. Systematic Review/ Metaanalysis  Search Period : 1950- March 2011	UAE versus Surgery (HE or MM) RCT : outcome QoL (SF-36) and complications SR and Metanalysis : idem	1. RCT : <b>Methodology</b> : 1 :1 Randomization by computer sequence generation. 63 UAE, 64 Surgery (10 HE, 54 MM all abdominal), Follow up 42 months <b>Results</b> : Technical feasibility : no problems <b>QoL</b> : SF-36 at 6 months : UAE group with significantly greater improvement in scores than the surgery group for five components (physical and social function, mental health, emotional role, vitality), p values < 0.05	Cave : results of SF 36 not provided for longer periods of assessment !  Not reported how satisfactory rate was measured  Kind of additional invasive procedures not for all events reported  Metaanalysis : All results with heterogeneity ( $I^2$ Recovery time and Hospital Stay >75% = substantial, Major complications= $I^2$ 42%= moderate)  Metaanalysis for minor complications	Emmy Trial(11) Mara 2008(8) Pinto 2003(7) Ruuskanen 2010(10) Jun 2012 (RCT)(5)	



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
	<p>Data Bases : Medline (1950 to March 2011) and EMBASE (1988 to March 2011) and manual search of citations in the relevant retrieved papers</p> <p>Inclusion Criteria : (1) RCTs; (2) compared UAE with surgery; (3) participants were patients with symptomatic uterine fibroids;</p>		<p>Complications :</p> <ul style="list-style-type: none"> <li>- <b>Minor complications</b> (no additional interventions, required no therapy or at most nominal therapy or overnight hospital stay for observation only, such as arterial spasm and surgical wound hematoma.)</li> </ul> <p>UAE : 31 (50%) Surgery : 14 (23%) p=0,03</p> <ul style="list-style-type: none"> <li>- <b>Major complications</b> (admission to hospital for therapy, life-threatening events, prolonged hospitalisation, permanent adverse sequelae or death)</li> </ul> <p>UAE group : 0 Surgery group 4 (6%) p=0,005</p> <ul style="list-style-type: none"> <li>- <b>Additional invasive</b></li> </ul>	<p>and reintervention rate not provided</p> <p><b>Cave</b> : Reporting bias in favour of UAE !</p>		



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<b>procedure</b> UAE group : n=12 (19%) Surgery Group : n= 9 (15%) p=0,02 - <b>Secondary UAE</b> UAE group : n=5 (8%) Surgery group : n= 0 p=0,005 - <b>Secondary myomectomy</b> UAE group : 1(2%) Surgery group : 6(10%) p=0,02 - <b>Patient satisfaction</b> UAE group : 52 (84%) Surgery group : 45 (73%) p=0,01 Not reported how satisfactory rate was measured <b>Systematic review/Metaanalysis</b> 5 RCT included : Emmy Trial Mara 2008			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Bemerkungen	Literaturbelege	Evidenz- niveau (SIGN/ Oxford)
			<p>Pinto 2003 Ruuskanen 2010 Jun 2012 Metaanalysis for Hospital Stay, Recovery time and Major complications : all results with heterogeneity</p> <p>a. <b>Hospital Stay</b> : mean difference – 2,71 days [95%CI : - 3,76, -1,65] p&lt;0,00001 I<sup>2</sup>=90%</p> <p>b. <b>Recovery time</b> : - 16,92days [95%KI : -22,55 ; -11,29] I<sup>2</sup>=86% p&lt;0,00001 I<sup>2</sup>86%</p> <p>c. <b>Major complications</b> : UAE group : 18/315 Surgery group : 24/325 Risk Ratio -0,42 [95%CI : 0,24, 0,76] I<sup>2</sup> 42% Fixed Effect Model</p>			





### 5.3. Evidenztabelle zu Hysterektomie versus medikamentöser Therapie und Hysterektomie plus additive präoperative medikamentöse Therapie bei Uterus myomatosus

Tabelle 5: Eingeschlossene Systematische Reviews/Metaanalysen zu hormoneller Therapie des Uterus myomatosus

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
<b>GnRH-Analoga</b>						
Metaanalyse <b>Zhang et al, 2014(13)</b> OBSTETRICAL AND GYNECOLOGICAL SURVEY « The Impact of Pre-operative Gonadotropin- Re-leasing Hormone Agonist Treatment on Women With Uterine Fibroids: A Meta-analysis	PubMed (from 1980 to June 2013) and EMBASE (from 1980 to June 2013) were searched to identify RCTs in <b>English-language</b> journals. Using the keywords "GnRH," "gonadotrophin-releasing hormone analogues," "uterine fibroid," "leiomyoma," "leiomyomatosis," and "randomized controlled trial" We also searched the related references of the retrieved studies and review articles from the bibliographic database. The corresponding authors in some studies were contacted.	<b>Patients</b> With uterine fibroids <b>Intervention/ Comparison</b> treatment with GnRH analoga versus other medical treatment, placebo, or no treatment when administered before surgery for uterine fibroids <b>Outcome</b> volume measurements of fibroid tumors, postoperative complications, myoma recurrence, and changes in fertility. Metaregression and subgroup analysis	183 hits, 26 RCT included, women underwent hysterectomy (=HE, 13x explicitly), myomectomy (=MM), or hysteroscopic resection of uterine fibroids. 20 studies observed the efficacy of preoperative GnRHa therapy compared with either no treatment or placebo; 6 RCT studies compared the efficacy of pretreatment between GnRHa and other analogs of progestin, selective progesterone-receptor modulators, selective estrogen receptor modulators, and dopamine receptor agonists. <b>Preoperative, intraoperative, and postoperative outcomes. no differences in</b>	1. Meta-analysis done only with <b>Random effects Modell</b> because of Heterogeneity expected (wider Confidence intervals than with fixed effects model) 2. <b>Publication bias</b> was examined using funnel plots and Egger regression test, indicating that	Friedman et al, 1989(82) MM Shaw et al, 1989(83) Fedele et al, 1990(84) MM Golan et al, 1993(85) MM+ HE Audebert et al, 1994(86) HE+ MM Cagnacci et al, 1994(87) Lumsden et al, 1994(88) Stovall et al, 1994(89) Balasch et al, 1995(90) HE Cetin et al, 1995	1a-2a (2a for outcomes with substantial heterogeneity)

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		were used to identify potential predictors of the effect sizes.	<p><b>-duration of surgery</b> data from 13 studies with HE+MM (some only MM!), <math>I^2</math> 48,8%, mean difference, -3.15minutes; 95%CI, -7.34 to 1.05minutes; <math>P = 0.243</math>), In addition to Lethaby et al, 2001 who found for HE a sign. shorter duration, only 1 study added after 2000 (Muzii et al, 2010, no HE, hyst. MM)</p> <p><b>-hospital stay</b> (SD -0.601 days; SE 0.342; <math>P = 0.079</math>),</p> <p><b>- rate of blood transition</b> (OR,0.603; 95% CI, 0.358-1.015; <math>Z = 1.904</math>; <math>P = 0.057</math>),</p> <p><b>- postoperative complications</b> (OR, 1.092; 95% CI, 0.527-2.261; <math>Z = 0.236</math>; <math>P = 0.813</math>),</p> <p>Data of 10 studies HE+MM, 2 studies after 2000</p> <p><b>-myoma recurrence</b> (OR, 4.155; 95% CI, 0.594-29.075; <math>Z = 1.435</math>; <math>P = 0.151</math>), and</p> <p><b>-changes in fertility</b> (OR, 0.490; 95%CI,</p>	<p>no significant publication bias was involved in the outcomes of this meta-analysis. Consequently , unpublished data were not further evaluated.</p> <p><b>3. Subgroup Analysis for Patients with hysterectomy is missing</b> in terms of operation time, blood loss, complications</p> <p><b>4. Substantial Heterogeneity</b> for outcomes = <math>I^2 &gt; 70\%</math>: Fibroid volume, Hb, Hk, duration</p>	<p>(Buserelin) Stovall et al. 1995(91) Benagiano 1996(92) Gerris 1996(93) Vercellini et al, 1998(94) Nikolov et al, 1998(95) Zullo 1998(96) Campo et Garcea 1999(97) Verspyck et al, 2000(33) Donnez 2003(98)HE Vercellini et al. 2003(99) Baytur et al. 2007(100) Melli et al, 2007(101) Sayyah-Melli et al. 2009(102) Mavrellos et al. 2010(103)</p>	



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>0.095Y2.532; Z = j0.852; P = 0.394) in the treated patients.</p> <p><b>Preoperative GnRHa treatment in women with uterine fibroids significantly reduced</b></p> <ul style="list-style-type: none"> <li>- <b>preoperative fibroid size</b> (SD, -0.493; SE, 0.190; Z = j2.594;P = 0.009) and</li> <li>- <b>increased the hemoglobin</b> (SD, 0.393; SE, 0.199; Z = 1.978; P = 0.048) <b>and hematocrit levels</b> before surgery (SD, 0.720; SE, 0.357; Z = 2.018;P = 0.044).</li> <li>- <b>The total score of preoperative pelvic symptoms</b> (SD, j1.656; SE, 0.120; Z = j13.774;P G 0.001)</li> <li>- <b>rate of vertical incision</b> (OR, 0.333; 95% CI,0.199Y0.556; Z = j4.209; P G 0.001) and</li> <li>-<b>a higher proportion of patients undergoing a vaginal procedure</b> (OR, 8.174; 95% CI,</li> </ul>	<p>of hospital stay – no sensitivity analysis given</p> <p>Moderate heterogeneity I<sup>2</sup> 40-70%: Duration of surgery, proportion with postoperative complications , proportion with recurrence of myomas</p> <p>5. Reporting of side effects of GnRH is missing</p>	<p>Muzii et al, 2010 hysteroscopy MM</p> <p>Donnez et al, 2012(30)</p>	



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>4.771Y14.005; Z = 7.647; P G 0.001).</p> <p>- the largest reduction in fibroid size was associated with hysterectomy, followed by myomectomy, and patients undergoing hysteroscopic resection were reported to have the smallest preoperative fibroid size.</p> <p>- Long-term preoperative GnRHa treatment (12 weeks) was more effective in reducing the fibroid size and enhancing the hemoglobin and hematocrit levels compared with shorter treatment of 8 weeks, especially in older women</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
Systematic Review with Meta- Analysis/Cochra ne Review  <b>Lethaby et al, 2001(14)</b> « Pre-operative GnRH analogue therapy before hysterectomy or myomectomy for uterine fibroids »	<b>Electronic searches</b> for relevant RCT trials of the Cochrane Menstrual Disorders and Subfertility Group Register of Trials, MEDLINE, EMBASE, the National Research Register, the National Library of Medicine's Clinical Trials Register and Current Contents. Attempts were also made to identify published trials from citation lists of review articles and direct contact with drug companies for unpublished trials. In most cases, the first author of each included trial was contacted for additional information.  The search was updated in October 2000.	<b>RCT</b> <b>Patients</b> Pre- menopausal women, without any other underlying uterine pathology, undergoing either hysterectomy (abdominal, vaginal or laparoscopic) or myomectomy (laparotomy, laparoscopy or hysteroscopy) for uterine fibroids <b>Intervention:</b> GnRH analogue treatment ((buserelin, goserelin, leuprorelin acetate, nafarelin or triptorelin) <b>Comparison:</b> placebo, no treatment, or other medical therapy prior to surgery, either myomectomy or hysterectomy, for uterine fibroids	26 RCT identified, 3 RCT waiting for assessment (data missing), 2 RCT excluded, <b>21 RCT included :</b> 14 RCT GnRH analogue therapy vs no therapy (total of 1005 patients), 6 RCT GnRH analogue therapy vs placebo (total of 825 patients), 1 RCT GnRH vs lynestrenol. <b>RCT with « no treatment arm »</b> Hysterectomy (HE) was performed in 4 trials, myomectomy (MM) in 5 trials, a combination of MM + HE in 4 trials, and unspecified surgery in one trial (Cagnacci 1994). <b>RCT with Placebo arm :</b> HE was performed in 4 trials, MM in 1 trial and a combination of HE and MM in 1 trial. HH+ME were performed in the trial comparing GnRH vs lynestrenol. Thus HE alone was performed in 8 trials, HE or	Fixed effect model used Meta- Analyses for operation time complications for HE extra Heterogeneity of outcomes not explained  Study quality: poor- moderate 8/21 RCT with adequate allocation concealment, 5/6 Placebo trials double blind, In no treatment comparison trials 3x surgeon blinded and 1x sonographer	D'Anna et al, 1994(104) Bustos-Lopez et al, 1995(105) Shaw 1996 unpublished data Friedman et al, 1989(82) Shaw et al, 1989(83) Fedele et al, 1990(84) Golan et al, 1993(85) Audebert et al, 1994(86) Cagnacci et al, 1994(87) Lumsden et al, 1994(88) Stovall et al, 1994(89) Balasch et al, 1995(90) Cetin et al, 1995 (Buserelin)	1a -2a (cave heterogenei ty)



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		<b>PRIMARY OUTCOMES</b> <b>1. Pre-operative assessment</b> a) Reduction in uterine volume and/or fibroid volume b) Change in haematologic indices (haemoglobin, haematocrit, ferritin) <b>2. Operative difficulties</b> a) Duration of operation b) Intra-operative blood loss c) Frequency of blood transfusions <b>3. Post-operative assessment</b> a) Post-operative morbidity (complications such as pyrexia, haematoma formation and incidence of post-	MM in 6 trials, MM in 6 trials, in 1 trials surgery was not specified. <b>Pre- and post-operative haemoglobin (Hb) and haematocrit (HCT) :</b> significantly improved by GnRH analogue therapy prior to surgery. <b>Uterine volume, uterine gestational size and fibroid volume :</b> all reduced. <b>Pelvic symptoms :</b> were also reduced but <b>Adverse events :</b> Some more likely during GnRH analogue therapy. Hysterectomy appeared to be easier after pre-treatment with GnRH analogue therapy; <b>Complication rate after HE :</b> GnRH : 36/308 events Control : 55/312 events OR 0.62 [0.39, 0.97] <b>Operating time :</b> -5.18 [ -8.62, -1.75 ] p<0,05	Power calculation only in 4 trials, Intention to treat analysis in 8 trials	Stovall et al. 1995(91) Benagiano 1996(92) Gerris 1996(93) Vercellini et al, 1998(94) Nikolov et al, 1998(95) Zullo 1998(96) Campo et Garcea 1999(97) Verspyck et al, 2000(33)	



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		operative adhesions)	<p><b>vaginal HE in stead of abdominal HE</b></p> <p>GnRH : 82/225</p> <p>Control : 27/230 OR 4.70 [2.97, 7.45 ] I<sup>2</sup>83%</p> <p><b>Duration of hospital stay :</b></p> <p>-1.06 [ -1.22, -0.90 ] p&lt;0,05 I<sup>2</sup>90%</p> <p><b>Blood loss :</b> -57.98 [ -75.66, -40.30 ]p&lt;0,05 I<sup>2</sup>=80%</p> <p><b>Rate of vertical incisions decreased :</b></p> <p>GnRH : .42/260</p> <p>Control: 88/269 OR 0,36 [ 0.23, 0.55 ]</p> <p>Evidence of increased risk of fibroid recurrence after GnRH analogue pre-treatment in myomectomy patients was equivocal and few data were available to assess change in post-operative fertility.</p> <p>Lynestrenol did not offer any advantage over GnRH analogue therapy before fibroid surgery. The increased costs associated with GnRH analogue</p>			





Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			therapy not assessed.			
<b>Progesterone / Progesteronereceptorantagonists</b>						
Systematic Review/ Cochrane Collaboration <b>Sangkomkamhang US et al, 2013(15)</b> « Progestogens or progestogen-releasing intrauterine systems for uterine fibroids »	<b>Electronic Search</b> in: Menstrual Disorders and Subfertility Group (MDSG) Specialised Register (from inception to 17 August 2012) in liaison with the Trials Search Coordinator; • Cochrane Central Register of Controlled Trials (CENTRAL) (from inception to 17.8.2012) in Ovid; • Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) (from inception to 17.8.2012); • Ovid EMBASE (1 January 2010 to 17 August 2012), EMBASE only one year back as the UK Cochrane Centre has hand-searched EMBASE to this point, these trials	<b>Patients</b> 1. Premenopausal women with uterine fibroids diagnosed by clinical manifestation and physical signs and confirmed by ultrasound scanning, computed tomography (CT), or MRI, or a combination of more than one of the procedures.	108 hits, 20 fulltext assessed, 3 Studies included in qualitative synthesis, 187 women, different comparisons: <b>1. Levonorgestrel-releasing intrauterine device (LNG-IUS) versus hysterectomy</b> <b>1. Inki 2002</b> , n=236 women, mean age 43 y, menorrhagia, a.o. not included: large enough fibroids to cause bowel or urinary symptoms, submucous fibroids. 117 LNG-IUS, 119 HE (done in	<b>1. Risk of bias included studies = serious</b> Random sequence generation unclear in Inki and Verspyck. Allocation concealment unclear in Sayed and Verspyck, Blinding for outcome	Verspyck et al, 2000(33) Inki et al, 2002(31) Sayed et al, 2011(32)	2a (formally downgraded because of risk of bias, clinically plausible results)

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
	are in CENTRAL;• Ovid Psyc-INFO (from inception to 17 .8. 2012). Other resources: ClinicalTrials.gov, World Health Organization (WHO) International Trials Registry Platform search portal	2. Premenopausal women with fibroid-related symptoms and palpable uterine fibroids without confirmation by imaging technology 3. Premenopausal women without symptoms but with uterine fibroids during routine gynaecological examination and confirmed by imaging techniques <b>Intervention/ Comparison</b> oral progestogens, depot medroxyprogesterone acetate (DMPA) intramuscular injections or progestin-releasing intrauterine	107 women, abd. HE 20%, vag. HE 28%, 52% lap. assisted, no HE performed in 10 women). Main outcome of study: comparison of ovarian cyst formation LNG-IUS versus HE. Assessment of uterus size by ultrasound at entry, 6 and 12 months. Fibroid size >2cm also recorded. <b>Primary outcome review: fibroid size and symptoms</b> <u>a.US examination at baseline</u> Uterus size: 58mm LNG-IUS group, 59mm HE group Fibroid>2cm: 32%LNG-IUS group mean size 28mm, 30% HE group mean size 29,4mm <u>b.US examination at 6 months</u> in 97 women with LNG-IUS (10 had HE, 10 had no LNG IUS anymore – mostly because of heavy bleeding/pain, 1 lost to follow up.): 19/98 (19,4%) with fibroids, mean size	assessment in none of the RCT reported, incomplete outcome data in Sayed and Verspyck, unclear in Inki, selective reporting unclear in all 3 RCT. 2. <b>Loss to follow up:</b> 9.3% to 27.6% (= incomplete outcome data in Verspyck and Sayed 2011)		



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		<p>devices (IUS). Control interventions included no treatment, placebo, medical therapy, or surgical procedures</p> <p><b>Outcomes</b> Primary outcomes</p> <p><b>1. Improvement in uterine fibroid-related symptoms,</b> abnormal uterine bleeding measured by objective disease measures such as Hb, Hk, or ferritin levels; pain assessed subjectively by the individual or with a visual analogue scale (VAS)</p> <p><b>2. Reduction in fibroid size</b></p> <p><b>Secondary outcomes</b></p>	<p>ca.30mm n. stat. sign.</p> <p><u>Symptoms at 6 months:</u> 28/97 (29%) reported amenorrhea or oligomenorrhea and 41/97 (42%) reported intermenstrual bleeding.</p> <p><u>c.US examination at 12 months</u> in 79 women (total 24 had HE, 10 no LNG-IUS anymore, 3 lost to follow up) fibroids 16/82 (19,5%), mean size ca. 24 mm n.stat. sign.</p> <p><u>Symptoms at 12 months:</u> 41/81 (51%) oligomenorrhoe/amenorrhoe, 26/81 (32%) intermenstruel bleeding. No absolute data available for Menstrual blood loss (MBL) reduction</p> <p>Patients who were found to have uterine fibroids at baseline were more likely to undergo hysterectomy during LNG-IUS use (46%).</p> <p><b>Secondary outcomes</b> Quality of life/ Recurrence rate with the possibility of</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		3. Quality of life 4. Recurrence rate with the possibility of necessitating additional therapy 5. Adverse events such as acne, weight gain, bloating, breast tenderness, and expulsion of the IUS 6. Cost effectiveness	<p>necessitating further additional therapy/ Adverse events/ Cost effectiveness: no data available.</p> <p>More ovarian cysts in LNG-IUS group, no symptoms. Endometrium line thinner at 6 and 12 months.</p> <p><b>2. Levonorgestrel-releasing intrauterine device (LNG-IUS) versus Combined oral contraception (COC)</b></p> <p><b>Sayed 2011</b> : n=58 women, 20-50 y , with fibroid-related menorrhagia (fibroids diagnosed by ultrasound) desiring contraception. Randomized to LNG-IUS and COC</p> <p>Excluded a.o. : submucous fibroids of any size distorting the cavity of the uterus or intramural or subserous fibroids &gt; 5 cm in diameter</p> <p><b>Primary outcomes :</b></p> <p><b>1. Fibroid related symptoms :</b></p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p><b>Primary outcome :</b> <b>reduction of blood loss measures</b></p> <p><b>a.by pictorial blood assessment chart (PBAC)</b> at baseline, at 6 month and 12 months : reduction was significantly greater in the LNG-IUS group (<math>88.0\% \pm 16.5\%</math> vs <math>53.5\% \pm 51.2\%</math>; <math>P=0.02</math>)</p> <p><b>b.by alkaline hematin method</b> at baseline and at 12 months : reduction of MBL was significantly greater in the LNG-IUS group (<math>90.9\% \pm 12.8\%</math> vs <math>13.4\% \pm 11.1\%</math>; <math>P&lt;0.001</math>).</p> <p><b>Hb :</b> with the LNG-IUS were significant higher than with the COC (MD 1.50, 95% CI 0.93 to 2.07 g/dl)</p> <p><b>2. fibroid size :</b> no significant difference between the two groups (MD 1.90 cm, 95% CI -8.04 to 11.84 cm)</p> <p><b>Secondary outcomes :</b> Quality of life/ Recurrence rate with the possibility of necessitating additional</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>therapy/Cost effectiveness: no data available. Adverse events: rate of LNG-IUS expulsion 0.1%.</p> <p><b>2. Lynestrenol versus leuprorelin</b></p> <p><b>Verspyck 2000</b> : 56 women with fibroids and symptoms indicating Surgery, 1 or more at least 5 cm or submucous. Preoperative 16 weeks randomized to lynestrenol 5 mg two tabs per day (5th to the 25th menstrual cycle) OR leuprorelin 3.75 mg sustained every 28 days</p> <p>1. <b>Primary outcomes at 16 weeks: reduction of fibroid size</b> : statistically significant in the leuprorelin group compared to lynestrenol (MD -15.93 mm, 95% CI -18.02 to -13.84 mm, 46 women)</p> <p><b>Fibroid symptoms</b> : no significant difference (pelvic pain) between the</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>lynestrenol and leuporelin groups, risk ratio (RR) of 1.20 (95% CI 0.56 to 2.56, 55 women) at 28 days and 1.48 (95% CI 0.59 to 3.71, 49 women)</p> <p><b>Hb</b> not significantly different between the two groups (MD 0.18, 95% CI 0.01 to 0.35 g/dl, 45 women)</p> <p><b>Secondary outcomes:</b> Quality of life/ Recurrence rate with the possibility of necessitating additional therapy/ Cost effectiveness: no data available.</p> <p><b>Adverse events:</b> no significant differences between lynestrenol and leuporelin : headache (RR 0.26, 95% CI 0.06 to 1.07, 56 women), nausea (RR 2.87, 95% CI 0.57 to 14.38, 56 women), and weight gain (RR 2.15, 95% CI 0.39 to 11.88, 56 women)</p>			
Systematic Review/	Search in: Specialised register of the-Cochrane Menstrua Disorders	Randomised controlled trials of	135 hits, 9 records screened, 3 RCT (112	<b>1. Risk of bias -</b>	Bagaria et al,	1a-



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
Metaanalyse/ Cochrane Collaboration <b>Tristan M, et al, 2012(16)</b> "Mife-pristone for uterine fibroids"	and Subfertility, the Cochrane Central Register of Controlled Trials (CENTRAL) ( <i>The Cochrane Library</i> 2011, Issue 4), MEDLINE, EMBASE, PsycINFO, and CINAHL (to November 2011). We hand-searched a number of journals, and searched reference lists, databases of ongoing trials and the Internet. There were no language restrictions.	mifepristone versus other forms of medical therapy or placebo in premenopausal women with confirmed uterine fibroids were included	participants) were included. Comparison interventions included different dosages of mifepristone (50 mg, 10 mg, 5 mg), placebo and vitamin B tablets. <b>Fibroid symptoms</b> There is evidence that treatment with mifepristone (2x 3 months, 1x 6 months) relieves heavy menstrual bleeding compared with placebo (PetoOR 17.84; 95%CI 6.72 to 47.38; 2 RCTs, 77 women, I <sup>2</sup> = 0%). Relief of dysmenorrhea (1 RCT, Bagaria): PetoOR 10,92[2,37-50,51] <b>Fibroid size/Uterus size</b> There was no evidence of an effect of mifepristone on the fibroid volume (standardized mean difference (SMD) -0.02; 95% CI -0.38 to 0.41; 99 women. 3 studies). The mean leiomyoma volume in the control groups was 118.3 ± 243 mL. The mean leiomyoma volume in the intervention groups was	<b>moderate</b> Sequence generation and allocation concealment ok, blinding ok, but specific side effects of mifepristone, selective outcome reporting possible, unclear if outcome assessors blinded 2. <b>Imprecision</b> n- small sample sizes, few events, wide confidence intervals. Sample size might have been	2009(26) Engman et al, 2009(25) Fiscella et al, 2006(24)	(- because of wide CI)





Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>0.10 lower (0.76 lower to 0.57 higher)</p> <p>There was no evidence of an effect of mifepristone on uterine volume (mean difference (MD) -77.24; 95% CI -240.62 to 86.14; 72 women, 2 studies).</p> <p>The mean uterine volume in the control groups was 281.1 ± 417 mL. The mean uterine volume in the intervention groups was 93.10 lower (317.07 lower to 130.87 higher)</p> <p><b>Adverse events</b></p> <p>The pooled data suggest an increased adverse event (abnormal endometrial histology) in the mifepristone group compared to placebo (OR 31.65; 95% CI 4.83 to 207.35; 2 RCTs; 54 women; I<sup>2</sup> = 0%).</p> <p>Only one study (Bagaria 2009) reported endometrial hyperplasia at the end of the therapy (12/19 women in the mifepristone group versus 0/16 in the placebo</p>	too small to even show differences		



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			group; OR 55.0; 95% CI 2.86 to 105.67). Engman 2009 found a significantly higher rate of cystic glandular dilatation in women in the mifepristone group (5/8 women biopsied) compared with the placebo group (1/11 women biopsied) (OR 16.67; 95% CI 1.36 to 204.03). <b>Quality of life</b> One study (Fiscella 2006) suggested significant improvements (P < 0.001) for specific quality of life outcomes.			
<b>Selective progesteron receptor modulator –Ulipristal</b>						
Systematic Review Canadian Agency for Drugs and Technologies in Health(27) 2013	Study Design : <b>RCT</b> Databases : EMBASE from 1974 to, Ovid MEDLINE In-Process & Other Non-Indexed Citations, Ovid MED-LINE Daily and Ovid MEDLINE 1946 to present Search date : 2013 June 4, Alerts	<b>Population :</b> Adult women of reproductive age with moderate to severe signs or symptoms from Uterine Fibroids (UFs), who are	196 hits, 2 RCT included <b>Study characteristics</b> <b>PEARL I :</b> placebo-controlled, superiority trial <b>co-primary end points :</b> % of patients with a pictorial bleeding assessment chart (PBAC) <sup>1</sup> score < 75 at 13	<b>I.</b> Conflicts of interest: Authors of RCT are partially: Scientific Advisory Board	1.PEARL I : Donnez et al, Ulipristal Acetate versus Placebo for Fibroid Treatment	1b

<sup>1</sup> [http://www1.wfh.org/docs/en/Resources/Assessment\\_Tools\\_PBAC.pdf](http://www1.wfh.org/docs/en/Resources/Assessment_Tools_PBAC.pdf)

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
	for Medline until October 16 Relevant websites from "Grey matters: a practical tool for evidence-based searching" ( <a href="http://www.cadth.ca/en/resources/finding-evidence-is/grey-matters">http://www.cadth.ca/en/resources/finding-evidence-is/grey-matters</a> )	eligible for surgical intervention <b>Intervention :</b> Ulipristal Acetat (UA) <b>5 mg daily</b> <b>Comparator :</b> GnRH agonists, Combined hormonal contraceptives, Progestin- releasing intrauterine system, Progestins, Placebo, Watchful waiting, Tranexamic acid, NSAIDs, Hysterectomy, Myomectomy, Uterine artery occlusion, Myolysis, Uterine artery embolization, <b>Outcome :</b> <b>Key efficacy outcomes:</b> Quality of life by validated	weeks, and the change in total fibroid volume from screening to week 13. <b>PEARL II :</b> active- controlled, non-inferiority trial of double-dummy design, GnRH agonist Leuprolide 3.75 mg intramusc.monthly as active comparator, <b>primary end point :</b> % of patients with, PBAC score < 75) at the end of week 13 <b>PEARL I and II :</b> both multinational, double-blind RCTs stratified randomization according to race (black or other); PEARL I additionally stratified patients according to hematocrit levels ( $\leq 28\%$ or $> 28\%$ ) Baseline characteristics generally well balanced between groups, 86% white, mean age of 41 years, body mass index of 25 kg/m <sup>2</sup> . Mean ferritin levels at the low end of normal PEARL I (12.7 mcg/L) and PEARL II	Members of Manufact er or working for manufact er <b>II. Sample size calculatio n:</b> PEARL I for diff. in myoma volume 20% with 90% power, PEARL II: non- inferiority was tested on percentag e of patients with a reduction in uterine bleeding as defined by a	before Surgery, NEJM, 2012(29) 2.PEARL II : Donnez et al, Ulipristal Acetate versus Leuprolide Acetate for Uterine Fibroids, NEJM, 2012(30)	



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		<p>instrument Symptom control (i.e., pain or discomfort)</p> <p><b>Other efficacy outcomes:</b> Number (%) of patients <i>not</i> proceeding to surgery after treatment Number (%) of invasive surgeries (i.e., laparotomic hysterectomy) avoided Control of bleeding</p>	<p>(24.1 mcg/L). Mean uterine volume at screening PEARL I (395 cm3) than PEARL II patients (238 cm3). Mean total myoma volume at screening was 140 cm3 in PEARL I Myoma volume evaluation was by magnetic resonance imaging (MRI) in PEARL I and transvaginal ultrasound in PEARL II</p> <p><b>Results :</b> <b>PEARL I : Screened 462, randomized 96 UA, 48 Placebo</b> <b>Control of bleeding PBAC score &lt; 75 week 13 :</b> ulipristal n=86 (91,5%) placebo: n=8 (18,2%) difference: 72.7% , 95% CI, 55.1% to 83.2%) <b>Short-form McGill Pain Questionnaire</b> Ulipristal: -5.0, Placebo: - 2,5 not significant (95%CI -0.0) <b>Measurement of</b></p>	<p>PBAC score &lt; 75 at week 13) using a one- sided CI at a significanc e level of P = 0.025 against a -20% non- inferiority margin — a clinical margin deemed acceptabl e by the clinical expert consulted.</p> <p><b>III. Appropri ate randomiz ation methods and allocation concealm ent (i.e.,</b></p>		



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p><b>Discomfort Due to Uterine Fibroids Questionnaire — Change from Baseline to Week 13</b></p> <p>Ulipristal -9.0, placebo:-6.0 Difference : -4.0, (-6.0 to -1.0) p&lt;0.001 clinical importance unclear</p> <p><b>Amenorrhea week 13</b></p> <p><b>Ulipristal</b> : 69 (73.4%), <b>Placebo</b> : 3 (6.3%)</p> <p><b>Number (%) of Patients Not Proceeding to Surgery after Treatment</b></p> <p><b>Ulipristal</b>: 61 (65.6%), <b>Placebo</b>: 35 (72.9%) n.s.</p> <p><b>PEARL II : Screened 400, randomized 102 UA5, 102 LA</b></p> <p><b>Proportion of Patients with PBAC Score &lt; 75 in week 13 per protocol</b></p> <p>Ulipristal : 88 (89.8%), Leucoprolid 87 (88.8%)</p> <p><b>Median Reduction in Fibroid Volume at w. 13</b></p> <p>Ulipristal 36% (10 mg 42%), leuprolide 53%</p>	<p>via an interactive voice or web response system) were used</p> <p><b>IV. Blinding</b> in PEARL II may have been compromised by the incidence of AEs — particularly, hot flashes — in the <a href="#">leuprolide</a> group; this is of importance, given the subjective nature of the primary outcome</p> <p><b>V. Since</b></p>		



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>Leuprolid was associated with a significantly greater reduction in uterine volume (47%) than was either ulipristal group (20 to 22%).</p> <p><b>Uterine Fibroid Symptom/Health-Related Quality of Life per protocol</b></p> <p>Symptom Severity:                      Ulipristal (n= 53) -28.2/                      Leucoprolid (n=46)-27.2                      n.s.</p> <p>HRQoL total score                      Ulipristal 20,3/Leucoprolid 17,8 n.s.</p> <p><b>Moderate-to-severe hot flashes</b></p> <p>11% of patients receiving 5 mg of ulipristal acetate, 10% of receiving 10 mg UA</p> <p>40% with leuprolide acetate (P&lt;0.001 for each dose of ulipristal acetate vs. leuprolide acetate)</p> <p><b>Short-form McGill Pain Questionnaire Change from Baseline to Week 13</b> all measures not significant, almost same</p>	<p>planned analyses involved comparisons of two doses of ulipristal acetate versus leuprolide acetate, a Bonferroni correction was used and all P values were doubled and confidence intervals were similarly adjusted.</p> <p>VI. The Hematin alkaline test is considered the gold standard for</p>		



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>results</p> <p><b>Surgery cancelled</b>  Ulipristal: 52 (55.9%),  Leucoprolid: 50 (53.8%)  n.s.</p> <p><b>Less invasive Surgery</b>  Ulipristal: 57 (62.0%),  Leucoprolid: 55 (59.1%)</p>	<p>quantifyin g menstrual blood loss, but was not used</p> <p><b>VII.</b> The  trials were  not  designed  to assess  difference  s in  surgical  outcomes  as a  function of  treatment;  an  important  limitation,  especially  given that  most of  the  literature  in this  therapeuti  c area  appears to  focus on</p>		



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
				<p>the effect of treatment on surgical outcomes, such as intra- or post-operative complication rates</p> <p>VIII. Unclear: how relevant is the assessment of quality of life is during this relatively short pre-surgical period compared with the post-operative period</p>		





Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
<b>Selective estrogen receptor modulator (SERM) – Raloxifene</b>						
Systematic Review/ Cochrane Collaboration <b>Deng et al, 2012(18)</b> « Selective estrogen receptor modulators (SERMs) for uterine Leiomyomas»	<b>Electronic Search</b> in: Cochrane Menstrual Disorders and Subfertility Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, PubMed, EMBASE, the Register of Chinese trials developed by the Chinese Cochrane Centre, and the Chinese MedDatabase (Chinese Biomedical Disc), VIP, and ChinaNational Knowledge Infrastructure. <b>Handsearch:</b> a number of journals and searched reference lists, <b>Other:</b> databases of ongoing trials and the Internet. The searches were conducted in March and April 2012.	RCT of selective estrogen receptor modulators versus other forms of medical therapy, placebo or no treatment in women of reproductive age (18 to 45 years old) with confirmed uterine fibroids	339 records screened, 6 full texts assessed, 3 RCT included, different comparisons, no metaanalysis possible. <b>Heterogeneous evidence :</b> <b>Jirecek et al. with positive result for 180mg, Palomba et al, 2002 (2 trials) with negative results for 60 and 180mg but with positive results for 60mg+ GnRH.</b> <b>1. Jirecek et al, 2004 : Raloxifene 180 mg vs no treatment 3 months: n=25</b> Randomised, single- blind, open-label, controlled clinical trial, women with <u>asymptomatic</u> fibroids and regular menstruation. 80% power to detect a 20% diff. between group. Baseline volume fibroids cm <sup>3</sup> : raloxifene group 59.0 +/- 48.1 no treatment group:	1. Quality of the evidence : Low to very low evidence Risk of bias potentially serious, because 1 RCT not blinded, 1 with unclear sequence generation, all with unclear allocation concealment and unclear risk of selective reporting bias 2. Jirecek et al : 2 coauthors working for manufacturer of Raloxifene (Lilly)	Jirecek et al, 2004(22) Palomba et al, 2002(20) Palomba et al, 2002a(106)	2a (formally downgrade d because of low quality evidence)

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>68.1+/- 48.0. Size at 3 months: raloxifene group 54.4 +/- 47.9 no treatment group: 78.4+/-62.3</p> <p><b>Effect on Fibroid size at 3 months:</b> significant difference between the groups in change from baseline in mean fibroid size, favouring the raloxifene group (MD -22.2%, 95% CI -42.2% to -2.2%, 23 women, p not given). <u>NO significant change from baseline in mean fibroid size in the raloxifene group (-9.1%, P = 0.31) but significant mean increase from baseline in the control group (+13.1%, P = 0.04).</u></p> <p><b>Adverse events:</b> 3 patients in raloxifene group (23%): 1 hot flashes, 1 weight gain, 1 dry skin, ovariancyste.</p> <p><b>2. Palomba et al, 2002 : Raloxifene 60mg (A) vs 180 mg (B) vs</b></p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p><b>placebo (polyvitamins= C) until 6 months:</b> n= 90, Prospective randomised (using a computer-generated list), single-blind placebo-controlled clinical trial, women with 1-2 asymptomatic fibroids min. 2cm. Sample size was calculated to be of 30 subjects per group to detect an effect on the size of 1 sd with an p-value of 0.05 (two-sided), a power 1-</p> <hr/> <p>of 0.8.</p> <p><b>Size fibroid in mm</b>  <b>Group A (R.60mg)</b> 51,7 +/-18,9, after 6 months: 57,4 +/-23.7; <b>Group B (R.180mg):</b> 47,4+/-16,3, after 6 months: 47,7+/-21,8, <b>C(placebo polyvitamin):</b> 49.0 +/-14.9, after 6 months 55.3 +/-17.9</p> <p><b>Effect on uterus/fibroid size at 3 and 6 months:</b> not significant. At 6 months only significant (<math>P = 0.05</math>) increase in mean uterine</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>and leiomyoma size in groups A and C in comparison with basal values and 3 (10.3%) and 4 (13.8%) cases of new tumoral formations in groups A and C. No sign. changes in group B.</p> <p><b>Effect on length and severity of bleeding:</b> not significant</p> <p><b>Adverse events:</b> 2 in group with raloxifene 180mg (7%)</p> <p><b>3. Palomba et al, 2002 : Raloxifene + GnRHa vs placebo :</b> n=100, parallel design, randomised, single-blind, placebo-controlled clinical trial. Randomisation using a computer-generated list. Analysis was by intention-to-treat. Included : 100 premenopausal women with symptomatic uterine leiomyomas. All women received leuprolide acetate depot at a dose of 3.75 mg/28 days combined with raloxifene hydrochloride at</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>a dose of 60 mg/day p.o. (group A) or placebo tablets (1 tablet/day; group B). Duration: 6x28 days each. Women of group A continued for another 12 cycles.</p> <p><b>Effect on uterus/fibroid size at 6 months (Percent size change in GHRH analogue treated women)</b></p> <p>+Raloxifene: -0.71 (0.08); Placebo: -0.4 (0.1) mean diff: -0.31 [ -0.35, -0.27 ] p&lt;0,05</p> <p><b>Effect on fibroid related symptoms at 6 months</b></p> <p>Menorrhagia, pelvic pressure, perlivc pain, urinary frequency, constipation were sign. better in both groups, no differences between groups. No menorrhagia and constipation was noted any more.</p> <p><b>Other outcomes in Palomba trials :</b> -fibroid recurrence with trend « less » for raloxifene, but</p>			



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			n.s.			
<b>Aromatasehemmer</b>						
Systematic Review/ Cochrane Collaboration <b>Song et al, 2013(17)</b> « Aromatase inhibitors for uterine fibroids. »	Search in : databases (from inception to August 21, 2013): Cochrane Menstrual Disorders and Subfertility Group Specialised Register, Cochrane Central Register of Controlled Trials (CENTRAL) ( <i>The Cochrane Library</i> ), MEDLINE, EMBASE, CINAHL and PsycINFO. In addition, the reference lists of included trials were searched, and experts in the field were contacted.  Included: RCTs. Only the first phase of cross-over studies was eligible. Quasi-RCTs were excluded.	<b>Patients:</b> Women of reproductive age with confirmed uterine fibroids diagnosed by ultrasound scanning, computerised tomography (CT), magnetic resonance imaging (MRI) or a combination of these procedures.  <b>Intervention:</b> use of aromatase inhibitors in the treatment of uterine fibroids versus other treatment or placebo.  <b>Primary Outcomes:</b> • Relief of symptoms: menstrual loss, as measured by object. assessments (e.g. menstrual volume, duration of flow); presence or severity of dysmenorrhoea, as assessed subjectively	84 records screened, 3 full texts assessed, 1 RCT included.  <b>Exclusion reasons:</b> Badawy 2012 targeted uterine adenomyosis, instead of uterine fibroids. Nassar 2009, which was intended to evaluate AIs for prevention of growth of uterine fibroids in perimenopausal women, was excluded because it had been withdrawn before enrolment as a result of lack of recruitment.  <b>Included study:</b> Parsanezhad 2010. Two- arm parallel-group design in multicentres (Iran and Germany). N= 70, randomly assigned to aromatase inhibitor group (letrozole, administered orally (2.5 mg/d regardless of the day of the menstrual period) or long-acting GnRHa group (triptorelin, control).	<b>Low quality of evidence</b>  <b>Risk of bias:</b> Allocation concealment unclear, assessor- blind design, risk of Per- formance bias was judged as high, whereas the risk detection bias was deemed low.  Intention-to- treat (ITT) analyses were not performed. The withdrawal rate after randomisation was 14.3% (10/70, two	Parsanezhad et al, 2010(23)	2b (formally downgrade d)



Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		<p>by participant or with the use of a scale</p> <p><b>Secondary outcomes</b></p> <ul style="list-style-type: none"> <li>• Adverse events: hot flushes, joint disorders (arthritis and arthralgia, or joint pain), hypercholesterolaemia, osteoporosis and fractures</li> <li>• Reduction in fibroid size, • Recurrence rate, • Live birth and pregnancy rates</li> <li>• Quality of life</li> <li>• Cost-effectiveness</li> </ul>	<p>Outcomes were measured at baseline and during treatment at 2, 4, 6 and 12 weeks after the start of treatment. According to the review protocol, only measures obtained at week 12 were taken into account.</p> <p><b>Primary outcomes:</b></p> <p><b>Relief of symptoms:</b> not reported in the included study.</p> <p><b>Secondary outcomes:</b></p> <p><b>Adverse events:</b> only the occurrence of hot flushes was reported. 96.3% of women in the GnRHa group experienced hot flushes with various degrees of severity, and no women in the aromatase inhibitor group reported hot flushes of any severity . The way the presence or severity of hot flushes was defined was not mentioned in the report. Analysis showed a statistically significant difference (<math>P = 0.00</math>). However, because one group reported no</p>	<p>from the letrozole group and eight from the triptorelin group), mainly because of irregular follow-up visits. The risk of attrition bias was judged as unclear.</p> <p>No protocol was available for the included study; the risk of selective reporting was unclear.</p> <p><b>Conclusion of authors:</b> The study failed to report important clinical outcomes.</p>		

Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>events (the AI group reported no cases of hot flushes), no OR could be calculated.</p> <p><b>Reduction in fibroid size:</b> measured by transvaginal ultrasound. Data presenting the reduction in fibroid volume (cm<sup>3</sup>) from baseline in both groups at week 12 showed that, for the GnRHa group, mean fibroid volume was reduced from 95.29 to 63.66; and for the aromatase inhibitor group, a reduction from 108.18 to 58.86 was noted. Data were presented as the percentage change from baseline: the total volume of fibroids declined by 33.2% at week 12 in the GnRHa group (P = 0.02) and by 45.6% at week 12 in the aromatase inhibitor group (P = 0.00). Analysis indicated no significant difference regarding the reduction in fibroid volume between those two groups. Standard deviations were not reported, so an odds</p>	<p>Another major quality issue was the small sample size. Chance could be a reasonable explanation for the reported findings, and this study was underpowered to determine any treatment effect. In addition, investigators did not report sufficient statistical information to permit calculation of ORs or MDs.</p>		





Studientyp Quelle	Untersuchte Studien	(verglichene) Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			ratio could not be calculated. <b>No other outcomes reported</b>			

Tabelle 6: Eingeschlossene Primärstudien zur medikamentösen Behandlung des Uterus myomatosus

Quelle/ Studientyp	Design/Population (Teilnehmer) (verglichene) Interventionen/ ggf. Dosierung/ggf. Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodische Bemerkungen	Evidenz- niveau
<b>RCT zu GnRH Analoga</b>					
Elzaher et al, 2013(19)	<b>Design:</b> RCT <b>Setting:</b> Obstetrics and gynecology departments of two hospitals in the Gulf area (Medical Teaching Center, Kingdom of Saudia Arabia, and Enjab Hospital, United Arab Emirates) over a 4-year period, between June	<b>-Primary end point:</b> Reduction of myoma size (weight, measurement by ultrasound) <b>-Additional end points:</b> -Duration of surgery -pain/analgetic use -length of	Only 88 patients were eligible for the study out of 230 patients <b>Weight of the uterine specimen /Decrease of size</b> significantly lower in VH group (511.7 +/-217 g) compared to TAH group (736.8 +/-212 g); P < 0.001. The mean objective decrease in clinical uterine bulk preoperatively in VH group was 20.1%. <b>Duration of surgery</b> nearly 1.5 times as long in VH groupI (119.6 +/-41.7 min) compared to TAH group (81.1 +/-34.1 min), P < 0.001 <b>pain/analgesia use</b> Mean pain score significantly lower in VH group	<b>Sample size Calculation:</b> at least 40 patients in each arm (using Minitab Statistical Computer program V.12) based on 20% reduction in the uterine size (axial uterine diameter at the sagittal plane by ultrasound), after GnRH injection in order to perform vaginal hysterectomy as a an alternative probability to abdominal hysterectomy rate of 45% for menorrhagia	1b-



Quelle/ Studientyp	Design/Population (Teilnehmer) (verglichene) Interventionen/ ggf. Dosierung/ggf. Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodische Bemerkungen	Evidenz- niveau
	<p>2008 and April 2012</p> <p><b>Patients:</b> Women scheduled for hysterectomy for menorrhagia with a non-prolapsing uterus of 14 to 20 weeks size (by clinical and sonographic assessments)</p> <p><b>Interventions</b></p>	<p>inpatient stay</p> <p>-surgical complications</p>	<p>compared to TAH group on both postoperative day 0 (2.4 +/- 1.6 vs 5.3 +/- 2.1 respectively) and postoperative day 1 (1.4 +/- 1.2 vs 2.9 +/- 1.4 respectively) (P &lt; 0.001 for each variable)</p> <p>analgesia use significantly lower in VH group 1 ( )</p> <p><b>length of inpatient stay</b> significantly shorter in Group 1 (2.6 +/- 1.3 days) compared to Group 2 (4.12 +/- 1.7 days), p &lt; 0.001.</p> <p><b>surgical complications</b> No significant difference between the two groups as regards the rate of occurrence of surgical complications.</p>	<p>with a power of 85.02%</p> <p><b>RCT should have compared VH with and without GNRH</b></p>	
<b>RCT zu selektivem Progesteronrezeptormodulator Ulipristal</b>					
<p>Donnez et al, 2014(28)</p> <p>NEJM</p> <p>PEARL III and PEARL III</p> <p>Extension</p> <p>Open labelled prospective trial +</p>	<p><b>Design:</b> Repeated intermittent open-label UPA courses, each followed by randomized double-blind norethisterone acetate (NETA) or placebo.</p> <p><b>Setting:</b> European clinical gynecology centers.</p> <p><b>Patient(s):</b> Two hundred</p>	<p>Objective: To investigate the efficacy and safety of ulipristal acetate (UPA) for long-term treatment of symptomatic uterine fibroids.</p> <p>Main Outcome Measure(s): Amenorrhea,</p>	<p><b>Amenorrhea after the first UPA course</b>, 79% of women, median onset of 4 days (interquartile range, 2–6 days). Rates were 89%, 88%, and 90% for the 131, 119, and 107 women who received treatment courses 2, 3, and 4, Median times to amenorrhea were 2, 3, and 3 days for treatment courses 2, 3, and 4,</p> <p><b>Median fibroid volume change</b> 45% (interquartile range, 66%; 25%). Median fibroid volume changes from baseline were 63%, 67%, and 72% after treatment courses 2, 3, and 4.</p> <p><b>endometrial biopsies</b> showed all benign histology</p>	<p><b>Internal validity:</b> Randomisation method not reported for NETA Sample Size Calculation not transparent ("We planned to enroll 200 women, with approximately 80% of participants expected to fulfill the efficacy endpoint of amenorrhea at the end of the first UPA treatment</p>	<p>3, 1b für NETA</p>



Quelle/ Studientyp	Design/Population (Teilnehmer) (verglichene) Interventionen/ ggf. Dosierung/ggf. Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodische Bemerkungen	Evidenz- niveau
extension	and nine women with symptomatic fibroids including heavy menstrual bleeding. <b>Intervention(s):</b> Patients received up to four 3-month courses of UPA 10 mg daily, immediately followed by 10-day double-blind treatment with NETA (10 mg daily) or placebo.	fibroid volume, endometrial histology.	without hyperplasia; <b>NETA did not affect fibroid volume or endometrial histology</b> <b>UPA and NETA :</b> sign. Less bleeding than Placebo (PBAC 14 vs 25), bleeding significant earlier <b>Menstrual bleeding (PBAC days 1–8)</b> progressively reduced from medians of 228 and 257 at the start of the first course to 55 and 13 after the end of the fourth course for women randomized to placebo or NETA, respectively (P0,02). 10-day progestin courses reduced the magnitude of menstrual bleeding during the off-treatment periods and also brought forward menstruation return (e.g., median of 15 days instead of 30 days for women receiving placebo after the end of the fourth UPA treatment course; P<.001). <b>Treatment emergent adverse events:</b> First Course: 120 women (57.4%); 8 (3,8%) severe. one TEAE (headache) led to treatment withdrawal. TEAEs occurring in >5% of women were headache (16.3%), nasopharyngitis (6.7%), and abdominal pain (5.3%). In women receiving multiple treatment courses, headaches, nasopharyngitis, abdominal pain, and hot flashes were the most frequent TEAEs, but the incidence did not increase over time and only five women discontinued UPA because of TEAEs. Alltogether: Hot flashes 9,1%, Headache 19,7%	course and allowing for a dropout rate of 10% during the first course of treatment. The planned sample size would provide an estimate of this percentage, with the corresponding 95% confidence interval (CI) being less than  6%. We considered 90 evaluable participants per treatment group to be sufficient to enable a reliable exploration of any differences between NETA and placebo treatment") Unclear what AE without NETA? <b>External validity:</b> 10 mg not licensed	



Tabelle 7: Ausgeschlossene Studien zur medikamentösen Behandlung des Uterus myomatosus

Autor, Jahr, Publikationstyp	Thema	Grund für Ausschluss
<b>Ausgeschlossene Studien zu Ulipristalacetat</b>		
Levens ED et al, 2008, Obstet Gynecol., RCT(107)	CDB-2914 for uterine leiomyomata treatment 10 mg (T1) or 20 mg (T2) daily or placebo	Only 22 patients involved, 18 completed
Nieman et al, 2011, Fertil Steril, RCT (108)	Premenopausal women with symptomatic uterine fibroids. Once-daily oral CDB (10 or 20 mg) or placebo (PLC) for 12 weeks (treatment 1). A second 3-month treatment with CDB (treatment 2) was offered.	Wrong dose - 10 mg not licensed
Pohl et al, 2013, J Clin Pharm Ther, RCT(109)	double-blind, placebo-controlled study randomized 32 healthy women of reproductive age to receive 10 consecutive daily doses of placebo, 10, 20 or 50 mg UPA. Safety assessments included vital signs, physical examination, ECG, clinical laboratory tests and reporting of adverse events. Blood samples for pharmacokinetic analysis were collected on Days 1 and 10 at intervals until 168 h after multiple dosing	Phase II Studie, Sicherheit von Ulipristal in verschiedenen Dosierungen, keine Therapie von Myomen
Williams et al, 2012, Int J Gynecol Pathol.(110), case series out of RCT	Endometrial morphology after treatment of uterine fibroids with the selective progesterone receptor modulator	No RCT, description of endometrial changes found in RCTs
Bouchard P, 2011, Fertil Steril(111), systematic Review	Selective progesterone receptor modulators in reproductive medicine: pharmacology, clinical efficacy and safety	Not up to date
Passaro MD, 2003, Hum Reprod(112), clinical trial (phase	We evaluated the biological activity, blood levels and safety of CDB-2914 at escalating single doses, in 36 normally cycling	not fibroid treatment, no RCT phase III,



II ?)	women at mid-luteal phase.	
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#### 5.4. Evidenztabelle zu Hysterektomie versus Endometriumablation bei dysfunktionellen Blutungsstörungen

Tabelle 8: Eingeschlossene Systematische Reviews/Metaanalysen zu Hysterektomie versus Endometriumablation bei Blutungsstörungen

Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
<b>Endometriumresektion/-ablation versus Hysterektomie</b>						
Systematic Review/ Cochrane Collaboration <b>Fergusson RJ et al, 2013(43)</b> “Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding”	Study types included: RCTs <b>Search period/databases:</b> Original search performed in 1999. Updated searches performed in 2008 and October 2013 in: The trial register of the Menstrual Disorders and Subfertility Group, MEDLINE (from 1966 : EMBASE (from 1980); PsycINFO (from 1972; the Cochrane Central	Intervention(s)/ control Endometrial resection and ablation (including first generation techniques, such as transcervical resection of the endometrium with loop electrode or rollerball, and second-generation techniques, such as endometrial ablation by thermal balloon, microwave, thermal free-fluid, radiofrequency and cryotherapy). Hysterectomy (by abdominal, vaginal and laparoscopic/laparoscopically assisted routes). Primary Outcome: Effectiveness (improvement in bleeding) - Woman's perception	<b>Selection of Studies</b> In addition to the seven studies included in the original version of the review, 62 studies were screened. Only two papers seemed to meet the inclusion criteria. One paper was a republication, so only one reference was added for the 2013 update. <b>Eight RCTs of endometrial resection/ablation versus hysterectomy with a total of 1,260 randomly assigned participants met the criteria for inclusion in the review.</b> <b>Main results</b> <b>1.1 Woman's perception of improvement in</b>	Methods: When possible, outcomes were pooled statistically. Measures of treatment effect For dichotomous data: numbers of events in the control and intervention groups of each study are used to calculate risk ratios (RRs). For continuous data if all studies report exactly the same outcomes, we will calculate mean differences	1. Crosignani et al 1997(48). <b>2. STOP-DUB: Surgical treatments outcomes project for dysfunctional uterine bleeding:</b> Dickersin K et al. 2003.(113) <b>Dickersin K et al. 2007(114).</b> Munro et al. 2011(115) 3. Dwyer et al, 1993 <b>a. Dwyer et al, 1993 (46)</b> b. Sculpher	1a

Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
	Register of Controlled Trials (CENTRAL; Inclusion criteria/ search algorithm: Women of reproductive years with heavy menstrual bleeding (including both heavy regular periods (menorrhagia) and heavy irregular periods (metrorrhagia)), measured objectively or subjectively. Search algorithms given – sensitive search Exclusion criteria	(proportion with improvement in bleeding symptoms). 1.2 PBAC (Pictorial Blood Loss Assessment Chart) score: 1.3 Requirement for further surgery. Acceptability 1.4 Proportion satisfied with treatment. Safety (adverse outcomes) 1.5 Adverse events: short term (intraoperative and immediately postoperative). 1.6 Adverse events: long term (after hospital discharge). Secondary Outcome: 1.7 Quality of life scores (continuous data). 1.8 Quality of life (proportion with improvement). 1.9 Duration of surgery. 1.10 Duration of hospital stay.	<b>bleeding</b> women with endometrial ablation were slightly less likely to show improvement in bleeding symptoms when compared with those assigned to hysterectomy at one year (RR 0.89, 95% confidence interval (CI) 0.85 to 0.93, four studies, 650 women, I <sup>2</sup> = 31%). Differences were also noted at later stages of follow-up, but these findings were only just within the range of statistical significance: at two years (RR 0.92, 95% CI 0.86 to 0.99, two studies, 292 women, I <sup>2</sup> = 53%) and at four years (RR 0.93, 95% CI 0.88 to 0.99, two studies, 237 women, I <sup>2</sup> = 79%); <b>1.2 Pictorial Blood Loss Assessment Chart (PBAC) score</b> Compared with pretreatment scores, the PBAC score was significantly reduced in	(MDs) between treatment groups. <b>Data were analysed on an intention-to-treat basis as far as possible;</b> otherwise only available data were analysed. When data were found to be missing, attempts were made to obtain this information from the original trial authors <b>Heterogeneity:</b> When statistical heterogeneity was found to be very substantial (> 90%), calculation of a summary effect measure was not considered appropriate, study data were not pooled.	M. et al, 1998(116) c. Sculpher MJ et al. 1993(117) d. Sculpher MJ, et al. 1996.(118) <b>4.Gannon et al, 1991 (119)</b> 5. O'Connor et al, 1997(50) “Medical Research Council randomised trial of endometrial resection versus hysterectomy in management of menorrhagia” 6. Pinion et al, 1994 a.Aberdeen	





Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
	<p>Postmenopausal bleeding (&gt; 1 year from the last period).</p> <p>HMB caused by uterine malignancy or endometrial hyperplasia.</p> <p>Iatrogenic causes of HMB (e.g. intrauterine coil devices).</p>	<p>1.11 Time to return to normal activity.</p> <p>1.12 Time to return to work.</p> <p>1.13 Total health service cost per woman.</p> <p>1.14 Total individual cost per woman.</p>	<p>both groups at one and two years postoperatively; This finding overall significantly favoured women randomly assigned to hysterectomy at one year (MD 24.40, 95% CI 16.01 to 32.79, one study, 68 women), and even more so at two years (MD 44.00, 95% CI 36.09 to 51.91, one study, 68 women)</p> <p><b>1.3 Requirement for further surgery</b></p> <p>Risk of repeat surgery was significantly more likely for TCRE/ablation than for hysterectomy at all follow-up periods</p> <ul style="list-style-type: none"> <li>- within the first year (RR 14.9, 95% CI 5.2 to 42.6, six studies, 887 women, I<sup>2</sup> = 0%),</li> <li>- at two years (RR 23.4, 95% CI 8.3 to 65.8, six studies, 930 women, I<sup>2</sup> = 0%),</li> <li>- at three years (RR 11.1, 95% CI 1.5 to 80.1, one study, 172 women) and</li> <li>- at four years (RR 36.4,</li> </ul>	<p>Risk of bias in included studies: overall moderate</p> <p>Allocation concealment: 5/8 studies provided sufficient detail on adequacy of randomisation method, 6/8 studies provided sufficient details of allocation concealment;</p> <p>Blinding</p> <p>3 more recent studies used single blinding for assessment of some outcomes, 5 studies did not appear to have any blinding of participants, investigators or assessors. All studies were therefore at high risk of bias in</p>	<p>Endometrial Ablation Trials Group(47).</p> <p>b. Alexander DA, et al. 1996(120).</p> <p>c.Cameron IM, et al. 1996.(121)</p> <p><b>d. Pinion SB et al. 1994.(122)</b></p> <p>7. Sesti et al, 2011(123)</p> <p>8. Zupi et al, 2003(49)</p>	





Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>95% CI 5.1 to 259.2, one study, 197 women;</p> <p><b>Proportion with HE:</b> Example: O'Connor 12/25 with further surgery</p> <p><b>1.4 Proportion satisfied with treatment</b></p> <p>Satisfaction (very or moderately satisfied) rates were comparable (five trials) although lower amongst those who had endometrial ablation at two years after surgery (RR 0.87, 95%CI 0.80 to 0.95, four studies, 567 women, I<sup>2</sup> = 0%).</p> <p>No significant differences were noted between post-treatment satisfaction rates in groups at other follow-up times (one and four years), although the trend favoured hysterectomy</p> <p><b>1.5 Adverse events short term (intraoperative and immediately postoperative)</b></p> <p>Most short-term complications were more</p>	<p>this category.</p> <p><b>Intention to treat, drop out:</b> 2/8 studies withdrawal from the study and/or missing data were greater than 10%, 1 trial, primary outcomes were analysed by an intention-to-treat method (satisfaction rate, quality of life and bleeding outcomes), but intraoperative and perioperative outcomes (adverse events, requirement for further surgery and hospital stay) were analysed according to surgery received. This</p>		



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>frequent after hysterectomy than after endometrial resection and ablation techniques. Women who had a hysterectomy were more likely to experience before their hospital discharge:</p> <p><b>Sepsis</b> (RR 0.2, 95% CI 0.1 to 0.3, four studies, 621 women, I<sup>2</sup> = 62%),</p> <p><b>blood transfusion</b> (RR 0.2, 95% CI 0.1 to 0.6, four studies, 751 women, I<sup>2</sup> = 0%),</p> <p><b>pyrexia</b> (RR 0.2, 95% CI 0.1 to 0.4, three studies, 605 women, I<sup>2</sup> = 66%),</p> <p><b>vault haematoma</b> (RR 0.1, 95% CI 0.04 to 0.3, five studies, 858 women, I<sup>2</sup> = 0%) and</p> <p><b>wound haematoma</b> (RR 0.03, 95%CI 0.00 to 0.5, one study, 202 women)</p> <p><b>women who underwent TCRE/ablation were more likely to have fluid overload</b> (RR 9.3, 95% CI 2.2 to 39.6, three studies, 611 women, I<sup>2</sup> = 0%)</p>	<p>trial also reported outcomes at three and four years' follow-up, but as women who were assigned later during the trial had shorter follow-up, these assessments are likely to be underpowered.</p> <p>Selective reporting</p> <p>7/8 insufficient information – risk of selective outcome reporting could not be excluded</p>		



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>No differences between groups were reported for haemorrhage, anaesthesia, perforation, gastrointestinal obstruction, laparotomy, cystotomy, cervical laceration, cardiorespiratory event, thromboembolic event or return to surgery as causes of postoperative complications,</p> <p><b>1.6 Adverse events: long term</b> (after hospital discharge)</p> <p>After hospital discharge, sepsis was more likely following hysterectomy in one study (RR 0.2, 95% CI 0.1 to 0.5, one study, 172 women), but no other significant differences were reported</p> <p><b>1.7 Quality of life scores (continuous data)</b></p> <p>Significant differences were detected in five domains of the SF-36 Scale measured one and two years after surgery. Women randomly</p>			



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>assigned to hysterectomy reported significantly higher scores on</p> <ul style="list-style-type: none"> <li>- the social functioning (one and two years), pain (two years), energy (one year) and general health perception (one and two years) domains (social functioning: one year: MD -21.2, 95% CI -24.7 to -17.7, one study, 181 women; two years: MD -10.1, 95% CI -13.55 to -6.58, three studies, 300 women, I<sup>2</sup> = 25%) (pain: two years: MD -9.5, 95% CI -12.8 to -6.2, four studies, 513 women, I<sup>2</sup> = 63%) (energy: one year: MD -11.0, 95% CI -14.5 to -7.5, two studies, 211 women, I<sup>2</sup> = 0%) (general health perception: one year: MD -7.3, 95%CI -10.7 to -3.8, two studies, 385 women, I<sup>2</sup> = 81%; two years:MD -7.4, 95% CI -12.8 to -6.21, four studies, 509 women, I<sup>2</sup> = 41%).</li> </ul> <p>Women randomly assigned to TCRE/ablation</p>			



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>reported significantly higher scores for emotional role limitation at two years (MD 10.2, 95% CI 5.5 to 15.0, three studies, 300 women, I<sup>2</sup> = 92%).</p> <p>No statistically significant differences in SF-36 scores were noted between the two interventions in the domains of physical role limitation, mental health and physical functioning</p> <p><b>1.8 Quality of life (proportion with improvement)</b></p> <p>Differences between groups were not reported in quality of life dimensions as measured by any of the other scales: Golombok Inventory, Euroqol Scale, Sabbatsberg Scale or HAD Scale. The dichotomous outcome of proportion with improvement in pain at two years was not significantly different</p>			



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>between surgical groups. However, a greater proportion of those who had undergone a hysterectomy reported an improvement in their general health one year after surgery when compared with those who had received TCRE/ablation (RR 4.2, 95% CI 1.5 to 11.9, one study, 185 women). At four years, this difference between groups had narrowed and was outside the level of significance</p> <p>1.9 Duration of surgery.</p> <p>1.10 Duration of hospital stay.</p> <p>1.11 Time to return to normal activity.</p> <p>1.12 Time to return to work.</p> <p><b>1.9-1.12: Statistically all in favour of TE with substantial heterogeneity</b></p>			



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
Systematic Review/ Meta-Analysis/ Cochrane Collaboration Lethaby A. et al, 2013 « Endometrial resection and ablation techniques for heavy menstrual bleeding »	<b>Included Studies:</b> RCT <b>Search in:</b> Cochrane Menstrual Disorders and Subfertility Group Specialised Register of controlled trials, Cochrane Central Register of Controlled Trials CENTRAL), MEDLINE, EMBASE, CINAHL, and PsycInfo, (from inception to June 2013). We also searched trials registers, other sources of unpublished or grey literature and reference lists of retrieved studies, and made contact with experts in the field and pharmaceutical	<b>women</b> with a complaint of heavy menstrual bleeding (HMB) without uterine pathology <b>Intervention:</b> comparing different endometrial ablation techniques (first and second generation) <b>Outcomes</b> included - reduction of HMB, - improvement in quality of life, - operative outcomes, - satisfaction with the outcome, - complications and - <b>need for further surgery or hysterectomy</b>	<b>Study selection</b> 21 Studies already included 2009, 14 new studies in update search 6/2013 all assessed as full texts, 4 studies included =  25 trials (4040 women) with sample sizes ranging from 20 to 372 were included in the review.  <b>Results:</b> <b>There was insufficient evidence to suggest superiority of a particular technique in the pairwise comparisons between individual ablation and resection methods.</b>  <b>Outcome : Requirement for further surgery (hysterectomy)</b> 15 trials compared hysterectomy rates after treatment « There was no evidence of significant differences for the other secondary outcomes	<b>Risk of bias:</b> A majority of the trials had a specified method of randomisation, adequate description of dropouts and no evidence of selective reporting. Less than half had adequate allocation concealment and most were unblinded.  <b>Study quality per outcome :</b> from very low (amenorrhoea rate at 1 year follow up) to high (Success of treatment- (PBAC<75 or acceptable improvement) at 12 months follow up Moderate quality	To be added	1b



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
	companies that manufacture ablation devices		<p>compared, that is inability to work, other complication rates and requirement for any additional surgery or hysterectomy. »</p> <p>Analysis 7.9 : Comparison of Electrode ablation (second generation) versus TCRE + rollerball (first generation), 1 Balloon system Corson 2000</p> <p>Electrode (second generation): 5xHysterectomy /132 3,7%</p> <p>TRCE+rollerball : 9xHysterectomy/123 7,3%</p> <p>RR : 0.52 [0.18, 1.50 ] not significant, wide confidence intervalls – imprecision</p> <p>The risk of requiring either further surgery of any kind or hysterectomy specifically was reduced with second-generation ablative methods compared to first-generation ablation up to 10 years after surgery (RR 0.69, 95% CI 0.48 to 0.99, 1 RCT; and RR 0.60, 95% CI 0.38 to 0.96, 1 RCT; both moderate quality evidence, respectively) but</p>	of evidence for outcome further requirement of surgery		





Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			not at earlier follow up. Additional research is required to confirm this finding.			
SR Matteson K. et al, 2012(45) « A Systematic Review comparing Hysterectomy to less invasive treatment for abnormal uterine bleeding »	<b>Studies included :</b> RCT <b>Search in :</b> Medline, inception to 1/2011, English,	Hysterectomy versus less invasive treatment (Endometrial ablation, LNG- IUS, medical therapies as treatments of AUB secondary to presumed ovulatory disorders (AUB-O) or endometrial hemostatic dysfunction (AUB-E), and reported an outcome of interest. 7 ranked critical/important: -bleeding, quality of life, pain, sexual health, patient satisfaction, need for subsequent surgical treatment, adverse events (major /minor – defined)	5503 citations, 117 eligible abstracts, 81 full texts, 18 articles from 9 RCT included. <b><u>Results Hysterectomy versus Endometrial Ablation</u></b> 7 trials HE vs EA (6x rated B, 1x rated A (Zupi)) - <b>Bleeding control:</b> better after HE - <b>Quality of life (6 studies):</b> Moderate quality of evidence Significant improvement above baseline for both, HE and ablation. Several studies found no difference between HE and EA (Dwyer, Sculpher, Alexander, Zupi, Dickersin) on various validated QoL assessment tools. 3 studies found statistical significant differences in various <b>SF-36</b> dimensions favouring HE: pain (Sculpher), general health	Methodological quality of each study: assessed using criteria from a 3 category system modified from the AHRQ. Studies were graded as good (A), fair (B), or poor (C) quality based on the likelihood of biases and the completeness of reporting. - To grade the overall strength of evidence, the Grades for Recommendatio n, Assessment, Development and Evaluation (GRADE) system was used, with four	See also Fergusson et al, 2013 Gannon 1991(119) Dwyer et al, 1993(46) Pinion et al, 1994(124) Alexander et al, 1996(120) Sculpher et al, 1996(118) Crosignani et al, 1997(48) (VE) O'Connor et al 1997(50) Abderdeen et al, 1999(47) Zupi et al,2003(49) (LH) Dickersin et al, 2007(114)	la-IIa

Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>and vitality (Crosignani, Zupi), social function (Zupi). 2/3 studies compared EA with laparoscopic HE approach (Zupi, Sculpher), 1/3 with vaginal approach (Crosignani)</p> <p><b>-Pain (5 studies):</b> low quality of evidence favoured HE over EA. Dysmenorrhea and pelvic pain less prevalent.</p> <p><b>-sexual health (5 studies:</b> Dwyer 1993, Aberdeen Endometrial Ablation Trials Group 1999, Crosignani 1997, Zupi 2003, O'Connor 1997 ): low quality of evidence. No difference in overall effect on sexual health ratings and sexual satisfaction. Only 1 study with validated questionnaire (Crosignani 1997)</p> <p><b>-satisfaction (5 Studies)</b> 4/5 defined satisfaction rate as primary outcome. (1. Trial UK: Dwyer (4Mo), Sculpher (2,8y), 2. Trial UK: Pinion (12 mo, Aberdeen, 4,8y) 3. Trial: Crosignani (3 years), 4.. Trial O'Connor (2 years),</p>	<p>ratings: high, moderate, low, and very low</p> <p><b>-Quality of life:</b> studies not powered to detect differences</p> <p><b>- sexual health:</b> only 1 study used validated questionnaire</p>		



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>5.Trial: Dickersin (2 years) Outcome measures varied among studies. The majority of women in both treatment arms reported being satisfied with their treatment option (50–95% for ablation, 52–96% for hysterectomy) at 1–4 years follow-up. 3 trials found no differences in satisfaction between the hysterectomy and ablation group. (Crosignani, Dickersin, O'Connor). 2 trials found significantly greater satisfaction after hysterectomy than ablation: 1 trial reported more women "very satisfied" 1 year after hysterectomy (88% vs. 78%, <math>p&lt;0.05</math>), but no significant difference at 4.8 years, possibly due to reduced statistical power due to dropouts (Pinion, Aberdeen). Another study found that at 4 months, 95% of the hysterectomy group was "quite satisfied" or "very satisfied" compared to 79% of ablation group (<math>p=0.002</math>). (Dwyer). Overall, the quality of evidence was very low for</p>			



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>satisfaction outcomes which were not different between hysterectomy and ablation.</p> <p><b>Additional Treatment (all studies) moderate quality</b></p> <p>At 1–4 years follow-up, 16–42% of participants assigned to ablation had undergone an additional surgical treatment for bleeding with 10–29% treated with hysterectomy.</p> <p>Sculpher (33Mo): 18/88 (20%), Aberdeen (48Mo): 24/102 (20%)</p> <p>Corsignani (24Mo)(4/41)10%, Dickersin (48)32/110 (29%), O'Connor (24) 12/199 (10%)</p> <p>Additional ablation: 2-19%</p> <p>Overall, the quality of evidence regarding additional treatments was moderate and favored hysterectomy over ablation.</p>			
HTA-Report S Bhattacharya et al. : Hysterectomy, endometrial	Study types included RCTs Search period/ databases	Intervention(s)/ control Hysterectomy, First-generation (hysteroscopic) EA Second- generation (non	<b>Selection of Studies:</b> 556 potentially relevant citations were identified by electronic searches. After detailed evaluation (see inclusion criteria), 30 trials	Methods: To minimise the possibility of bias individual		<b>1b</b> downgraded due to the methodological weakness



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
ablation and Mirena® for heavy menstrual bleeding: a systematic review of clinical effectiveness and costeffectiveness analysis. Health Technology Assessment 2011; Vol. 15: No. 19 (125)  This HTA – report comprises three parts: A metaanalysis derived from RCTs A retrospective registry evaluation (Scottish Morbidity Returns (SMR) analysing a cohort of	The Cochrane Library, MEDLINE (1966–2010), EMBASE (1980 to May 2010) and CINAHL databases (1982 to May 2010)  We also hand-searched the bibliographies of all relevant primary Articles  Experts were contacted to identify further studies.  The Meta-Register of Controlled Trials, the International Standard Randomised Control Trial Number register  <b>Inclusion criteria/</b>	hysteroscopic) EA LNG-IUS  Outcome: -Level of satisfaction. Dissatisfaction rates are presented to simplify interpretation of statistical output.  -For a small number of studies surrogate outcomes for satisfaction were used.  -bleeding scores (ranging from a minimum of zero to no upper limit), -amenorrhoea rate -heavy bleeding rate -EQ-5D utility score, -SF-36 scores -duration of surgery/hospital stay, -general anaesthesia rates, postoperative pain score ( time to return to work/normal activities/sexual activity, dysmenorrhoea/dyspareunia rate	were eligible for inclusion in the review comprising 4305 women  Of these trials, seven compared hysterectomy with ED techniques comprising 1127 women.  <b>Satisfaction/dissatisfaction</b>  Hysterectomy vs first-generation EA: More women were dissatisfied at 12 months following first-generation EA than hysterectomy [12.6% vs 5.3%; (57/454 vs 23/432); OR 2.46; 95% CI 1.54 to 3.93; p = 0.0002]  First- versus second-generation EA techniques: unsatisfactory outcomes were comparable with first- and second-generation EA techniques [12.2% (123/1006) vs 10.6% (110/1034); OR 1.20, 95% CI 0.88 to 1.62; p = 0.2],  Hysterectomy vs second-generation EA (indirect	patient data (IPD) and aggregate data (AD) were combined in a two-stage approach. IPD were reduced to AD to allow studies with AD only to be combined with those where IPD were obtained.  Point estimates and 95% confidence intervals (CIs) were calculated for individual studies at each time point.  For the primary outcome measure, differences in		of some trials included.



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
48,419 women having either hysterectomy or EA -a cost-effectiveness analysis Only the first part, the metaanalysis was considered in this evidence report.	<b>search algorithm:</b> databases were searched using relevant terms and word variants for population [e.g. menorrhagia, hypermenorrhea, (excessive) menstrual blood loss, HMB, dysfunctional uterine bleeding] and interventions (e.g. hysterectomy, vaginal hysterectomy, total abdominal hysterectomy, subtotal abdominal hysterectomy, laparoscopic hysterectomy, LNG IUS, Mirena coil and all types and	proportion undergoing subsequent ablation/hysterectomy discontinuing use of Mirena. Pre-defined subgroups age at randomisation ( $\leq 40$ vs $> 40$ years), parity (nulliparous vs parous), uterine cavity length ( $\leq 8$ vs $> 8$ cm), p presence or absence of fibroids/polyps and, where available, severity of bleeding at baseline	comparison): Indirect estimates (Figure 6) suggest that hysterectomy is also preferable to second-generation EA [5.3% vs 10.6% (23/432 vs 110/1034); OR 2.32; 95% CI 1.27 to 4.24; $p = 0.006$ ] in terms of patient dissatisfaction. Predictors of dissatisfaction: For second-generation EA, IPD showed that uterine cavity length was the strongest predictor of dissatisfaction ( $p = 0.02$ ), with shorter uterine cavity length ( $\leq 8$ cm vs $> 8$ cm) associated with reduced rates (OR 0.59; 95% CI 0.38 to 0.93; $p = 0.02$ ) <b>Other outcomes</b> Hysterectomy versus EA EA offered quicker surgery (WMD 32 minutes; 95% CI 30 to 34 minutes; $p < 0.0001$ ), shorter hospital stay (WMD 3.0 days; 95% CI	effect estimates between trials and the pre-defined subgroups of patients are displayed using odds ratio (OR) plots; Heterogeneity was investigated using Cochran's Q, $I^2$ statistics and Higgins et al.8 Only a limited amount of data were available for studies comparing Mirena with ED, so Mirena was compared with first- and second-generation studies		



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
	variants of first- and second- generation ablative techniques). exclusion criteria Not mentioned		<p>2.9 to 3.1 days; <math>p &lt; 0.00001</math>), faster recovery periods (time to return to normal activities: WMD 5.2 days; 95% CI 4.7 to 5.7 days; <math>p &lt; 0.00001</math>) and less pain postoperatively (WMD 2.5 points; 95% CI 2.2 to 2.9 points; <math>p &lt; 0.0001</math>), although estimates of differences for some of these parameters should be used with caution given the high variability between studies</p> <p>One study suggested no obvious difference in EQ- 5D utility scores, while another suggested differences in favour of hysterectomy in the general health (WMD 9.6 points; 95% CI 5.7 to 13.5 points; <math>p &lt; 0.0001</math>), social function (WMD 24 points; 95% CI 21 to 27 points; <math>p &lt; 0.0001</math>) and vitality (WMD 13 points; 95% CI 9.3 to 16 points; <math>p &lt; 0.0001</math>) domains of the</p>	<p>combined as well as separately. Assumption- free 'fixed- effect' methods were used to combine dichotomous outcome measures and estimate pooled ORs using the method of Peto et al., and, for continuous variables, weighted mean differences (WMD) were calculated at each time point. Data at less than 12 months were combined and are described</p>		



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>SF-36 questionnaire.</p> <p>First- versus second-generation EA techniques</p> <p>The proportion of women with amenorrhoea or still experiencing heavy bleeding was similar in both groups at all time points apart from at 2 years, where there was a borderline significant difference in favour of second-generation techniques (amenorrhoea: OR 0.64, 95% CI 0.41 to 0.99, <math>p = 0.04</math>; HMB: OR 1.85, 95% CI 1.04 to 3.32, <math>p = 0.04</math>)</p> <p>Two studies using the SF-36 questionnaire and one small study<sup>94</sup> using the EQ-5D questionnaire showed no consistent difference between first- and second-generation techniques, in terms of change from baseline results.</p> <p>Second-generation EA was quicker (WMD 15 minutes; 95% CI 14 to 15 minutes; <math>p &lt; 0.0001</math>) and</p>	<p>as results at 6 months.</p> <p>Limitations:</p> <p>A lot of comparisons show a high or borderline heterogeneity of the trials included, so many of the results are doubtful.</p> <p>The methodological quality of the trials differs between the different comparisons analysed (see Fig. 2)</p> <p>It is very difficult to follow the process of data extraction from trials and especially the reduced number of analysed</p>		





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			<p>less likely to need general anaesthesia than first generation (OR 0.16; 95% CI 0.12 to 0.20; <math>p &lt; 0.0001</math>),</p> <p>Less frequent use of general anaesthesia with second-generation EA translated to a slightly quicker time to return to work (WMD 1.36 days; 95% CI 0.69 to 2.03 days; <math>p &lt; 0.0001</math>) and time to return to normal activities (WMD 0.48 days; 95% CI 0.20 to 0.75 days; <math>p = 0.0008</math>),</p> <p>Postoperative pain was similar following either method of EA,</p> <p>but perioperative complications such as uterine perforation (OR 0.20; 95% CI 0.07 to 0.57; <math>p = 0.003</math>), excessive bleeding (OR 0.14; 95% CI 0.07 to 0.55; <math>p = 0.005</math>), fluid overload (OR 0.12; 95% CI 0.04 to 0.36; <math>p = 0.0001</math>) and cervical laceration (OR 0.12; 95% CI 0.05 to 0.33; <math>p &lt;</math></p>	<p>women when compared to the number of women included in the selected trials is sometimes unclear.</p> <p>Moreover, at least for Fig. 3, there is a discrepancy between the number of analysed women and the number mentioned in the corresponding text.</p>		



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>0.0001) were lower with second-generation EA.</p> <p>The number of women requiring a subsequent hysterectomy was lower for second-generation EA, but these differences were not large enough to be statistically significant within the first 2 years (12 months: OR 0.77, 95% CI 0.47 to 1.24, <math>p = 0.3</math>; 2 years OR 0.68, 95% CI 0.41 to 1.13, <math>p = 0.1</math>).</p> <p>.</p>			



## 5.5. Evidenztabellen zu Hysterektomie versus lokale (intrauterine) Hormontherapie bei dysfunktionellen Blutungsstörungen

Tabelle 9: Eingeschlossene Systematische Reviews/Metaanalysen zu Hysterektomie versus lokaler (intrauteriner) Hormontherapie bei dysfunktionellen Blutungsstörungen

Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
<b>Hysterectomy versus Levenorgestrel - Intrauterine-System (LNG-IUS)</b>						
SR Matteson et al, 2012	<b>Studies included :</b> RCT <b>Search in :</b> Medline, inception to 1/2011, English,	Hysterectomy versus less invasive treatment (Endometrial ablation, <b>LNG- IUS</b> , medical therapies as treatments of AUB secondary to presumed ovulatory disorders (AUB-O) or endometrial hemostatic dysfunction (AUB- E), and reported an outcome of interest. 7 ranked critical/ important: -bleeding, quality of life, pain, sexual health,	<b>Selection of Studies: HE-LNG-IUS</b> 1 "A" quality RCT (with six publications) compared hysterectomy to LNG-IUS was identified (from Finland); 598 women referred with menorrhagia to five university hospitals in Finland and screened (1994-97), 184 not eligible, 178 not willing (Preference for hysterectomy =71, preference for medical treatment =37), preference for endometrial ablation (3), refusal of any treatment (28), still planning pregnancy (11), other (28). n=236 women with heavy menstrual bleeding (blood loss 129ml) were followed for 6 months to 10 years after treatment. Mean age 43y, BMI 25- 26kg/qm <sup>2</sup> , Women with diagnosed submucous fibroids and women with "irregular bleeding" as a main complaint were excluded; 49% of participants had uterine fibroids. Groups: LNG-IUS=119, HE=117	- <b>Overall quality of the evidence</b> for these studies was moderate for each outcome domain. - <b>primary outcome measure was health-related quality of life at 12-month follow-up.</b> Analyses were by intention to treat <b>Study size:</b> Calculation of a target of 115 patients in each treatment group.	Hurskainen R, et al, Lancet 2001(126) Hurskainen R et al, Acta Obstet Gynecol Scand. et al, 2004(127) Hurskainen R, et al, JAMA. 2004;(128) Halmesmäki K, et al, BJOG. 2007;(129) Heliövaara- Peippo S, et al, Acta Obstet	lb



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		patient satisfaction, need for subsequent surgical treatment, adverse events (major /minor – defined)	<p>In the hysterectomy group 107 underwent surgery 20% (n=21) had a TAH, 28% (n=30) had a TVH, and 52% (n=56) had a laparoscopic approach..</p> <p><b>Results according to endpoints</b></p> <p><b>1. Bleeding at 12 month/5 years</b> (measured by the alkaline haematin method). Proportion of participants who reported amenorrhea or oligomenorrhea with the LNG-IUS still “in-situ” was 51% (41/81) at 12 months and 75% (43/57) at 5 years. Women who discontinued use of the LNG-IUS (n=50, 42%) did so because of intermenstrual bleeding (70%) and heavy bleeding (30%). Overall, the evidence favored hysterectomy over LNG-IUS for bleeding control.</p> <p><b>2. Quality of life measures</b>—Both the EuroQOL-5D and the SF-36 were used to measure quality of life.(27–29) Overall, the evidence revealed no differences in quality of life outcomes between hysterectomy and LNG-IUS.</p> <p><b>Pain (critical importance)</b>—At 6 and 12 month follow-up, a greater proportion of participants in the LNG-IUS group reported lower abdominal pain. At 12 months, this difference was statistically significant (30% LNG-IUS vs. 14% hysterectomy, p=0.02). No difference was found at 5 years. Overall, the</p>	<p>On the basis of an EQ-5D score SD of 19% (derived from a Finnish 34–49-year-old female population) and p=0.05, the study had 80% power to detect a 7.5% difference between the groups</p> <p>-</p>	<p>Gynecol Scand. 2009; (130) Heliövaara-Peippo S, et al, BJOG, 2010(131)</p>	



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>evidence on pain revealed no differences between hysterectomy and LNG-IUS.</p> <p>Back Pain at 5 years: ca. 30% in both groups</p> <p><b>Sexual health (high importance)—</b> Sexual function was compared between LNG-IUS and hysterectomy at 6 months, 1 year, and 5 years using McCoy sex scale scores. Compared to hysterectomy, the LNG-IUS group reported more sexual problems at 6 months (<math>p=0.03</math>), however, this effect was not seen at 12 months or 5 years. No differences were found in sexual problems at other time points or in sexual satisfaction scores at any time point. Overall, evidence for sexual health revealed no differences between hysterectomy and LNG-IUS.</p> <p><b>Satisfaction (high importance)—</b> Satisfaction rates at 5 years were very high for both the LNG-IUS group (93%) and the hysterectomy group (94%).(Hurskainen JAMA 2004) Overall, the evidence regarding satisfaction showed no difference in satisfaction between LNG-IUS and hysterectomy.</p> <p><b>Additional treatment (Moderate importance)—</b>Among women randomized to LNG-IUS, 20% had undergone hysterectomy by 12-months,</p>			



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<p>42% by 5 years, and 46% by 10 years. Overall, the evidence on additional treatments favored hysterectomy over LNG-IUS.</p> <p><b>Adverse events:</b>                      LNG-IUS: 1 major complication (a recurrent thromboembolic event) occurred (1%) and no minor complications(0%).                      Hysterectomy: 12 major complications (10%) and 32 minor complications (27%)                      The authors reported that 30% of participants in the hysterectomy group had "post-operative complications".                      Overall, the evidence for adverse events was moderate quality and favored LNG-IUS over hysterectomy.</p>			
<p>HTA-Report</p> <p>S Bhattacharya et al. :                      Hysterectomy, endometrial ablation and Mirena® for heavy menstrual bleeding: a systematic review of clinical effectiveness and</p>	<p>Study types included RCTs</p> <p>Search period/ databases</p> <p>The Cochrane Library, MEDLINE (1966–2010), EMBASE (1980 to May 2010) and CINAHL databases (1982 to May 2010)</p> <p>Handsearch of bibliographies of all</p>	<p>Intervention(s)/ control</p> <p>Hysterectomy, LNG-IUS</p> <p>Outcome:</p> <p>-Level of satisfaction.</p> <p>Dissatisfaction rates are presented to simplify interpretation of statistical</p>	<p><b>Selection of Studies:</b> 556 potentially relevant citations were identified by electronic searches. After detailed evaluation (see inclusion criteria), 30 trials were eligible for inclusion in the review comprising 4305 women</p> <p><b>One study compared hysterectomy with Mirena</b> (236 women), eight studies compared Mirena with EA, three of which were first generation (190 women) and five second generation (304 women)</p> <p>Main results from individual patient</p>	<p>Only a limited amount of data were available for studies comparing Mirena with ED, so Mirena was compared with first- and second-generation studies combined as well as</p>		<p><b>1b</b></p> <p>(only 1 trial HE vs Mirena).</p>



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
<p>costeffectiveness analysis. Health Technology Assessment 2011; Vol. 15: No. 19 (125)</p> <p>This HTA – report comprises three parts: A metaanalysis derived from RCTs</p> <p>A retrospective registry evaluation (Scottish Morbidity Returns (SMR) analysing a cohort of 48,419 women having either hysterectomy or EA</p> <p>-a cost-effectiveness analysis</p> <p>Only the first part, the metaanalysis was considered</p>	<p>relevant primary Articles</p> <p>Experts were contacted to identify further studies.</p> <p>The Meta-Register of Controlled Trials, the International Standard Randomised Control Trial Number register</p> <p><b>Inclusion criteria/ search algorithm:</b></p> <p>databases were searched using relevant terms and word variants for population [e.g. menorrhagia, hypermenorrhea, (excessive) menstrual blood loss, HMB, dysfunctional uterine bleeding] and interventions (e.g. hysterectomy, vaginal hysterectomy, total abdominal hysterectomy, subtotal abdominal hysterectomy,</p>	<p>output.</p> <p>-For a small number of studies surrogate outcomes for satisfaction were used.</p> <p>-bleeding scores (ranging from a minimum of zero to no upper limit),</p> <p>-amenorrhoea rate</p> <p>-heavy bleeding rate</p> <p>-EQ-5D utility score,</p> <p>-SF-36 scores</p> <p>-duration of surgery/hospital stay,</p> <p>-general anaesthesia rates,</p> <p>postoperative pain score, time to return to work/normal activities/sexual</p>	<p>data meta-analysis</p> <p><b>Satisfaction/dissatisfaction</b></p> <p><b>Hysterectomy vs Mirena</b> (indirect comparison):</p> <p>The evidence to suggest hysterectomy is preferable to Mirena was weak [5.3% vs 17.2% (23/432 vs 22/128); OR 2.22; 95% CI 0.94 to 5.29; p = 0.07], but given the lack of precision from Mirena comparisons this was not a surprising result and should be cautiously interpreted.</p> <p><b>Mirena versus endometrial ablation techniques:</b></p> <p>Rates of dissatisfaction with Mirena and second-generation EA were similar [18.1% vs 22.5% (17/94 vs 23/102); OR 0.76; 95% CI 0.38 to 1.53; p = 0.4] although the latter rate was twice as high as that seen for second-generation EA when it was compared with first-generation EA. Heterogeneity of estimates overall was of borderline statistical significance (p = 0.09; I<sup>2</sup> = 54%).</p> <p>Predictors of dissatisfaction: For second-generation EA, IPD showed that uterine cavity length was the strongest predictor of dissatisfaction (p = 0.02), with shorter uterine cavity length (≤ 8 cm vs &gt; 8 cm) associated with reduced rates</p>	<p>separately.</p> <p>Limitations:</p> <p>A lot of comparisons show a high or borderline heterogeneity of the trials included, so many of the results are doubtful.</p> <p>The methodological quality of the trials differs between the different comparisons analysed (see. Fig. 2)</p> <p>It is very difficult to follow the process of data extraction from trials and especially the reduced number of analysed women when</p>		

Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
in this evidence report.	laparoscopic hysterectomy, LNG IUS, Mirena coil and all types and variants of first- and second- generation ablative techniques).exclusion criteria Not mentioned	activity, dysmenorrhoea/ dyspareunia rate  proportion undergoing subsequent ablation/ hysterectomy, discontinuing use of Mirena. Pre-defined subgroups  age at randomisation (≤ 40 vs > 40 years), parity (nulliparous vs parous), uterine cavity length (≤ 8 vs > 8 cm), p presence or absence of fibroids/polyps and, where available, severity of bleeding at	(OR 0.59; 95% CI 0.38 to 0.93; p = 0.02)  <b>Other outcomes</b> Hysterectomy versus Mirena No differences in EQ-5D scores were seen at 6 or 12 months in the single study comparing hysterectomy with Mirena, while the only statistically significant effect observed in the SF-36 questionnaire was in the pain domain, which favoured hysterectomy (WMD 9.6 points; 95% CI 2.7 to 16.6 points; p = 0.007). Mirena vs EA techniques Fewer women experienced HMB after Mirena at 6 months (OR 0.23; 95% CI 0.09 to 0.57; p = 0.001) and at 2 years (OR 0.08; 95% CI 0.01 to 0.50; p = 0.007), although total numbers here were small compared with the estimate at 12 months, where there was no evidence of any difference (OR 0.74; 95% CI 0.34 to 1.61; p = 0.5) Changes in bleeding scores favoured EA at 12 months only (WMD 38 points; 95% CI 15 to 60 points; p = 0.0009), Other outcome measures could not separate the two treatments.	compared to the number of women included in the selected trials is sometimes unclear. For Fig. 3, there is a discrepancy between the number of analysed women and the number mentioned in the text.		





Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		baseline				

Tabelle 10: Eingeschlossene Primärstudien zu Hysterektomie versus lokaler (intrauteriner) Hormontherapie bei dysfunktionellen Blutungsstörungen

Quelle/ Studien typ	Populatio n (Teilnehm er)	Interventio n/ggf Dosierung/ Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodisch e Bemerkung en	Evidenz -niveau (CEBM Oxford)
<b>HE vs LNG-US</b>						
Follow up of RCT Heliöva ra- Peippo et al, 2013(13 2)	236 women, aged 35- 49 years, referred for menorrha gia to 5 university hospitals in Finland	-random assignment to treatment with LNG-IUS (n= 119) or hysterectomy (n = 117) Follow up 10 years	main outcome measures were healthrelated <b>QOL (HRQOL), psychosocial well-being, and cost- effectiveness</b>	A total of 221 (94%) women were followed for 10 years. 55 (46%) women assigned to the LNG-IUS subsequently underwent hysterectomy. The overall costs in the LNG-IUS group (\$3423) were substantially lower than in the hysterectomy group (\$4937). Levels of HRQOL and psychosocial well-being improved during first 5 years but diminished between 5 years and 10 years and the improved HRQOL returned close to the baseline level. There were no significant differences between LNG-IUS and hysterectomy groups.	Drop out rate acceptable (<10%)	Ib
Sesti et al, 2012(13 3)  Levonor gestrel-	The trial was performed at Tor Vergata University Hospital,	72 women requiring treatment for HMB were randomly allocated into two treatment	<b>Primary outcome :</b> effects on menstrual bleeding (pictorial blood loss	<b>1. Menstrual bleeding (pictorial blood loss assessment chart [PBAC]) at 12 months</b> PBAC score was significantly reduced in both treatment groups <b>2. Quality of life</b> The Medical Outcomes Survey Short Form 36 (SF-36) score improved in both groups. A more significant improvement in the parameters Role and Mental health	Imprecision because of low patient numbers	1b-



Quelle/ Studien typ	Populatio n (Teilnehm er)	Interventio n/ggf Dosierung/ Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodisch e Bemerkung en	Evidenz -niveau (CEBM Oxford)
releasing intrauteri ne system versus laparosc opic supracerv ical hysterec tomy for the treatmen t of heavy menstru al bleeding : a randomi zed study	Rome.	arms: LNG- IUS (n=36) or LSH (n=36).	assessment chart [PBAC]) at 12 months. <b>Secondary outcomes</b> quality of life, improvement in bleeding patterns, intensity of postoperative pain, and early postoperative complications . A p<0.05 was considered statistically significant.	was observed after LNG-IUS <b>Conclusion of the authors:</b> LNG-IUS can be considered as first option for the treatment of HMB unresponsive to drug therapy, and it is particularly suitable for women who want to preserve an acceptable menstrual flow. LSH may be considered the best surgical option in women with HMB unresponsive to any medical treatment		
Follow up of RCT Leminen et al, 2012(13)	236 women, aged 35- 49 years, referred for menorrha	See above Follow up 5 years Here: questionnaire s at baseline,	<b>Here: occurrence of premenstrua l symptoms</b>	Questionnaires were completed by the participants and study gynecologists before the randomization and at each follow-up visit. Anxiety was measured using the validated Finnish version of the Spielberger 20-item State-Trait Anxiety Inventory, with a range of 20–80 (12). Depression was measured with the 13-item version of the Beck Depression Inventory with a scale of 0–39 <b>Results</b>	Validated questionnai res No primary endpoint, but low	Ib



Quelle/ Studien typ	Populatio n (Teilnehm er)	Interventio n/ggf Dosierung/ Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodisch e Bemerkung en	Evidenz -niveau (CEBM Oxford)
4)	gia to 5 universi-ty hospitals in Finland	follow-up visits six and 12 months after the treatment and five years after the randomizatio n.		Premenstrual symptoms decreased significantly in both groups by six months ( $p \leq 0.028$ ) without significant differences between the groups In LNG-IUS group the decrease of breast tenderness was seen first by 12 months ( $p = 0.048$ ). Even though 42% of the women assigned to treatment with LNG-IUS were hysterectomized during the follow-up period, the results of intention-to-treat and actual treatment analyses were comparable	drop out rate	
Follow up of RCT Heliövaara- Peippo et al, 2011(13 5)	See above	See above Followup 5 years	Waist circumferenc e, BMI, RR, levels of blood lipids, serum high- sensitivity CRP, tumor necrosis factor alpha were measured, and use of medication for hypertension, diabetes, hypercholest erolemia, and ischemic	After 5 years, an increase in the use of diabetes medication during the follow-up was only detected in the hysterectomy group (from 1.7% to 6.7%, $P = 0.008$ vs from 5.1% to 8.4%, $P = 0.08$ ), as well as they had significantly higher serum levels of TNF- (108.59 pg/ml vs 49.02 pg/ml, $P = 0.001$ ) and hsCRP (1.55 _____g/ml vs 0.78 _____g/ml, $P = 0.038$ ) at 5- and 10-years. There was no difference between the groups in the use of cardiovascular medication, neither was there difference in blood pressure, waist circumference, BMI, or concentrations of blood lipids.	No primary endpoint Cave : multiple testing !	?



Quelle/ Studien typ	Populatio n (Teilnehm er)	Interventio n/ggf Dosierung/ Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodisch e Bemerkung en	Evidenz -niveau (CEBM Oxford)
			heart disease was analyzed.			
Follow up of RCT Heliöva -ra- Peippo et al, 2010(13 1)	236 premenop ausal women referred for menorrh agia to five university hospitals	randomly assigned to treatment with hysterectomy (n = 117) or LNG-IUS (n = 119)	Lower urinary tract symptoms (LUTS) among women treated for menorrhagia baseline, after 6,12 months, 5, 10 years	<p>Medications and operations for urinary incontinence were confirmed from medical records and national registries.</p> <p>221 (94%) women took part in the 10-year follow-up evaluation. As 55 (46%) women originally randomised to the LNG-IUS group underwent hysterectomy, the results were analysed by actual treatment</p> <p><b>Medication for urinary incontinence</b></p> <p>Hysterectomy : 12%</p> <p>LNG-IUS : 1% , OR 9.45, 95% CI 1.24-71.87, P = 0.006</p> <p><b>Surgery for stress incontinence</b></p> <p>Hysterectomy : 3 women</p>		



Quelle/ Studien typ	Populatio n (Teilnehm er)	Interventio n/ggf Dosierung/ Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodisch e Bemerkung en	Evidenz -niveau (CEBM Oxford)
			evaluated by Questionnair es	<p>LNG-IUS : 1 woman</p> <p><b>Urinary tract infections (UTIs)</b></p> <p>Hysterectomy versus LNG-IUS users : OR 3.20, 95% CI 1.47-6.96, P = 0.002. A multivariate model showed that UTIs were associated with hysterectomy (P = 0.004)</p> <p><b>Symptoms :</b></p> <p>- Feeling of incomplete emptying HE versus LNG-IUS : OR 3.00, 95% CI 1.00-9.05, P = 0.04) - Stress incontinenc : OR 1.83, 95% CI 1.01-3.32, P = 0.04)</p> <p>No differences between the study arms were noted in urge urinary incontinence or by the Urinary Incontinence Severity Score.</p>		
RCT Halmes mäki K et al, 2004(13 6)	236 premenop ausal women referred for menorrh agia to five university hospitals	randomly assigned to treatment with hysterectomy (n = 117) or LNG-IUS (n = 119)	FSH, estradiol (baseline, 6 and 12 months) Menopausal symptoms characterized by the Kupperman menopausal distress test	<p>After 6 months : no difference between the groups,</p> <p>After 12 months : hysterectomized women had higher FSH levels than women with LNG-IUS (P = 0.005).</p> <p>Signicant association between FSH levels and treatment modality (P = 0.020).</p> <p>Hot flushes increased significantly in the hysterectomy group (P = 0.02).</p> <p>Signicant association between hot flushes and both treatment modality and age (P = 0.02 and P = 0.01, respectively).</p> <p>CONCLUSION: Hysterectomy may impair ovarian function shown by rising serum FSH levels and hot flushes. Results should be interpreted with caution, longer follow-up is needed.</p>		1b



## 5.6. Evidenztabelle zu Hysterektomie versus systemische Hormontherapie bei dysfunktionellen Blutungsstörungen

Tabelle 11: Eingeschlossene Studie zu Hysterektomie versus systemische Hormontherapie bei dysfunktionellen Blutungen

Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
<b>Hysterectomy versus Medical Treatment</b>						
From : SR Matteson K. et al, 2012(45) « A Systematic Review comparing Hysterectomy to less invasive treatment for abnormal uterine bleeding »	<b>Studies included :</b> RCT <b>Search in :</b> Medline, inception to 1/2011, English	Hysterectomy versus less invasive treatment (Endometrial ablation, LNG-IUS, medical therapies as treatments of AUB secondary to presumed ovulatory disorders (AUB-O) or endometrial hemostatic dysfunction (AUB- E), and reported an outcome of interest. 7 ranked critical/important: -bleeding, quality of life, pain, sexual health, patient satisfaction, need for subsequent surgical treatment,	<b>Study selection</b> 1 RCT (rated as "A" or "B" quality for different outcomes) compared hysterectomy to medical therapy in 63 women with AUB presumably from DUB with follow up for 2 years. In the hysterectomy group 36% (n=10) had a TAH and 64% (n=18) had a TVH. The trial included women already on medical treatment and randomized to HE Or expanded medical treatment The trial did not mandate a specific medication regimen and therapies used in this study included combined oral contraceptive pills (38%), cyclic progesterin (16%), continuous progesterin (6%), conjugated estrogen with progesterin (25%), and conjugated estrogen alone (6%); 53% received a prostaglandin synthetase inhibitor, usually with a hormonal therapy. <b>Results per endpoint</b> <b>Bleeding control (critical importance)</b> — not reported for this trial. <b>Quality of life measures (critical importance)</b> —No differences were found in the change of any SF-36	<b>-Overall quality of the evidence</b> for these studies was low to very low for each outcome domain. <b>-cave :</b> women randomized were already dissatisfied with medical treatment <b>-sample size :</b> A larger sample powered to detect a smaller effect was originally planned, but major	Kuppermann M, et al, JAMA. 2004;(137) Learman LA, et al, Obstet Gynecol. 2004(138) (Varner et al, Control Clin Trials, 2004(139))	IIB- downgraded  Sample size patient group selection

Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
		adverse events (major /minor – defined)	<p>scores between medication and hysterectomy groups. Overall, the quality of evidence for quality of life measures was low and revealed no differences between hysterectomy and medications.</p> <p><b>Pain (critical importance)</b>—No differences were found in pain between groups. Overall, the quality of evidence for pain outside the post-operative period was very low and revealed no differences between hysterectomy and medications.</p> <p><b>Sexual health (high importance)</b>—No differences were found in SF-36 sexual satisfaction scores between groups. Overall, the quality of evidence on sexual health outcomes was low and revealed no differences between hysterectomy and medications.</p> <p><b>Satisfaction (high importance)</b>—No differences were found in change in satisfaction with symptom level between groups. Overall, the quality of evidence for satisfaction was low and revealed no differences between hysterectomy and medications.</p> <p><b>Additional treatment (Moderate importance)</b>—Although “additional treatment” can be inferred from “crossed-over” to hysterectomy, it was not specifically assessed nor reported as an explicit “outcome” for this study.</p> <p>At 2 year follow-up, 53% of the group randomized to medication had “crossed-over” to the hysterectomy group. One patient in the hysterectomy arm required a trachelectomy 15 months after hysterectomy for persistent bleeding. Therefore an evidence profile was not generated.</p>	<p>difficulties in the early stages of recruitment and a failed effort to randomize women in a similar trial led our data and safety monitoring board to endorse a decision to reduce the recruitment goal to 60.</p> <p>60 participants would allow us to reject the null hypothesis of no difference in MCS improvements between hysterectomy and medical treatment with 90% power in a 2-sided test</p>		



Studientyp Quelle	Untersuchte Studien	Interventionen/ (ggf. Dosierung)	Ergebnisse	Methodische Bemerkungen	Literatur belege	Evidenz niveau
			<b>Adverse events</b> Medication : no reported complications in the medication group.(0%) Hysterectomy : 3 major complications (10%) and 1 minor complication (3%). Overall, the quality of evidence for adverse events was low and favored medication over hysterectomy.	with an p of .05 if the true effect size was 6.8 units or greater. This difference of 6.8 units represents approximately 70% of an SD and, although large, is similar to 1-year MCS change scores for patients who were classified as having improved in 1 of 5 tracer conditions in the MOS study		





## 5.7. Nicht eingeschlossene Publikationen zu Interventionen bei dysfunktionellen Blutungsstörungen (nach Volltextscreening, aufgeführt ab 2000)

Tabelle 12: Nicht eingeschlossene Publikationen zu Interventionen bei dysfunktionellen Blutungsstörungen (nach Volltextscreening)

Author, Year, study- or publication typ	Subject/Topic	Reason for exclusion
Sesti F et al, 2011(123) RCT	Thermal balloon ablation versus laparoscopic supracervical hysterectomy for the surgical treatment of heavy menstrual bleeding: a randomized study.	Included in systematic review Fergusson et al, 2013
Cooper K et al, 2011(140) retrospective cohort study	Outcomes following hysterectomy or endometrial ablation for heavy menstrual bleeding: retrospective analysis of hospital episode statistics in Scotland	Retrospective analysis specific for Scotland – study design not adequate
Middleton et al, 2010(141) Systematic Review, Metaanalysis	Hysterectomy, endometrial destruction, and levonorgestrel releasing intrauterine system (Mirena) for heavy menstrual bleeding: systematic review and meta-analysis of data from individual patients.	Included in Health Technology Assessment of Bhattacharya S. et al.2011(51)
Heliövaara-Peippo et al, 2010(131)  Follow up of RCT	Effect of hysterectomy and levonorgestrel-releasing intrauterine system (LNG-IUS) on lower urinary tract symptoms (LUTS) among women treated for menorrhagia	Included in systematic review Matteson et al, 2012
Heliövaara-Peippo et al, 2009(130)	Effect of hysterectomy or levonorgestrel-releasing intrauterine system on lower abdominal pain and back pain among women treated for menorrhagia: a	Included in systematic review Matteson et al, 2012



Author, Year, study- or publication typ	Subject/Topic	Reason for exclusion
Follow up of RCT	five-year randomized controlled trial	
Frick et al, 2009, secondary analysis of RCT	Financial and quality-of-life burden of dysfunctional uterine bleeding among women agreeing to obtain surgical treatment	Full text not available
Dickersin et al ,2007, RCT(114)	Hysterectomy compared with endometrial ablation for dysfunctional uterine bleeding: a randomized controlled trial	Included in systematic reviews Fergusson et al, 2013, Matteson et al, 2012
Clegg et al, 2007(142) Modelling out of RCT	Cost-utility of levonorgestrel intrauterine system compared with hysterectomy and second generation endometrial ablative techniques in managing patients with menorrhagia in the UK.	Economic Model specific for UK
Halmesmäki et al, RCT, 2007(129)	The effect of hysterectomy or levonorgestrel-releasing intrauterine system on sexual functioning among women with menorrhagia: a 5-year randomised controlled trial.	Included in systematic review Matteson et al, 2012
Learman et al, RCT, 2004(138)	Hysterectomy versus expanded medical treatment for abnormal uterine bleeding: clinical outcomes in the medicine or surgery trial	Included in systematic review Matteson et al, 2012
Kuppermann et al, RCT, 2004(137)	Effect of hysterectomy vs medical treatment on health-related quality of life and sexual functioning:	Included in systematic review Matteson et al, 2012



Author, Year, study- or publication typ	Subject/Topic	Reason for exclusion
	the medicine or surgery (Ms) randomized trial.	
Hurskainen et al, RCT, 2004(127)	Levonorgestrel-releasing intrauterine system or hysterectomy in the treatment of essential menorrhagia: predictors of outcome In this study the amount of menstrual blood loss (MBL) turned out to be the single most important outcome predictor of these treatments. However, the treatment with LNG-IUS seemed to be an appropriate alternative to hysterectomy for all women who perceived their MBL heavy.	Included in systematic review Matteson et al, 2012
Varner et et al, RCT, 2004(139)	randomized clinical trial comparing hysterectomy and medical treatment in premenopausal women with abnormal uterine bleeding.	Included in systematic review Matteson et al, 2012
Marjoribanks J, Lethaby A, Farquhar C. Cochrane Review 2003	Surgery versus medical therapy for heavy menstrual bleeding.	more up-to-date- review available (2006)



## 5.8. Evidenztabelle zu Hysterektomie versus lokale oder systemische Hormontherapie bei Adenomyosis uteri

Tabelle 13: Eingeschlossene Primärstudien zu Hysterektomie versus lokaler (intrauteriner) Hormontherapie bei Adenomyosis uteri

Quelle/ Studientyp	Population (Teilnehmer)	Interventionen/ggf Dosierung/ Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodische Bemerkungen	Evidenz- niveau (CEBM Oxford)
<b>Adenomyosis uteri : HE vs LNG-US</b>						
RCT Ozdegirmenci et al, 2011(143) « Comparison of levonor- gestrel intrauterine system versus hysterectomy on efficacy and quality of life in patients with adenomyosis	Women with clinical suspicion of adenomyosis complaining of menorrhagia and/or dysmenorrhea were referred to our Gynecology Department. Menorrhagia was defined as menstrual blood loss above 80 mL/menstruation. Adenomyosis was diagnosed via transvaginal ultrasound and MRT	LNG-US vs HE Follow up 1 year	QoL (WHOQOL- BREF TR has four domains: physical health, psychological health, social relationships, and environment) Efficacy on symptoms (Bleeding/Pain) Clinical measures of menstrual bleeding as the number of used pads/day during menstruation, hemoglobin	N=86 women included, 75 continued, 11 Loss to Follow up (43 LNG-US mean age 44y, 32 HE mean age 46 n.s., both parity :3, gravity 5), All hysterectomies were performed via the abdominal route. Postoperative pathology findings confirmed the presence of adenomyosis in 21 (65.6%), myomas in six (18.8%), adenomyosis with coexisting myoma in three (9.4%), and normal uterus in two (6.2%) womenAll LNG-US were inserted without anesthesia. <b>Results per Endpoint:</b> <b>WHOQOL-BREF TR (Quol):</b> <b>pretreatment period</b> : all the domain scores were comparable between groups <b>Posttreatment 6 and 12 months:</b> all five domain scores were not statistically different between groups. When pretreatment and post-treatment scores of groups were compared, three of the five mean domain scores (physical, environmental, environmental-TR) were increased in patients treated with hysterectomy, while in patients	For <b>QOL evaluation</b> , the World Health Organization Quality of Life- Short Form, Turkish Version (WHOQOL- BREF TR) was used. The validity and reliability of the Turkish version was studied by Eser et al. <b>Sample size</b> : 90% power to detect a 30% difference (endpoint not specified) with 72 women <b>Randomization</b>	Ib-



Quelle/ Studientyp	Population (Teilnehmer)	Interventionen/ggf Dosierung/ Follow-up	Outcomes (Endpunkte)	Ergebnisse	Methodische Bemerkungen	Evidenz- niveau (CEBM Oxford)
			(Hb) levels, and health-related QOL variables were evaluated at preinsertion period (pretreatment).	<p>managed with LNG-IUS, all five mean domain scores were increased</p> <p><b>Amenorrhoe 6 months:</b> LNG-IUS : n=10, 23.8%  <b>Oligomenorrhoe 6 months :</b>LNG-US :18 (42.8%), <b>both : n=28, 66,6%</b></p> <p><b>Amenorrhoe 12 months :</b> LNG-US : n=22, 51.4%,  <b>Oligomenorrhoe 12 months :</b>LNG-US : n=15,35.7% <b>both n=37, 87,1%</b></p> <p><b>Bleeding :Amount of Pads Used :</b> From pretreatment 2/day to1/day after 6 months and 12 months (p&lt;0,001), no statistically significant difference in Hb levels between groups, increased in both groups</p> <p><b>Conversion to hysterectomy :</b> n=1 after spontaneous expellation of LNG-US ;  <b>Continuation rate after 1 year :</b> 97,7%</p> <p><b>Side effects :</b>  <b>LNG-US :</b> most common side effects as follows: headache (11.9%), breast tenderness (7.1%), acne (4.8%), and transient depressive episode (2.4%). No woman requested removal of the device secondary to the side effects of LNG-IUS</p> <p><b>HE :</b> One (3.1%) patient had postoperative wound infection and required secondary suture. No other complications were observed in this group.</p>	by computer generation.	



### 5.9. Nicht eingeschlossene Publikationen zu Interventionen bei Adenomyosis (nach Volltextscreening)

Tabelle 14: Nicht eingeschlossene Publikationen zu Interventionen bei Adenomyosis (nach Volltextscreening)

Author, Year, study- or publication typ	Subject/Topic	Reason for exclusion
Grimbizis GF, Mikos T, Tarlatzis B. Fertil Steril. 2014 Feb;101(2):472-87	Uterus-sparing operative treatment for adenomyosis.	No randomized controlled trials, no comparison with hysterectomy
Pan HS, Ko ML, Huang LW, Chang JZ, Hwang JL, Chen SC. Minim Invasive Ther Allied Technol. 2008;17(5):318-22.	Total laparoscopic hysterectomy (TLH) versus coagulation of uterine arteries (CUA) at their origin plus total laparoscopic hysterectomy (TLH) for the management of myoma and adenomyosis.	Not randomized, adenomyosis results not reported seperately



## 5.10. Evidenztabelle zum Vergleich der Hysterektomieverfahren

Tabelle 15: Eingeschlossene Publikationen zum Vergleich der Hysterektomieverfahren

Systematischer Review, Metaanalyse, HTA

Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
<b>Vergleich abdominale, vaginale und laparoskopische Hysterektomie</b>						
Guo Y1, Tian X, Wang L 2013(55) Laparoscopically assisted vaginal hysterectomy vs vaginal hysterectomy: meta analysis.	Study types : RCT  Search period/ databases  Search up to 11/2011 in Medline, ISI EMBASE, ISI Web of Knowledge (from 1990) CPCI-S, and the Cochrane Library (4/2011)  Outcomes	Randomized controlled trials to compare LAVH vs VH. Outcomes : complications, conversion rate, operative time, hospital stay, blood loss, paralytic ileus duration, and weight of the surgically treated uterus.	<b>Study selection:</b> 61 RCT identified, after abstract- and fulltextscreening included : 9 randomized controlled trials with 629 patients, 312 were allocated to the VH group, and 317 to the LAVH group. <b>Results:</b> <b>1. Perioperative Complications inclusive paralytic ileus duration/ Blood loss</b>  No significant difference between VH	<b>the methodologic quality of trials included was evaluated with the Jadad Score.</b> The median Jadad score of the methodologic quality of the included studies was 3 (from a Maximum of 5 points). The primary study limitations pertained to both justification of sample size and double blinding. For example, only	<b>1. Summitt RL</b> Jr, Stovall TG, Lipscomb GH, Ling FW. Randomized comparison of laparoscopy- assisted vaginal hysterectomy with standard vaginal hysterectomy in an outpatient setting. Obstet Gynecol. 1992; 80:895. <b>2. Ottosen C,</b> Lingman G, Ottosen L. Three methods for	1a

Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	evaluated were :		<p>and LAVH,</p> <p><b>Complications</b>  <b>overall: 38 in LAVH,</b>  <b>32 in VH n.s. I<sup>2</sup>40%.</b>                      Reported in 8 Studies</p> <p><b>1a. Duration of paralytic ileus:</b>                      reported in 3 Studies,                      2 studies with VH shorter,                      1 study with LAVH shorter,                      weighted mean difference + 2,22                      LAVH but 95%CI +6,99 to 11,4 n.s.                      .I<sup>2</sup>98%</p> <p><b>1b.Blood loss:</b>                      reported in 5 Studies.  <b>In 4 Studies (Ottosen, Hwang,Sesti, Zhu)</b>  <b>less blood loss in VH,</b>                      in 1 study less blood loss in LAVH                      (Summitt) – therefore overall less blood loss for VH (53ml), but not statistically significant,                      Random Effects</p>	<p>2 studies described the double blinding (Ottosen et al, 2000, Sesti et al, 2008).</p> <p>Cave: no sensitivity analysis, significant heterogeneity in metaanalyses!</p>	<p>hysterectomy: a randomised, prospective study of short term outcome. BJOG. 2000;107:1380.</p> <p><b>3.Soriano D, Goldstein A, Lecuru F, Darai E.</b> Recovery from vaginal hysterectomy compared with laparoscopy-assisted vaginal hysterectomy. Acta Obstet Gynecol Scand. 2001;80:337–341.</p> <p><b>4. Darai E, Soriano D, Kimata P, Laplace C, Lecuru F.</b> Vaginal hysterectomy for enlarged uteri, with or without</p>	





Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>Model, Heterogeneity 95%</p> <p><b>Cave:</b> Summitt with greater estimated blood loss, but hematocrit measure postoperative at day 2 significant lower in LAVH than VH! (35,2+/-4,6 versus 32,6 +/-4,6)</p> <p><b>Other complications:</b></p> <p><b>2. Conversion Rate</b></p> <p>No significant difference between VH and LAVH: 15 conversions in LAVH versus 6 in VH (<math>I^2 = 0\%</math>), OR 2,21 but not significant (95%CI 0,92-5,31)</p> <p><b>3. Operative Time</b></p> <p>LAVH required longer operating time than VH did (weighted mean difference, + 39.59; 95% confidence interval, 20:00-59.18)</p>		<p>laparoscopic assistance: randomized study. Obstet Gynecol. 2001;97:712.</p> <p><b>5.Hwang JL,</b> Seow KM, Tsai YL, Huang LW, Hsieh BC, Lee C. Comparative study of vaginal, laparoscopically assisted vaginal and abdominal hysterectomies for uterine myoma larger than 6 cm in diameter or uterus weighing at least 450 g: a prospective randomized study. Acta Obstet Gynecol Scand. 2002;81:1132–1138.</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>minutes; <math>p &lt; .001</math>; <math>\chi^2(2)</math> <math>p &lt; .001</math>; <math>I(2) = 97\%</math>, with evidence of significant heterogeneity (<math>\chi^2(2) = 209.14</math>; <math>p &lt; .001</math>).</p> <p><b>4. Hospital Stay</b> Reported in 5 Studies. No significant difference between VH and LAVH, +1,17 days more for LAVH but 95%CI -0,1 to 2,43 n.s. <math>I^2=97</math> because of 1 study (Sesti et al, 2008 with 1 day longer stay for LAVH!, all other studies n.s.)</p> <p><b>5. Uterusweight</b> No significant difference between VH and LAVH,</p>		<p><b>6. Ribeiro S,</b> Ribeiro R, Santos N, Pinotti J. A randomized study of total abdominal, vaginal and laparoscopic hysterectomy. Int J Gynecol Obstet. 2003;83:37–43.</p> <p><b>7. Sesti F,</b> Ruggeri V, Pietropolli A, Piccione E. Laparoscopically assisted vaginal hysterectomy versus vaginal hysterectomy for enlarged uterus. JSLS. 2008 ;12:246.</p> <p><b>8. Zhu L,</b> Lang JH, Liu CY, Shi H, Sun Z, Fan R. Clinical assessment for</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
					<p>three routes of hysterectomy. Chin Med J (Engl). 2009;122:377–380.</p> <p><b>9. Drahonovsky J,</b> Haakova L, Otcenasek M, Krofta L, Kucera E, Feyereisl J. A prospective randomized comparison of vaginal hysterectomy, laparoscopically assisted vaginal hysterectomy, and total laparoscopic hysterectomy in women with benign uterine disease. Eur J Obstet Gynecol Reprod Biol. 2010;148:172–176.</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
Yi YX, Zhang W, Zhou Q et al, 2011(54) Laparoscopic-assisted vaginal hysterectomy vs abdominal hysterectomy for benign disease: a meta-analysis of randomized controlled trials.	<b>Study types:</b> randomized controlled trials <b>Search Period/databases:</b> 20/2/ 2010 to 2/7/ 2010 Medline (PubMed), EMBASE, Web of Science, ProQuest, Cochrane Library, China Biological Medicine Database, and screening the references cited in the acquired articles <b>Inclusion/Exclusion criteria:</b> No language restrictions, Published trials comparing LAVH with AH for benign	LAVH versus AH for patients with benign disease of the uterus	<b>Study selection:</b> 54 full text assessed, 23 included (6 more than Nieboer 2009) <b>Results:</b> <b>1. Operation time :</b> LAVH sign longer than AH (15 studies, ca. 700 pat.) MD + 13.62 min [4.60, 22.65] p<, cave Heterogeneity I <sup>2</sup> 96%! Some studies with shorter operation time! <b>2. Blood loss</b> LAVH sign less than AH (13 studies; ca. 600 pat.) MD -47.92 ml [-77.79, -18.06] cave Heterogeneity I <sup>2</sup> 91%!	<b>Additional studies compared to Nieboer et al, 2009:</b> 1. Lin SQ, 2001, 2. Atabekoglu C, 2004, 3. Zhang P, 2004, Sesti F, 2008, 5. Yue Q, 2009 6. Zhu L 2009 <b>Random effects models</b> <b>Cave: often significant heterogeneity</b> <b>Overall study quality</b> (assessed with Cochrane risk of bias tool); moderate. Overall assessment in % of studies: Adequate sequence generation > 75% Incomplete outcome data	<b>Kunz G</b> , Plath T, Leyendecker G.. Geburtsh Frauenheilk 1996; 56:453–7. <b>Langebrekke A</b> , Eraker R, Nesheim BI, Urnes A, Busund B, Sponland G., Acta Obstet Gynecol Scand 1996;75:404–7. <b>Summitt RL</b> , Stovall TG, Steege JF, Lipscomb GH. Obstet Gynecol 1998 <b>Falcone T</b> , Paraiso MFR, Mascha E. Am J Obstet Gynecol 1999;180:955–62. <b>Marana R</b> , Busacca M, Zupi E, Garcea N, Paparella P, Catalano GF. Am	1a



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	disease, documented the case selection criteria for LAVH and AH, reported on at least one of the outcomes mentioned below. Studies were excluded if the laparoscopic technique was not LAVH, the outcomes were not clearly reported, it was impossible to extract data, there was considerable overlap between studies.		<p>Some studies with higher loss in LAVH !</p> <p><b>3. Hospital stay</b> LAVH sign less than AH (13 studies; ca. 590 pat.) MD -2.11 days [-2.63, -1.59] Cave: I<sup>2</sup> 90%, all studies shorter for LAVH but great range, between 0,8 and 6 days</p> <p><b>4. Postoperative Pain (day 1 and day 2)</b> LAVH with sign. less pain compared to AH <b>Day 1</b> 3 studies, 150 patients MD -1.48 [-1.95, -1.01] no sign. I<sup>2</sup> <b>Day 2</b> 3 studies, 150 patients,</p>	<p>addressed &gt;75%</p> <p>Free of other bias: ca. 70%</p> <p>Most often no blinding (&gt;70%)</p> <p>allocation concealment not reported ca 50%</p> <p>selective outcome reporting ca. 50%</p> <p>8 studies not with suitable results for inclusion in metaanalysis with similar results concerning the effects of LAVH versus AH</p>	<p>J Obstet Gynecol 1999;180:270–5.</p> <p><b>Ferrari MM</b>, Berlanda N, Mezzopane R, Ragusa G, Cavallo M, Pardi G. BJOG 2000;107:620–5.</p> <p><b>Lumsden MA</b>, Twaddle S, Hawthorn R, et al. BJOG 2000;107:1386–91.</p> <p><b>Ottosen C</b>, Lingman G, Ottosen L. BJOG 2000;107:1380–5.</p> <p><b>Lin SQ</b>, Bai J, Felix W. Clin Med J China 2001;8:483–4.</p> <p><b>Hwang JL</b>, Seow KM, Tsai YL, Huang LW, Hsieh BC, Lee C. Acta Obstet</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>MD -2.07 [-2.49, -1.66] no sign. I<sup>2</sup> Day 3 2 studies, 120 patients MD -1.81 [-2.25, -1.37]</p> <p><b>5. Haemoglobin drop (g/100ml)</b> LAVH with significant less drop compared to AH 4 studies, 200 patients MD -0.52 [-0.73, -0.31]</p> <p><b>6. Return to normal activities</b> LAVH with significant shorter return compared to AH 6 studies, 260 patients MD -13.32 days [-16.77, -9.88] cave: I<sup>2</sup> 71%</p>		<p>Gynecol Scand 2002;81:1132–8. <b>Schutz K</b>, Possover M, Merker A, Michels W, Schneider A. Surg Endosc 2002;16:121–5. <b>Tsai EM</b>, Chen HS, Long CY, et al. Gynecol Obstet Invest 2003;55:105–9. <b>Atabekoglu C</b>, Sonmezer M, Gungor M, Aytac R, Ortac F, Unlu C. J Am AssocGynecol Laparosc 2004;11:467–72. <b>Zhang P</b>, Ling F, Zeng Y. ShangHai Med J 2004 ;27:736–8. <b>Muzii L</b>, Basile S, Zupi E, et al. J Minim Invasive Gynecol</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>heterogeneity</p> <p><b>7. Major complication</b> LAVH with significant more major complications compared to AH 8 studies, ca. 450 patients OR 2.54 [1.13, 5.70], <math>^2 = 0</math></p> <p><b>8. Minor complications</b> LAVH with significant less minor complications compared to AH 18 studies, 770 patients, OR 0.50 [0.36, 0.70]</p>		<p>2007;14:610– <b>5.Sesti F</b>, Calonzi F, Ruggeri V, Pietropolli A, Piccione E. Int J Gynecol Obstet 2008;103:227– 31. <b>Yue Q</b>, Ma R, Mao DW, et al. J Int Med Res 2009;37:855– 61. <b>Zhu L</b>, Lang JH, Liu CY, Shi HH, Sun ZJ, Fan R. Chin Med J (Engl) 2009;122:377– 80. <b>Olsson JH</b>, Ellstrom M, Hahlin M. BJOG 1996;103:345– 50. <b>Härkki-Sirén P</b>, Sjöberg J, Toivonen J, Tiitinen A. Acta Obstet Gynecol Scand 2000;79:866–71. <b>Yuen PM</b>, Mak</p>	



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			<p><b>9. Overall complications</b> LAVH with significant fewer overall complications OR 0.60, 95% CI 0.44 to 0.81; p = 0.0008</p> <p>“Quality of life is likely to be the key outcome to evaluate the approach for hysterectomy, but further research is needed.”</p> <p>“Kluivers et al. reported that the quality of life following LAVH was better than that following AH at 6 weeks after surgery, but the difference was not significant after 1 year.”</p>		<p>TW, Yim SF, et al. Am J Obstet Gynecol 1998;179:1–5.</p> <p><b>Seracchioli R</b>, Venturoli S, Vianello F, et al. J Am Assoc Gynecol Laparosc 2002;9:333–8.</p> <p><b>Ellström M</b>, Olsén MF, Olsson JH, Nordberg G, Bengtsson A, Hahlin M. Acta Obstet Gynecol Scand 1998;77:923–8.</p>	
Duru C1, Jha S, Lashen	<b>Study type:</b>	Patients with hysterectomy and	<b>Study selection:</b> Twenty-one studies	<b>Limitations:</b>	<b>Ei Toukhy TA</b> , Hefni M, Davies	





Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
H.(58) Urodynamic outcomes after hysterectomy for benign conditions: a systematic review and meta-analysis.	prospective <b>Search period/Databases:</b> English articles on MEDLINE from 1950 to February 2009 and on Web of Knowledge for all years were searched. <b>Inclusion/Exclusion criteria:</b> Included: Urodynamically assessed bladder and lower urinary tract function before and after total hysterectomy for benign conditions. Studies with dichotomous	assessment of urinary incontinence (urodynamic) before and after hysterectomy	reported information on urinary and lower urinary tract function after TAH for benign conditions. 12 studies were included in the review. <b>Results:</b> <b>1. Urinary incontinence before and after hysterectomy</b> 6 Studies included, 320 patients Risk Ratio: 1,37 [1.01-1.84] after hysterectomy $I^2 = 38\%$ <b>2. Detrusor overactivity before and after hysterectomy</b> 8 Studies included, ca. 720 patients RR 1,58 [1,16-2,16] $I^2 = 0\%$ <b>3. Urodynamic stress incontinence before</b>	Most of the studies reviewed contained only a small number of patients. Many were not prospective and few were randomized. The exclusion of non-English language studies adds to and may strengthen the inherent selection bias. This may be that investigators are more likely to report in international journals if the findings of their study are positive and report them in local journals if they are negative. Therefore, by including only English studies, negative findings, which might be	A, et al. J Obstet Gynaecol. 2004;24: 420–425. <b>Prior A</b> , Stanley K, Smith AR, et al. Effect of hysterectomy on anorectal and urethrovesical physiology. Gut. 1992; 33: 264–267. <b>Lalos O</b> , Bjerle P. Eur J Obstet Gynecol Reprod Biol. 1986; 21: 143–150. <b>Thakar R</b> , Ayers S, Clarkson P, et al. N Engl J Med. 2002; 347:1318–135. <b>Coughlan BM</b> , Smith JM, Moriarity CT. Ir J Med Sci. 1989;158:215–216. <b>Hansen BM</b> , Bonnesen T, Hvidberg JE, et al. Urol Int.	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	and continuous data regarding prevalence of perceived and urodynamically confirmed UI. Excluded: Radical hysterectomy. Hysterectomy for gynecological cancer. Nonhuman hysterectomy and non-English studies. Retrospective studies and those that did not examine the patients before hysterectomy.		<b>and after hysterectomy</b> 4 studies included, 260 pat. RR 0,89[0,58-1,38] n.s. , I <sup>2</sup> =%	reported in non-English local journals, would be missed. There were different time points of follow-up, and different units for the urodynamic parameters. A random effects model was used for adjustment.	1985;40:224–226. <b>Kaya H</b> , Sezik M, Ozbasar D, et al. Int Urogynecol J Pelvic Floor Dysfunct. 2004;15: 171–174. <b>Kujansuu E</b> , Teisala K, Punnonen R. Gynecol Obstet Invest. 1989; 27: 105–106. <b>Langer R</b> , Neuman M, Ron-el R, et al. Obstet Gynecol. 1989; 74: 205–207. <b>Parys BT</b> , Haylen BT, Hutton JL, et al. Aust NZ J Obstet Gynaecol. 1990; 30: 161–165. <b>Vervest HA</b> , van Venrooij GE, Barents JW, et al. Acta Obstet Gynecol Scand.	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
					1989; 68: 221–229. <b>Wake CR.</b> Br J Obstet Gynaecol. 1980; 87:901–902.	
Systematic Review/ Metaanalysis Gendy R. et al, 2011(53) “Vaginal hysterectomy versus total laparoscopic hysterectomy for benign disease”	Study Type : Randomized Controlled Trials Search period: 1/1989-6/2010 <b>Databases :</b> PubMed, Medline, SCOPUS, and Cochrane searched for combinations of the terms “laparoscopic,” “hysterectomy,” “vaginal,” “outcome,” “randomiz(s)ed,” and “benign.” <b>In-/Exclusion criteria :</b> see next	RCT comparing patients with vaginal hysterectomy (VH) with patients with Total Laparoscopic Hysterectomy (TLH) Studies with laparoscopically assisted HE were not included.	<b>Study Selection</b> 269 abstracts screened, 31 potentially eligible citations identified. Of these, 19 were not RCTs and were excluded. Of the remaining 12 studies, 7 studies described “laparoscopically assisted hysterectomy,” which did not meet a strict definition of TLH. The other 5 <b>papers reported results from RCTs comparing VH with TLH and were included in the present analysis</b> <b>Results:</b>	<b>Jadad-Score:</b> <b>Study quality poor to moderate</b> <b>Ribeiro and Morelli: 1</b> (only inclusion/exclusion criteria specified) <b>Candiani and Drahonovsky: 2</b> (inclusion/exclusion criteria described and randomization process described) <b>Ghezzi: 3</b> (inclusion/exclusion criteria described and randomization	Ribeiro et al, 2003 Morelli et al 2007(144) Candiani et al 2009(145) Drahonovsky et al 2010(42) Ghezzi et al 2010(69)	2a



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>Complications: <b>(DINDO classification of surgical complications used: Grade I :</b> Any deviation from normal postoperative course, without the need for pharmacological intervention (except antipyretics, analgesics, antiemetics, electrolytes, diuretics) / <b>Grade II</b> Requiring pharmacological treatment with drugs not included in grade I; also blood transfusions and TPN/<b>Grade III</b> Requiring surgical, endoscopic, or radiological intervention (not under GA IIIa; under GA IIIb))</p>	<p>process described and power calculation and withdrawals explained)</p>		



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>no significant differences in the rate of any complication were found between VH (89 of 331) and TLH (113 of 332); pooled OR, 0.87; 95% confidence interval [CI], 0.38 – 2.00; P .74;</p> <p>No significant differences in the incidence of grade II complications were demonstrated between VH (52 of 331) and TLH (64 of 332); pooled OR, 1.32; 95% CI, 0.87–2.00; P .198</p> <p>No significant differences in the incidence of grade III complications (requiring surgical, endoscopic, or radiological interevent) were</p>			



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>demonstrated between VH (5 of 331) and TLH (19 of 332; pooled OR, 2.48; 95% CI, 0.73–8.41; P.144;</p> <p>Evidence of heterogeneity and publication bias</p> <p><b>Operating time</b></p> <p>Overall, TLH was associated with a longer operating time compared with VH (WMD 29.31 minutes; 95% CI, 13.33–45.30 minutes; P_.003). Evidence of significant heterogeneity between the trials (Cochran'sQ _65.45; P_.001). No evidence of bias (Egger__2.40; P_.31).</p> <p><b>Blood loss (3 trials)</b></p> <p>no difference</p>			



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			<p>between the 2 operative approaches (WMD 42.24 mL; 95% CI, 101.18 to 16.71 mL; <math>P = .16</math>). No evidence of heterogeneity (Cochran's <math>Q = 4.85</math>; <math>P = .08</math>). There were insufficient trials to undertake a test for bias.</p> <p><b>Conversion to laparotomy (3 trials)</b></p> <p>No difference between the 2 groups (pooled OR, 1.26; 95% CI, 0.49–3.27; <math>P = 0.63</math>). No evidence of heterogeneity (Cochran's <math>Q = 0.000006</math>; <math>P = .99</math>). Too few trials to test for bias.</p> <p><b>Postoperative pain (3 trials)</b></p> <p>Postoperative pain</p>			



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>scores on the day of surgery were reported by 3 trials using visual analog scales (VAS). One trial reported VAS scores at 1, 3, and 8 hours postoperatively. We chose the middle value (3 hours) for the purposes of the metaanalysis. TLH was associated with significantly lower VAS pain scores on the day of surgery than VH (WMD 2.13; 95% CI, 4.08 to 0.18; P .0326;). However, we found evidence of heterogeneity (Cochran's Q 26.42; P&lt;.0001), and there were too few trials to test for bias.</p> <p><b>Length of postoperative stay (4 trials)</b></p>			





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			TLH was associated with a shorter length of stay compared with VH (WMD, 0.62 days; 95% CI, 0.89 to 0.35 days; P < .0001; There was no evidence of either heterogeneity or bias.			
Uccella S, Ghezzi F, Mariani A et al, 2011(60) Vaginal cuff closure after minimally invasive hysterectomy: our experience and systematic review of the literature.	<b>Study type:</b> cohort studies including at least 30 minimally invasive hysterectomies no case reports <b>Search period/databases:</b> Jan. 1,1989, to May 31, 2010, systematic search of PubMed <b>Inclusion criteria:</b>	Patients with malignant or benign uterine disease with minimal invasive hysterectomy	<b>Study selection:</b> The search identified 57 cohort studies on minimally invasive hysterectomy that met our inclusion criteria. 47 were series of laparoscopic hysterectomies, 10 were series of robotic hysterectomies, and 1 was a series including both robotic and laparoscopic hysterectomies. These studies included a total of 13,030 women, of which 8481 underwent TLH with laparoscopic	Methodological quality of studies was not assessed	Will be added	2a



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	Articles reporting series of laparoscopic- or robotic-assisted hysterectomies. Only papers written in English. We excluded case reports, reviews of previous studies, articles enrolling cases that were included in subsequent larger studies, series of subtotal hysterectomies and radical hysterectomies.		cuff closure, 2672 had TLH with transvaginal cuff suturing (3337 including our 665 cases), and 1887 had robotic hysterectomy. <b>Results:</b> pooled incidence of vaginal cuff dehiscence after laparoscopic cuff closure: 0.64% (54/8481, 95%CI, 0.47–0.79), After transvaginal cuff closure 0.18% (6/3337, 95% CI, 0.09–0.44), After robotic cuff closure 1.64% (31/1887, 95% CI, 1.16–2.32) <b>Transvaginal cuff closure was associated with a significantly lower rate of vaginal</b>			



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p><b>dehiscence</b> compared with both laparoscopic (OR, 0.28; 95% CI, 0.12– 0.65; <math>p &lt; .0017</math>) and robotic closure (OR ,0.11; 95% CI, 0.04–0.26; <math>P .0001</math>).</p> <p>The rate of postoperative vaginal bleeding was lower after transvaginal cuff closure than afterlaparoscopic cuff suturing (<math>P &lt; 0 .026</math>).</p> <p>The need for vaginal cuff resuturing was statistically less likely when transvaginal closure was performed compared with both laparoscopic (<math>P &lt; .005</math>) and robotic cuff closure (<math>P &lt; 0.0001</math>).</p> <p>Vaginal infection/abscess rate did not differ significantly using</p>			



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			different suture techniques.			
Nieboer TE, et al, Surgical approach to hysterectomy for benign gynaecological disease. Cochrane Database of Systematic Reviews 2009, Issue 3. (34)	<b>Study types</b> randomised controlled trials <b>Search period/databases</b> The Cochrane Menstrual Disorders and Subfertility Group Specialised Register of controlled trials (15 August 2008), <b>CENTRAL</b> (The Cochrane Library 2008, Issue 3), <b>MEDLINE</b> (1950 to August 2008), <b>EMBASE</b> (1980 to August 2008), Biological Abstracts (1969 to August 2008), the National	Intervention(s)/ control approaches to hysterectomy for benign disease: -abdominal hysterectomy (AH), vaginal hysterectomy (VH), and laparoscopic hysterectomy (LH). -Laparoscopic hysterectomy further subdivisions: 1. <b>LAVH</b> is where the laparoscopic component does not involve ligation of the uterine vessels; 2. <b>LH(a)</b> is where the uterine vessels are ligated laparoscopically	Study selection 55 trials identified, 34 included Exclusion: details not reported, not fully published, other reasons ; -Trials evaluating different surgical approaches to subtotal hysterectomy: If a minority of the trial women had a subtotal hysterectomy and the comparison was made between any of the three approaches outlined, the trial was included. Included Studies: -Three compared VH versus AH -19 compared LH versus AH (including one LH-BSO versus AH-BSO) and -one LAVH versus	Methodological Quality of studies: moderate, almost no blinding, ca. 50% no adequate allocation concealment, ca. 40% selective outcome reporting, ca. 50% not clear if free from other bias  -Data analysed using intention-to-treat where available. - Dichotomous data: expressed as odds ratios for meta-analysis using the Peto-modified Mantel-Haenszel method. - Continuous data combined for meta-analysis using the	<b>Agostini et al 2006</b> , American Journal of Obstetrics and Gynecology 2006;194(2):351–4., <b>Benassi et al. 2002</b> American Journal of Obstetrics and Gynecology 2002;187:1561–5., <b>Darai et al. 2001</b> , Gynaecological Endoscopy Supplement: Paris,2000:5., Obstetrics and Gynecology 2001;97(5):712–6., <b>Drahonovsky et al. 2006</b> Ceska Gynekol 2006;71(6):431–, <b>Ellstrom et al.</b>	1a



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	<p>Research Register and relevant citation lists.</p> <p>Inclusion criteria/ search algorithm:</p> <ul style="list-style-type: none"> <li>• RCT ; Keywords for the NATIONAL RESEARCH REGISTER and the CLINICAL TRIAL REGISTER:</li> <li>○ 1. Hysterectomy, 2. Abdominal, 3. Vaginal, 4</li> </ul>	<p>but there is still some vaginal component; and 3.TLH is where the entire hysterectomy is completed laparoscopically with no vaginal component other than the removal of the uterus.</p> <p>To assess the most beneficial and least harmful surgical approach to hysterectomy for women with benign gynaecological conditions.</p> <p>Primary Outcome:</p> <ul style="list-style-type: none"> <li>• Return to normal activities</li> <li>• Satisfaction and quality of</li> </ul>	<p>minilaparotomy AH;</p> <ul style="list-style-type: none"> <li>-six compared LH versus VH;</li> <li>-two compared LAVH versus TLH</li> <li>-one compared both LH versus AH and LH versus VH</li> <li>-and three compared LH versus AH versus VH</li> </ul> <p>Main results</p> <ul style="list-style-type: none"> <li>• 34 included studies with 4495 women.</li> <li>• The benefits of VH versus AH were</li> <li>○ speedier return to normal activities (mean difference (MD) 9.5 days),</li> <li>○ fewer febrile episodes or unspecified infections (odds</li> </ul>	<p>mean difference (MD).</p> <ul style="list-style-type: none"> <li>- Outcome variables reported only graphically were not included -</li> <li>Statistical heterogeneity was examined by inspecting the scatter in the data points on the graphs, the overlap in their CI and, more formally, by checking the results of Chi<sup>2</sup> tests and I<sup>2</sup> statistics.</li> <li>- outcomes were pooled statistically where no clinical heterogeneity was apparent. A fixed-effect model was used where statistical heterogeneity was absent.</li> <li>-Where statistical</li> </ul>	<p><b>1998</b> Acta Obstetrica et Gynecologica Scandinavica 1998; 77:923–8., <b>Falcone et al.</b></p> <p><b>1999</b> American Journal of Obstetrics &amp; Gynecology 1999;180: 955–62. <b>Ferrari et al.</b></p> <p><b>2000</b> British Journal of Obstetrics and Gynaecology 2000; 107:620–5. <b>Garry et al.</b></p> <p><b>2004</b> British Medical Journal 2004;328(7432): 129–33. <b>BMJ</b> 2004;328(7432): 134. <b>Harkki-Siren et al.</b></p> <p><b>2000</b> Acta Obstetrica et Gynecologica Scandinavica 2000;79: 866–71. <b>Hwang et al.</b></p>	



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		<p>life</p> <p>-Intra-operative visceral injury (Bladder, Ureter Urinary tract (bladder or ureter), Bowel, Vascular</p> <p>-Major long-term complications (Fistula, Pelvi-abdominal pain, Urinary dysfunction, Bowel dysfunction, Pelvic floor condition (prolapse), dysfunction</p> <p>Secondary Outcome:</p> <p>-Operation time</p> <p>-Other intra-operative complication (Sequelae of ) bleeding, Substantial bleeding, Haemoglobin or</p>	<p>ratio (OR) 0.42),</p> <ul style="list-style-type: none"> <li>○ and shorter duration of hospital stay (MD 1.1 days).</li> <li>• The benefits of LH versus AH were</li> <li>○ speedier return to normal activities (MD 13.6 days),</li> <li>○ lower intraoperative blood loss (MD 45 cc),</li> <li>○ a smaller drop in haemoglobin (MD 0.55 g/dl),</li> <li>○ shorter hospital stay (MD 2.0 days),</li> <li>○ and fewer wound or abdominal wall infections (OR 0.31)</li> <li>○ at the cost of more urinary</li> </ul>	<p>heterogeneity was apparent after pooling of data, this was noted and statistically significant results interpreted cautiously after further analysis using a random-effects statistical model.</p>	<p><b>2002</b> Acta Obstetrica et Gynecologica Scandinavica 2002;81:1132–8. <b>Kluiters et al. 2007</b> Journal of Minimally Invasive Gynecology 2007;14(2):145–52. <b>Kunz et al. 1996</b> Geburtshilfe und Frauenheilkunde 1996;56: 453–7. <b>Langebrekke et al. 1996</b> Acta Obstetrica et Gynecologica Scandinavica 1996;75:404–7. <b>Long et al. 2002</b> Gynecologic and Obstetric Investigation 2002;53:214–9. <b>Lumsden et al. 2000</b> British Journal</p>	



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		haematocrit drop, Transfusion, Pelvic haematoma, Unintended laparotomy for approaches not involving routine laparotomy -Short-term outcomes and complications -Length of hospital stay -Infections (Vaginal cuff, Abdominal wall or wound, Urinary tract infection, Febrile episodes or unspec. infections) - Thromboembolism -cost	tract (bladder or ureter) injuries (OR 2.41) <ul style="list-style-type: none"> <li>○ and longer                              operation time                              (MD 20.3                              minutes).</li> <li>• The benefits of                              LAVH versus                              TLH were</li> <li>○ fewer febrile                              episodes or                              unspecified                              infection (OR                              3.77) and</li> <li>○ shorter operation                              time (MD 25.3                              minutes).</li> <li>• There was no                              evidence of                              benefits of LH                              versus VH and                              the operation                              time (MD 39.3                              minutes) as                              well as                              substantial                              bleeding (OR</li> </ul>		Obstetrics and Gynecology 2000; <b>107</b> :1386– 91. <b>Marana et al.</b> <b>1999</b> American Journal of Obstetrics and Gynecology 1999; <b>180</b> : 270– 5. <b>Miskry et al.</b> <b>2003</b> XVI FIGO World Congress Abstract Book 3. Washington DC, 2000:44. Acta Obstetrica et Gynaecologica Scandinavica 2003; <b>82</b> :351–8. <b>Morelli et al.</b> <b>2007</b> Minerva Ginecologica 2007; <b>59</b> (2):99– 105. <b>Muzii et al.</b> <b>2007</b> Journal of Minimally Invasive Gynecology	



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			<p>2.76) were increased in LH.</p> <ul style="list-style-type: none"> <li>For some important outcomes, the analyses were underpowered to detect important differences or they were simply not reported in trials.</li> <li>Data were absent for many important long-term outcome measures.</li> </ul>		<p>2007 ;14(5): 610–5. <b>Ollson et al. 1996.</b> British Journal of Obstetrics and Gynaecology 1996;103:345–50. <b>Ottosen et al. 2000</b> British Journal of Obstetrics and Gynaecology 2000;107:1380–5. <b>Perino et al. 1999</b> Human Reproduction 1999; 14:2996–9. <b>Persson et al. 2006</b> British Journal of Obstetrics and Gynecology 2006;113:1023–30. <b>Raju et al. 1994</b> British Journal of Obstetrics &amp; Gynaecology 1994;101: 1068–71. <b>Ribiero et al.</b></p>	





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					<b>2003</b> International Journal of Gynecology and Obstetrics 2003; <b>83</b> : 37–43. <b>Richardson et al. 1995</b> Lancet 1995; <b>345</b> :36–41. <b>Schutz et al. 2002</b> Surgical Endoscopy 2002; <b>16</b> :121–5. <b>Seracchioli et al. 2002</b> The Journal of the American Association of Gynecologic Laparoscopists 2002; <b>9</b> (3):333–8. <b>Silva Filho et al. 2006</b> Archives of Gynecology and Obstetrics 2006; <b>274</b> (1):21–4. <b>Soriano et al. 2001</b> Acta Obstetrica et Gynaecologica	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
					Scandinavia 2001; 80:337–41. <b>Summitt et al. 1992</b> Obstetrics and Gynecology 1992; 80: 895–901. <b>Summitt et al. 1998</b> Obstetrics and Gynecology 1998;92: 321–6. <b>Tsai et al. 2003</b> Gynecologic and Obstetric Investigation 2003;55: 105–9. <b>Yuen et al. 1998</b> American Journal of Obstetrics and Gynecology 1998;179: 1–5.	
Lethaby A, Mukhopadhyay A, Naik R. Total versus subtotal hysterectomy for benign gynaecological conditions. Cochrane Database Syst	Search: Cochrane Menstrual Disorders and Subfertility Group	Inclusion: Randomised controlled trials of women undergoing either total or subtotal	Included: Nine RCT with participants 1553 <b>Primary outcomes of meta-analysis:</b> 1. Urinary	+ Publikationen zu Langzeitfolgen dieser Studien bis 7/2011 <b>Methodological</b>	<b>Asnafi N</b> , Basirat Z, Hajian-Tilaki KO. Outcomes of total versus subtotal abdominal	1a



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
Rev. 2012	Specialised Register of controlled trials (July 2011), CENTRAL (July 2011), MEDLINE (1966 to July 2011), EMBASE (1980 to July 2011), CINAHL (January 2005 to July 2011), Biological Abstracts (1980 to December 2005), the National Research Register and relevant citation lists.	hysterectomy for benign gynaecological conditions (abdominal and laparoscopic)	function <b>No evidence of a significant difference in the prevalence of stress incontinence</b> (within 2 years: OR 1.45, 95% CI 0.85 to 2.47; 4 studies; >2 years: OR 1.15, 95%CI 0.63 to 2.08; 1 study), <b>incomplete emptying</b> (within 2 years: OR 0.94, 95% CI 0.59 to 1.47, three studies; > 2 years: OR 0.69, 95% CI 0.37 to 1.29, 1 study) or <b>urinary urgency</b> (within 2 years: OR 1.05, 95% CI 0.47 to 2.37, 1 study; > 2 years: OR 1.26, 95% CI 0.68 to 2.32; 1 study) <b>between randomised groups having either abdominal or laparoscopic</b>	<b>Quality of studies:</b> moderate. 7/9 randomization per computer (4x block randomization), 7/9 adequate allocation concealment, 5/9 adequate outcome reporting, only 1/9 blinding (cave: only if no self examination done!)	hysterectomy. Eastern Mediterranean Health Journal 2010;16(2):176–9. <b>Ellstrom</b> Engh MA, Jerhamre K, Junsog K. A randomized trial comparing changes in sexual health and psychological well-being after subtotal and total hysterectomies. Acta Obstetrica et Gynecologica 2010;89:65–70. <b>Flory</b> N, Bissonnette F, Amsel RT, Binik YM. The psychosocial outcomes of total and subtotal hysterectomy: a randomized controlled trial.	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p><b>surgery.</b></p> <p>2. Bowel Function</p> <p><b>No evidence of a difference in the rates of constipation</b> (within 2 years: OR 0.8, 95% CI 0.49 to 1.31, 2 studies; &gt; 2 years: OR 1.52, 95% CI 0.67 to 3.45, 1 study) <b>or incontinence of stools</b> (&gt; 2 years: OR 0.52, 95% CI 0.05 to 5.83, 1 study). Bowel function outcomes were not measured by the trials where laparoscopic surgery was undertaken. Substantial heterogeneity (<math>I^2 = 73\%</math>) was found in the analysis of constipation rates within two years between the</p>		<p>Journal of Sexual Medicine 2006;3:483–91. <b>Gimbel H</b>, Zobbe V, Andersen BA, Filtenborg T et al, Randomised controlled trial of total compared with subtotal hysterectomy with one-year follow up results. BJOG 2003;110:1088–98. <b>Gorlero F</b>, Lijoi D, Biamonti M, et al, Hysterectomy and women satisfaction:total versus subtotal technique. Archives of Gynecology and Obstetrics 2008;278:405–10. <b>Learman LA</b>, Summitt RL,</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>abdominal subtotal and total hysterectomy. When the data were carefully checked, the values for each outcome were dissimilar at baseline for groups in the Thakar trial.</p> <p>3. Sexual Function</p> <p>6 trials: multiple outcomes related to sexual function measured in different ways, making it inappropriate to pool the results.</p> <p>5 trials: some measure of sexual satisfaction, using dichotomous or continuous data. There was no evidence of a difference in sexual satisfaction between randomised groups</p>		<p>Varner RE, et al, A randomized comparison of total or supracervical hysterectomy: surgical complications and clinical outcomes. Obstetrics and Gynecology 2003;102(3):453–62. <b>Morelli M</b>, Noia R, Chiodo D, et al, Laparoscopic supracervical hysterectomy vs laparoscopic total hysterectomy: a prospective randomized trial Minerva Ginecologica 2007;59:1–10. <b>Persson P</b>, Brynhildsen J, Kjolhede P.</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>in meta-analyses (dichotomous data:OR 1.04, 95%CI 0.68 to 1.59, 2 studies; continuous data SMD -0.15, 95% CI -0.43 to 0.13, 2 studies). One other trial that couldn't be pooled (Ellstrom 2010) also reported no evidence of significant differences. Substantial heterogeneity (I<sup>2</sup> = 76%) was found in the analysis of sexual satisfaction within two years (dichotomous data) between the abdominal subtotal and total hysterectomy. In these two pooled trials, satisfaction was assessed differently</p>		<p>Short-term recovery after subtotal and total abdominal hysterectomy – a randomised clinical trial. Gynecological Surgery 2010;117:469–78. <b>Thakar R</b>, Ayers S, Clarkson P et al. Outcomes after total versus subtotal abdominal hysterectomy. New England Journal of Medicine 2002;347 (17):1318–25.</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p><b>4 Trials: Dyspareunia (pain during intercourse).</b> There was no evidence of a difference in dyspareunia (defined as either deep dyspareunia or dyspareunia not otherwise specified) between randomised groups (&lt; 2 years: OR 0.87, 95% CI 0.46 to 1.67, 2 studies; &gt; 2 years: OR 0.56, 95% CI 0.25 to 1.23, 1 study). Substantial heterogeneity (I<sup>2</sup> = 71%) was found in the analysis within two years between the abdominal subtotal and total hysterectomy, likely to have arisen from different ways of measuring</p>			



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			<p>dyspareunia.</p> <p><b>Secondary outcomes</b></p> <p><b>1. 5 trials: Quality of life.</b> There was no evidence of a statistically significant difference in any of the quality of life scales measured within two years of surgery, although only a few studies contributed data to each outcome. In the majority of studies, quality of life improved from baseline (before surgery), regardless of the type of surgery</p> <p><b>2. 4 /5 trials: Length of operation - recovery.</b> Surgery was significantly shorter for subtotal abdominal hysterectomy when compared with total abdominal</p>			





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			<p>hysterectomy (MD - 11.26 mins, 95%CI - 15.1 to -7.5) no significant difference between the laparoscopic subtotal or total hysterectomy (MD 5.0, 95% CI - 14.8 to 4.8, 1 study). no evidence of significant differences between types of hysterectomy for hospital stay or time to resume normal activities (hospital stay - abdominal hysterectomy:MD- 0.17, 95%CI -0.39 to 0.04, 5 studies; hospital stay - laparoscopic hysterectomy: MD - 0.2, 95% CI -0.6 to -0.2, 1 study; normal activities - abdominal hysterectomy: MD - 0.14, 95% CI -0.53 to</p>			



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>0.25).</p> <p><b>3. Complications:</b></p> <p><b>blood loss</b> Abdominal subtotal hysterectomy was associated with significantly less intraoperative blood loss than total hysterectomy (MD -56.6, 95% CI -99.6 to -13.7, three studies); one other trial not suitable for pooling also found a reduction in blood loss with subtotal hysterectomy.</p> <p><b>Transfusion:</b> no evidence of significant differences between randomized groups in the proportion of women who required blood transfusions</p> <p><b>Pyrexia and urinary retention</b> were significantly</p>			



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			<p><b>reduced with the</b>  subtotal when  compared to total  hysterectomy  (pyrexia: OR  0.48, 95% CI 0.31 to  0.75, 5 studies;  urinary retention: OR  0.23, 95% CI 0.06 to  0.81, 5 studies).  There was no  evidence of  significant  differences in the  rates of other short  term complications  such as surgical  injury, pelvic  haematoma, vaginal  bleeding, wound  infection, or bowel  obstruction between  groups having a  subtotal or total  hysterectomy.</p> <p><b>4. Intermediate outcomes</b></p> <p>Ongoing cyclical bleeding was</p>			



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>significantly increased with the subtotal when compared to total hysterectomy (OR 16.0, 95% CI 6.1 to 41.6, 5 studies). There was no evidence of significant differences in the rates of other intermediate outcomes: persistent pain after discharge, removal of the cervical stump, pelvic prolapse or gynaecological cancer.</p> <p><b>5. Long term outcomes</b></p> <p>At a mean of nine years after surgery, one trial found no significant difference in the rate of pelvic prolapse between randomised groups.</p>			



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			The included trials did not have long enough followup to compare the odds of gynaecological cancer in the two groups			
<b>Systematic Review</b> Robert M, Soraisham A, Sauve R. Postoperative urinary incontinence after total abdominal hysterectomy or supracervical hysterectomy: a metaanalysis. Am J Obstet Gynecol 2008;198:264.e1-264.e5.	<b>Study types included</b> <ul style="list-style-type: none"> <li>randomized clinical trials</li> </ul> <b>Search period/databases</b> <ul style="list-style-type: none"> <li>1966-February 2007</li> <li>PUBMED</li> <li>EMBASE</li> <li>Cumulative Index to Nursing</li> <li>Allied Health Literature (CINHAL)</li> <li>Biological</li> </ul>	<b>Intervention(s)/control</b> <ul style="list-style-type: none"> <li>A metaanalysis of randomized trials was conducted to evaluate if the type of hysterectomy, total abdominal hysterectomy or supracervical hysterectomy, has an impact on the development of urinary incontinence</li> </ul> <b>Primary Outcome:</b>	<b>Selection of Studies</b> <ul style="list-style-type: none"> <li>After the online search, a total of 734 abstracts were identified of which 11 were deemed eligible for full review.</li> <li>Reviewing bibliographies identified 2 additional articles</li> <li>Full reviews of these 13 studies identified 3 studies that met eligibility. [15-17]</li> <li>Reasons for exclusion were: 4 had duplicate data,</li> </ul>	<b>Methods:</b> <ul style="list-style-type: none"> <li>Data abstraction was performed independently by two investigators by using standard data collection forms.</li> <li>Both the investigators reviewed the abstracted data before analysis and disagreements were resolved by discussion.</li> <li>The methodologic</li> </ul>	<b>Thakar R, Ayers S, Clarkson P, Stanton S, Manyonda I.</b> Outcomes after total versus subtotal abdominal hysterectomy. N Engl J Med 2002;347:1318-25.  <b>Learman LA, Summitt RL Jr, Varner RE, et al.</b> A randomized comparison of total or supracervical hysterectomy: surgical	1a



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	<ul style="list-style-type: none"> <li>Abstracts</li> <li>Cochrane Library</li> <li>Cochrane Central Register of Controlled Trials</li> <li>the National Institutes of Health (NIH) Clinical Trials Registry</li> <li>the Current Controlled Trials.</li> <li>supplemented by scanning bibliographies and contacting experts.</li> <li>In addition, abstracts presented at major American and international</li> </ul>	<ul style="list-style-type: none"> <li>The primary outcome measure was the development of urinary incontinence (stress and/or urge urinary incontinence).</li> </ul> <p><b>Secondary Outcome:</b></p> <ul style="list-style-type: none"> <li>Secondary outcome measures were urinary frequency and incomplete emptying.</li> </ul>	<p>1 did not have 1-year follow-up, 1 compared different TAH procedures (not SCH), 2 were observational, and 2 were nonrandomized.</p> <p><b>Main results</b></p> <ul style="list-style-type: none"> <li>SCH did not demonstrate a higher risk of stress urinary incontinence developing compared with TH (relative risk, 1.3 95% CI, 0.94-1.78)</li> <li>Nor were the results statistically significantly different for urge incontinence, frequency, or incomplete emptying</li> <li>The Begg's plot was used to measure bias indicating no</li> </ul>	<p>quality of the included trial was independently scored by using the validated Jadad 5-point scale. Higher scores indicating better reporting.</p> <ul style="list-style-type: none"> <li>Relative risk was calculated for each outcome variable.</li> <li>Metaanalysis was carried out with the use of a fixed effect model to calculate summary relative risk estimates and 95% CIs.</li> <li>The <math>\chi^2</math> test was used to measure heterogeneity and considered significant if</li> </ul>	<p>complications and clinical outcomes. Obstet Gynecol 2003; 102: 453-62.</p> <p><b>Gimbel H, Zobbe V, Andersen BJ, et al.</b> Lower urinary tract symptoms after total and subtotal hysterectomy: results of a randomized controlled trial. Int Urogynecol J Pelvic Floor Dysfunct 2005;16:257-62.</p>	



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	<p>urogynecology meetings were searched by hand, from 2003-2005.</p> <p><b>Inclusion criteria/ search algorithm:</b></p> <ul style="list-style-type: none"> <li>• "hysterectomy AND "ncontinence."</li> <li>• relevant articles in any language</li> <li>• Abstracts were considered for full review if they contained original data</li> <li>• randomized trial comparing total abdominal</li> </ul>		<p>publication bias or study effect bias (<math>p = .24</math>).</p> <p><b>Single study description</b></p> <p><b>15. Thakar et al 2002</b></p> <ul style="list-style-type: none"> <li>• Patients: SCH: 133, TH. 146</li> <li>• <i>Method:</i> standardized questionnaires</li> <li>• <i>Follow-up:</i> 12 months</li> <li>• <i>Results:</i> no significant difference for stress incontinence and urge incontinence</li> <li>• <i>Statistics:</i> not relevant due to metaanalysis</li> <li>• <i>Countries/centres:</i> ethnic groups reported/multicenter</li> </ul> <p><b>16. Learman et al 2003</b></p>	<p><math>p &lt; .05</math>.</p> <ul style="list-style-type: none"> <li>• We assessed for presence of bias with the funnel plot for asymmetry (Begg's plot).</li> </ul> <p><b>Limitations Overview:</b></p> <ul style="list-style-type: none"> <li>• The primary objective of the trial by Learman et al [16] was to compare surgical complications. Urinary incontinence was a secondary outcome unlike the two other trials.</li> <li>• There were differences in the patient characteristics Menopausal status and</li> </ul>		



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	<p>hysterectomy (TAH) and SCH</p> <ul style="list-style-type: none"> <li>urinary incontinence as an outcome.</li> </ul> <p><b>exclusion criteria</b></p> <ul style="list-style-type: none"> <li>Trials involving radical hysterectomy or</li> <li>prolapse surgery were excluded.</li> </ul>		<ul style="list-style-type: none"> <li><i>Patients:</i> SCH: 68, TH. 67</li> <li><i>Method:</i> standardized questionnaires</li> <li><i>Follow-up:</i> 24 months (12 months results used for metaanalysis)</li> <li><i>Results:</i> no significant difference for stress incontinence and urge incontinence</li> <li><i>Statistics:</i> not relevant due to metaanalysis</li> <li><i>Countries/centres:</i> ethnic groups reported/multicenter</li> </ul> <p><b>17. Gimbel H et al 2005</b></p> <ul style="list-style-type: none"> <li><i>Patients:</i> SCH: 161, TH. 158</li> <li><i>Method:</i> standardized</li> </ul>	<ul style="list-style-type: none"> <li>bilateral salpingo-oophorectomy was well documented in two trials [15,16] but not described in the trial by Gimbel et al. [17]</li> <li>There was a large diversity amongst the trials in ethnic background.</li> <li>Learman et al [16] performed 3 incontinence surgeries concomitantly in both groups.</li> <li>Each trial developed its own method of reporting urinary symptoms by using standardized questionnaires.</li> </ul>		





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			<p>questionnaires</p> <ul style="list-style-type: none"> <li>• <i>Follow-up:</i> 12 months</li> <li>• <i>Results:</i> no significant difference for stress incontinence and urge incontinence</li> <li>• <i>Statistics:</i> not relevant due to metaanalysis</li> <li>• <i>Countries/centres:</i> ethnic groups not reported/multicenter</li> </ul>	<p><b>Study characteristics:</b></p> <p><b>15. Thakar et al 2002</b></p> <ul style="list-style-type: none"> <li>• <i>Jadad-score:</i> 4</li> <li>• <i>Randomization:</i> yes, method not reported</li> <li>• <i>allocation concealment:</i> not reported</li> <li>• <i>blinding:</i> yes</li> <li>• <i>Intention to treat analysis:</i> yes</li> <li>• <i>Drop out/Loss to follow-up:</i> 32</li> </ul> <p><b>16. Learman et al 2003</b></p> <ul style="list-style-type: none"> <li>• <i>Jadad-score:</i> 3</li> <li>• <i>Randomization:</i> yes, method not reported</li> <li>• <i>allocation concealment:</i> not reported</li> <li>• <i>blinding:</i> no</li> </ul>		



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
				<ul style="list-style-type: none"> <li>• <i>Intention to treat analysis: yes</i></li> <li>• <i>Drop out/Loss to follow-up: 10</i></li> <li>• <b>17. Gimbel H et al 2005</b></li> <li>• <i>Jadad-score: 3</i></li> <li>• <i>Randomization: yes, method not reported</i></li> <li>• <i>allocation concealment: not reported</i></li> <li>• <i>blinding: no</i></li> <li>• <i>Intention to treat analysis: yes</i></li> <li>• <i>Drop out/Loss to follow-up: 42</i></li> </ul>		
SR/Meta-analysis Walsh CA et al, 2009 "Total abdominal hysterectomy versus total laparoscopic hysterectomy for benign"	Study Type : Randomized Controlled Trials Search period: 1989-8/2007 <b>Databases :</b>	Comparison of patients with total laparoscopic (TLH) versus total abdominal hysterectomy ) benign disease	Study selection 391hits/24fulltexts/3 studies included (Flow Chart) 201 patients (103 = total abdominal hysterectomy/ 98=	3 small RCT with moderate – high risk of bias Jadad Score: <b>1.Perino = 1</b> No inclusion/excl	<b>1.Perino A,</b> Cucinella G, Venezia R, et al, Total laparoscopic hysterectomy versus total	1a-



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
Disease“	PubMed/Medline, Cochrane Library (Systematic Reviews, Controlled Trials) In-/Exclusion criteria : Randomized Controlled Trials, Comparison of patients with total laparoscopic (TLH) versus total abdominal hysterectomy (TAH) for benign disease	Primary outcome: Incidence of complications <b>Major complications:</b> visceral damage (bladder, ureter or bowel), vaginal vault dehiscence and other life-threatening complications, such as thromboembolic disease <b>Minor complications:</b> pelvic haematoma, febrile morbidity(not specified),the need for blood transfusion and other miscellaneous complications, including anaesthetic problems and	total laparoscopic hysterectomy) 1. Total peri-operative complications TAH: 31/103 TLH: 9/98 pooled Odds Ratio 0.19[0.07-0.50] p=0,0008 2. <b>Patients with complications</b> TAH:24/103 TLH: 9/98 pooled OR 0.31 [0.13–0.75] p= 0.009 3. <b>Major complications</b> TAH: 3/103 TLH: 4/98 pooled OR 1.35 [0.32–5.73] 0.68 4. <b>Minor complications</b> TAH: 28/103 TLH: 5/98 pooled OR 0.12 [0.04–0.35] p=0.0001 (n.s : blood transfusion (3 vs 0), febrile morbidity (11	inclusion criteria specified; randomisation not good explained, no blinding, no power calculation No substantial baseline differences <b>2.Ribeiro = 1</b> inclusion/exclusion criteria specified; randomisation not good explained, no blinding, no power calculation, No substantial baseline differences? <b>3.Kluiers= 2</b> Inclusion/exclusion	abdominal hysterectomy: an assessment of the learning curve in a prospective randomized study. Hum Reprod 1999;14 (December 12)): 2996–9. <b>2.Ribeiro SC,</b> Ribeiro RM, Santos NC, Pinotti JA. A randomized study of total abdominal, vaginal and laparoscopic hysterectomy. Int J Gynaecol Obstet 2003; 83(October (1)):37–43. <b>3. Kluiers KB,</b> Hendriks JC, Mol BW, et al. Quality of life and	



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		<p>vault</p> <p>Granulation</p> <p><b>Secondary outcomes:</b></p> <p>operative time, estimated blood loss, hospital stay, post-operative pain scores and costeffectiveness.</p>	<p>vs 4), borderline significant hematoma (8 vs 0)</p> <p>Insufficient data were available to draw conclusions on pain scores or the relative cost-effectiveness of the two surgical approaches.</p> <p><b>Operative time</b> :significantly longer in the laparoscopic group (WMD 22 min; 95% CI 5–39 min; p = 0.01). evidence of heterogeneity =Cochran's Q 0.007) rate of conversion to laparotomy 2% (2/98) in TLH</p> <p><b>Estimated blood loss</b>, two series .TLH with a significant decrease in the estimated blood loss compared to TAH (WMD 183 ml; 95%</p>	<p>n criteria specified; randomisation good explained, no blinding, power calculation, No substantial baseline differences?</p>	<p>surgical outcome after total laparoscopic hysterectomy versus total abdominal hysterectomy for benign disease: a randomized, controlled trial. J Minim Invasive Gynecol 2007; 14(Mar–April (2)):145–52.</p>	



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			<p>CI 346 ml to 21 ml; p = 0.03). Evidence of heterogeneity (Cochran's Q &lt; 0.0001).</p> <p><b>Hospital stay</b> (2 studies), non-significant trend towards reduced hospital stay in the TLH group (WMD - 2.5 days; 95% CI -5.1 to 0.01; p = 0.05), evidence of heterogeneity (Cochran's Q &lt; 0.0001).</p>			
<p>Agdi M1, Al-Ghafri W, Antolin R, 2009</p> <p>Study and Systematic Review</p> <p>Vaginal Vault Dehiscence after Hysterectomy</p>	<p><b>Study type:</b> Not specified</p> <p><b>Search period, Data bases:</b> Search period not specified, Search in MEDLINE, EMBASE, and the Cochrane Database</p>	<p>Patients after hysterectomy</p>	<p><b>Definition vault dehiscence:</b> We defined vault dehiscence as separation or rupture of the vaginal vault edges and pelvic peritoneum with or without evisceration of the pelvic-abdominal contents.</p>	<p>No methodological assessment</p>	<p><b>Hur HC</b>, Guido RS, Mansuria SM, Hacker MR, Sanfilippo JS, Lee TT. J Minim Invasive Gynecol. 2007; 14: 311–317.</p> <p><b>Iaco PD</b>, Ceccaroni M, Alboni C, et al. Eur J Obstet</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	of Systematic Reviews using keywords "vault dehiscence," "vaginal vault dehiscence," "vault prolapse," and "hysterectomy," and conducted the		<p><b>Study selection:</b> not mentioned</p> <p><b>Results of study and systematic review:</b></p> <p><b>Study:</b> n=16 after total hysterectomy</p> <p><b>Review:</b> n= 38 in</p> <p><b>Combined:</b> When we combined groups A and B, among the 3 types of hysterectomy, <b>51.9% of vaginal vault dehiscence occurred after laparoscopic hysterectomies, whereas 33.3% and 14.8% occurred after abdominal and vaginal hysterectomies, respectively.</b> Menorrhagia, myoma uterus, and chronic pelvic pain were the</p>		<p>Gynecol Reprod Biol. 2006; 125:134–138.</p> <p><b>Somkuti SG,</b> Vieta PA, Daugherty JF, Hartley LW, Blackmon EB Jr. Am J Obstet Gynecol. 1994 ; 171: 567–568.</p> <p><b>Aharoni A,</b> Kaner E, Levitan Z, Condrea A, Degani S, Ohel G. Int J Gynaecol Obstet. 1998;63:29–32.</p> <p><b>Ramirez PT,</b> Klemer DP. Obstet Gynecol Surv. 2002; 57: 462–467.</p> <p><b>Mousa AZA,</b> Tulandi T. J Obstet Gynecol Can. 2008</p> <p><b>Narducci F,</b> Sonoda Y, Lambaudie E,</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>most common indications for hysterectomy in all cases.</p> <p><b>Of a total 10 632 hysterectomies, the incidence of vault dehiscence was higher after laparoscopic hysterectomy (1.14%) than after TAH (0.1%, <math>p &lt; 0,0001</math>, OR 11.5) and after vaginal hysterectomy (0.14%, <math>p &lt; 0,001</math>, OR 8.3).</b></p>		<p>Leblanc E, Querleu D. Gynecol Oncol. 2003; 89: 549–551. <b>Powell JL</b>. Am. J Obstet Gynecol. 1973; 115: 276–277. <b>Cullins V</b>, Anastasi J, Huggins GR. J Reprod Med. 1989; 34: 426–428. <b>Guttman A</b>, Afilalo M. Am J Emerg Med. 1990; 8: 127–128. <b>Kowalski LD</b>, Seski JC, Timmins PF, Kanbour AI, Kunschner AJ, Kanbour-Shakir A. J Am Coll Surg. 1996; 183: 225–229. <b>Ferrera PC</b>, Thibodeau LG. J Emerg Med. 1999; 17: 665–667. <b>Pelikan</b></p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
					HM, Engelen MJ. Ned Tijdschr Geneesk. 2007;151:2281–2283	
Systematic Review Kluivers et al. 2008: Comparison of laparoscopic and abdominal hysterectomy in terms of quality of life: A systematic review. European Journal of Obstetrics & Gynecology and Reproductive Biology 136 (2008) 3–8	Study types included RCT Search period/databases PUBMED Jan 1966 – Jan 2006 EMBASE Jan 1980 – Jan 2006 Inclusion criteria/ search algorithm: (laparoscop* OR abdominal) AND RCT AND postoperative health and quality of life	Intervention(s)/ control • Laparoscopic vs. abdominal hysterectomy Primary Outcome: • None Secondary Outcome: • postoperative health and quality of life as a secondary outcome	Selection of Studies -29 full texts from 670 studies in PUBMED, 24 full texts from 579 studies in EMBASE, 1 study listed in EMBASE but not in PUBMED = 30 full texts. -7 studies reported postoperative QoL comprising 1450 women undergoing hysterectomy. 874 women were randomized to a laparoscopic approach (LH) and 576 women were randomized to abdominal surgery (AH). Only benign	<b>Limitations</b> - Overview: Four studies [11,18,25,28], especially the older studies, made use of non-validated measurement methods to evaluate postoperative health and quality of life, of which one study used both a validated and a non-validated method [18]. These studies failed to describe the methods used [11,18,25] or did	[25] Raju KS, Auld BJ. A randomised prospective study of laparoscopic vaginal hysterectomy versus abdominal hysterectomy each with bilateral salpingoophorectomy. Br J Obstet Gynaecol 1994; 101(December (12)): 1068–71. [9] Ellstrom M, Ferraz-Nunes J, Hahlin M, Olsson	2a (downgraded due to the low quality RCTs included)





Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>lesions were included.</p> <p>Main results</p> <p>-Four studies [11,18,25,28], failed to describe the methods used [11,18,25] or did not adequately present the results [28], thus hampering interpretation of the data.</p> <p>-Nonetheless, three out of four studies concluded that laparoscopic hysterectomy was more favourable over abdominal hysterectomy [11,25,28].</p> <p>Single study description</p> <p>Raju [25] 1994</p> <ul style="list-style-type: none"> <li>Patients: LH n = 40, AH n = 40,</li> <li>Method: Questioning</li> </ul>	<p>not adequately present the results [28], thus hampering interpretation of the data.</p> <p>-Different approaches to laparoscopic surgery were used, ranging from LAVH to TLH and LSH. Although three studies used more than one laparoscopic approach, the quality of life data were not presented per subgroup [18,28,13]. In four studies [9,10,25,28] the abdominal procedure was only described briefly whereas the other three studies [11,13,18] did not</p>	<p>JH. A randomized trial with a cost-consequence analysis after laparoscopic and abdominal hysterectomy. Obstet Gynecol 1998;91(January (1)):30-4.</p> <p>[11] Falcone T, Paraiso MF, Mascha E. Prospective randomized clinical trial of laparoscopically assisted vaginal hysterectomy versus total abdominal hysterectomy. Am J Obstet Gynecol 1999;180 (April (4)): 955-62.</p> <p>[18] Lumsden MA, Twaddle S, Hawthorn R, et</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p><i>Follow-up:</i> 6 weeks  <i>Results:</i> LH better than AH  <i>Statistics:</i> not reported  <i>Countries/centres:</i> UK/ 1</p> <p>Ellstrom [9] 1998</p> <ul style="list-style-type: none"> <li><i>Patients:</i> LH n = 38, AH n = 38  <i>Method:</i> SF 36 health survey  <i>Follow-up:</i> 1,3,12 weeks  <i>Results:</i> LH better than AH  <i>Statistics:</i> not reported  <i>Countries/centres:</i> Sweden/ not reported</li> </ul> <p>Falcone [11] 1999</p> <ul style="list-style-type: none"> <li><i>Patients:</i> LH n = 24, AH n = 24  <i>Method:</i> Daily diary</li> </ul>	<p>provide any information on the surgical technique.</p> <p>-Only two out of the four studies that used validated quality of life measurement resulted in significant differences between the treatment groups and showed better quality of life after laparoscopic hysterectomy in the early postoperative period, i.e. in the first 6 weeks [9,13].</p> <p>..... The follow-up period was longer than 6 weeks in all studies, but no statistically significant differences between study groups were found</p>	<p>al. A randomised comparison and economic evaluation of laparoscopic-assisted hysterectomy and abdominal hysterectomy. BJOG 2000;107(November (11)): 1386–91.</p> <p>[28] Schutz K, Possover M, Merker A, Michels W, Schneider A. Prospective randomized comparison of laparoscopic-assisted vaginal hysterectomy (LAVH) with abdominal hysterectomy (AH) for the treatment of the</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p><i>Follow-up:</i> 6 weeks</p> <p><i>Results:</i> LH better than AH</p> <p><i>Statistics:</i> not reported</p> <p><i>Countries/centres:</i> USA/1</p> <p>Lumsden [18] 2000</p> <ul style="list-style-type: none"> <li><i>Patients:</i> LH n = 100, AH n = 100</li> <li><i>Method:</i> Achievement of milestones, VAS Euroqol 5D</li> <li><i>Follow-up:</i> Baseline, 1 month, 6 months, 12 months</li> <li><i>Results:</i> no difference between both groups</li> <li><i>Statistics:</i> not reported</li> <li><i>Countries/centres:</i></li> </ul>	<p>beyond this time point.</p> <p>-Quantitative data are not reported. Only for Garry [13] 2004 it was mentioned that the great number of patients yielded to a significant but clinically irrelevant difference.</p> <p>-Heterogeneity of the studies can not be calculated</p> <p>Study characteristics:</p> <p>Raju [25] 1994</p> <p>-Randomization yes, allocation concealment yes, blinding: not reported, Intention to treat analysis not reported, Drop out / Loss to follow-up 0%</p> <p>Ellstrom [9] 1998</p>	<p>uterus weighing &gt;200 g. Surg Endosc 2002;16(January (1)):121–5.</p> <p><b>[10]</b> Ellstrom MA, Astrom M, Moller A, Olsson JH, Hahlin M. A randomized trial comparing changes in psychological well-being and sexuality after laparoscopic and abdominal hysterectomy. Acta Obstet Gynecol Scand 2003;82(September (9)):871–5.</p> <p><b>[13]</b> Garry R, Fountain J, Mason S, et al. The evaluate study: two parallel randomised</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>es UK/3 Schutz [28] 2002</p> <ul style="list-style-type: none"> <li>Patients: LH n = 28, AH n = 20 Method: 18 items questionnaire Follow-up: 12 month Results: LH better than AH Statistics: not reported Countries/centres: Germany/1</li> </ul> <p>Ellstrom [10] 2003 Series 1</p> <ul style="list-style-type: none"> <li>Patients: LH n = 36, AH n = 38 Method: Psychological General Well-Being Index Follow-up: Baseline, 1 year</li> </ul>	<p>-Randomization: yes, allocation concealment: not reported, blinding: not reported, Intention to treat analysis: not reported, Drop out / Loss to follow-up: not reported</p> <p>Falcone [11] 1999</p> <p>-Randomization: yes, allocation concealment: yes, blinding: no, Intention to treat analysis: yes, Drop out / Loss to follow-up: not reported</p> <p>Lumsden [18] 2000</p> <ul style="list-style-type: none"> <li>Randomization: yes, allocation concealment: yes, blinding: not reported, Intention to treat analysis: yes, Drop out / Loss to follow-up: up to</li> </ul>	<p>trials, one comparing laparoscopic with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. BMJ 2004;328 (January (7432)):129.</p> <p>[29] Sculpher M, Manca A, Abbott J, Fountain J, Mason S, Garry R. Cost effectiveness analysis of laparoscopic hysterectomy compared with standard hysterectomy: results from a randomised trial. BMJ 2004;328 (January</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>Results: no difference between both group</p> <p>Statistics: not reported</p> <p>Countries/centres: Sweden/1</p> <p>Series 2</p> <ul style="list-style-type: none"> <li>Patients: LH n = 29, AH n = 33</li> <li>Method: McCoy Scale</li> <li>Follow-up: Baseline, 1 year</li> <li>Results: no difference between both groups</li> <li>Statistics: not reported</li> <li>Countries/centres: Sweden/1</li> </ul> <p>Garry [13] 2004<sup>1)</sup>,</p> <ul style="list-style-type: none"> <li>Patients: LH n = 584, AH n = 292</li> </ul>	<p>53% within 12 months</p> <p>Schutz [28] 2002</p> <ul style="list-style-type: none"> <li>Randomization: yes, allocation concealment: yes, blinding: not reported, Intention to treat analysis: not reported, Drop out / Loss to follow-up: not reported</li> </ul> <p>Ellstrom [10] 2003</p> <ul style="list-style-type: none"> <li>randomization: not reported, allocation concealment: not reported, blinding: not reported, Intention to treat analysis: no, Drop out / Loss to follow-up: not reported</li> </ul> <p>Garry [13] 2004<sup>1)</sup>, Sculpher [29] 2004<sup>1)</sup></p>	(7432):134.	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p><i>Method:</i> SF 12 health survey, Body image scale, Sexual activity questionnaire</p> <p><i>Follow-up:</i> Baseline, 6 weeks, 4 months, 12 months</p> <p><i>Results:</i> LH better than AH</p> <p><i>Statistics:</i> not reported</p> <p><i>Countries/centres:</i> UK, South Africa/30</p> <p>Sculpher [29] 2004<sup>1)</sup></p> <ul style="list-style-type: none"> <li><i>Patients:</i> LH n = 573, AH n = 286</li> </ul> <p><i>Method:</i> Euroqol 5D and QALYs</p> <p><i>Follow-up:</i> Baseline, 6 weeks, 4 months, 12 months</p>	<ul style="list-style-type: none"> <li>Randomization: yes, allocation concealment: yes, blinding : not reported, Intention to treat analysis: yes, Drop out / Loss to follow-up: up to 50% depending upon follow-up period and method used</li> <li><sup>1)</sup> same study population</li> </ul>		



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			months Results: LH better than AH Statistics: not reported Countries/centres: UK, South Africa/30 1) same study population			
<b>Systematic Review</b>  Brandsborg B. et al. 2008 : Chronic pain after hysterectomy, Acta Anaesthesiol Scand 2008; 52: 327–331	<b>Study types included</b> <ul style="list-style-type: none"> <li>Retrospective studies</li> <li>Prospective observational studies</li> <li>One RCT with randomization between general and spinal anaesthesia</li> </ul> <b>Search period/ databases</b> A computerized search in the	The review summarizes studies on chronic pain following hysterectomy. The underlying mechanisms and risk factors for the development of chronic posthysterectomy pain are discussed	<ul style="list-style-type: none"> <li><b>Selection of Studies</b></li> <li>Eleven studies were identified</li> <li>No information about the selection process is available</li> <li><b>Results</b></li> <li>Pain as a pre-operative symptom was reported by as many as 60–100% (8–18),</li> <li>pain was the</li> </ul>	<b>Limitations</b> Overview <ul style="list-style-type: none"> <li>In the present review, a direct comparison between the studies was difficult because the indications for hysterectomy, types of surgery and the methods of pain assessment were different.</li> <li>Pain data were obtained through</li> </ul>	8. Stovall TG, Ling FW, Crawford DA. Hysterectomy for chronic pelvic pain of presumed uterine etiology. Obstet Gynecol 1990; 75: 676–9. 9. Carlson KJ, Miller BA, Fowler FJ Jr. The Maine Women's Health Study: I. Outcomes of hysterectomy. Obstet Gynecol 1994; 83: 556–65.	2a- (prognosis)



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	<p>PubMed and EMBASE search engines was performed during June 2007</p> <p><b>Inclusion criteria/ search algorithm:</b></p> <ul style="list-style-type: none"> <li>... combining and exploring the words: 'pain, chronic pain, pelvic pain, neuropathic pain, visceral pain, neuroplasticity, post-surgical, postoperative, gynaecology, hysterectomy, Pfannenstiel, Joel-Cohen, vertical incision, nerve entrapment, incisional hernia and incisional</li> </ul>		<p>main indication for surgery in three studies (8, 10, 11).</p> <ul style="list-style-type: none"> <li>The pain prevalence 1–2 years after surgery varied between 4.7% and 31.9%, and therefore, surgery did relieve pain in the majority of patients.</li> <li>Pain as a new symptom at follow-up ('acquired pain') was reported in 1–14.9% (9, 16, 18), and 'increased pain' was found in 2.9–5% of women with pre-operative</li> </ul>	<p>interviews or questionnaires (9–18) or through a review of medical records(8).</p> <ul style="list-style-type: none"> <li>In nine studies, pain was described in verbal ratings such as 'present/not present', 'big/medium/small/no problem' and 'very often/fairly often/a few times/not at all'; Only in two studies a numerical rating scale was used (NRS 0–10) (17, 18).</li> </ul>	<p>10. Hillis SD, Marchbanks PA, Peterson HB. The effectiveness of hysterectomy for chronic pelvic pain. <i>Obstet Gynecol</i> 1995; 86: 941–5.</p> <p>11. Tay SK, Bromwich N. Outcome of hysterectomy for pelvic pain in premenopausal women. <i>Aust NZ J Obstet Gynaecol</i> 1998; 38: 72–6.</p> <p>12. Meltomaa SS, Makinen JI, Taalikka MO et al. One-year cohort of abdominal, vaginal, and laparoscopic hysterectomies:</p>	





Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	<p><i>endometriosis</i>.</p> <ul style="list-style-type: none"> <li>• Original studies in English</li> <li>• on hysterectomy for a benign condition were included</li> <li>• if they contained information about pain at least 3 months after surgery.</li> </ul>		<p>pelvic pain (8, 10). Detailed</p> <ul style="list-style-type: none"> <li>• information about the impact of chronic pain on daily life and consumption of analgesics was only presented in one study; pain affected daily life a lot/very much in 5.6% of patients and opioids were used by 6.1% (18).</li> <li>• Pre-operative pain was associated with a higher risk of having pelvic pain at follow-up (15, 18).</li> <li>• The prevalence of</li> </ul>		<p>complications and subjective outcomes. J Am Coll Surg 1999; 189: 389–96.</p> <p>13. Thakar R, Ayers S, Clarkson P et al. Outcomes after total versus subtotal abdominal hysterectomy. N Engl J Med 2002; 347: 1318–25.</p> <p>14. Gimbel H, Zobbe V, Andersen BM et al. Randomised controlled trial of total compared with subtotal hysterectomy with one-year follow up results. Br J Obstet Gynaecol 2003; 110: 1088–98.</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>chronic pain was similar in women who had abdominal and those who had vaginal hysterectomy (8, 9, 16, 18).</p> <ul style="list-style-type: none"> <li>Likewise, no differences in pain frequency were found between total and subtotal abdominal hysterectomy (13, 14) or abdominal, vaginal and laparoscopic hysterectomy (12).</li> <li>One study found concomitant oophorectomy to be associated with poor</li> </ul>		<p>15. Hartmann KE, Ma C, Lamvu GM et al. Quality of life and sexual function after hysterectomy in women with preoperative pain and depression. Obstet Gynecol 2004; 104: 701–9.</p> <p>16. Kjerulff KH, Langenberg PW, Rhodes JC et al. Effectiveness of hysterectomy. Obstet Gynecol 2000; 95: 319–26.</p> <p>17. Sprung J, Sanders MS, Warner ME et al. Pain relief and functional status after vaginal hysterectomy: intrathecal versus general</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>outcome, but it was not specified if this referred to pain (16), and other studies found no influence of oophorectomy on chronic pain (8, 9).</p> <ul style="list-style-type: none"> <li>In two studies, 19.3% and 38.5% of women with chronic pain reported pain located to the scar (11, 18).</li> <li>Previous caesarean section was related to chronic pain in one study (18).</li> <li>General vs. spinal anaesthesia did not affect pain scores</li> </ul>		<p>anesthesia: [Can J Anaesth 2006; 53: 690–700.</p> <p>18. Brandsborg B, Nikolajsen L, Hansen CT et al. Risk factors for chronic pain after hysterectomy: a Nationwide Questionnaire and Database Study. Anesthesiology 2007; 106: 1003–12.</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>after 12 weeks in one randomized study (17).</p> <ul style="list-style-type: none"> <li>• In contrast, a reduced risk of chronic pain after spinal anaesthesia was found in a multiple regression model of risk factors for hysterectomy, but patients were not randomized (17).</li> <li>• The histopathological diagnosis (e.g. fibromyoma, adenomyosis) was not related to pain in two studies (8, 16), but one study</li> </ul>			



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>found that 'no abnormal histopathology' was associated with pain in women with pre-operative chronic pelvic pain</p> <ul style="list-style-type: none"> <li>• (10). Women with pre-operative depression had chronic pain more frequently, and they also had less improved quality of life after hysterectomy (15).</li> <li>• Other risk factors for chronic post-hysterectomy pain were two or more</li> </ul>			



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			pregnancies and being 'economically disadvantaged' (10).			
<b>Cochrane Review</b> Orozco LJ, Salazar A, Clarke J, Tristán M. Hysterectomy versus hysterectomy plus oophorectomy for premenopausal women. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD005638. DOI: 10.1002/14651858.CD005638.pub2.	<b>Study types included</b> <ul style="list-style-type: none"> <li>Randomised controlled and</li> <li>controlled trials</li> </ul> <b>Search period/databases</b> the Cochrane Menstrual Disorders and Subfertility Group Trials Register (December 2005 to October 2007), CENTRAL (The Cochrane	<b>Intervention(s)/control</b> <ul style="list-style-type: none"> <li>hysterectomy (using any surgical approach) without oophorectomy versus hysterectomy (using any surgical approach) with bilateral oophorectomy in premenopausal women with benign gynaecological </li></ul>	<b>Selection of Studies:</b> -We identified a total of 119 abstracts which were retrieved and screened for inclusion by three review authors (LJOS, AS, MT). -No RCTs were identified. Three abstracts were identified as potentially relevant studies and two of these abstracts were included in the review (Aziz 2005a; Aziz 2005b). We excluded the third abstract since it was neither an RCT or a	<b>Limitations Overview:</b> <ul style="list-style-type: none"> <li>The results from both reports should be taken in the context of the methodological limitations of the studies.</li> </ul> <b>Study characteristics:</b> <b>Aziz 2005a, b</b> <ul style="list-style-type: none"> <li>Randomization: no</li> <li>allocation concealment:</li> </ul>	<b>Aziz 2005a :</b> Aziz A, Bergquist C, Nordholm L, Moller A, Silfverstolpe G. Prophylactic oophorectomy at elective hysterectomy Effects on psychological well-being at 1-year follow-up and its correlations to sexuality. Maturitas 2005;51:349-57. <b>Aziz 2005b</b>	2b no more than 1 study population identified



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	Library 2007, Issue 4), MEDLINE (January 1966 to October 2007), EMBASE (January 1985 to October 2007), LILACS (January 1982 to October 2007), NHS Economic Evaluation Database (inception to October 2007), Biological Abstracts (January 1968 to October 2007), Health Technology Assessment Database (inception to October 2007), the Meta RCTs (inception to October 2007). Reference lists	conditions. <b>Primary Outcome:</b> (1) <b>Mortality</b> (ovarian cancer, breast cancer, colon cancer, myocardial infarction, stroke, thrombo-embolism, all cause) (2) <b>Future gynaecological surgical interventions</b> (unilateral or bilateral oophorectomy, any type of pelvic or gynaecological surgery, <b>Secondary Outcome:</b> (1) <b>Adverse events</b> • ovarian neoplasia • pathological fractures as	CCT (Teplin 2007). <b>-The included abstracts were two different publications reporting the same controlled clinical trial (CCT) of 362 women, comparing hysterectomy without bilateral oophorectomy (HYS only) versus hysterectomy plus bilateral salpingo-oophorectomy (HYS + BSO).</b> <b>Main results</b> -We could not find any information from controlled trials about mortality, future gynaecological surgical interventions or adverse events. - The only trial included in this review showed evidence of very low quality of an unclear effect in terms of	no • blinding: no • Intention to treat analysis: per protocol analysis • Drop out / Loss to follow-up: unclear	Aziz A, Brännström M, Bergquist C, Silfverstolpe G. Perimenopausal androgen decline after oophorectomy does not influence sexuality or psychological well-being. Fertility and Sterility ;83(4): 1021–8.	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	<p>of relevant articles</p> <p><b>Inclusion criteria/ search algorithm:</b> "hysterectomy*" AND "oophorectomy*"</p> <ul style="list-style-type: none"> <li>• Randomized controlled trials</li> <li>• Controlled trials</li> <li>• Premenopausal</li> <li>• Benign conditions</li> </ul> <p><b>exclusion criteria</b></p> <ul style="list-style-type: none"> <li>• Women with gynaecological cancer or</li> <li>• postmenopausal women</li> </ul>	<p>defined by trial authors</p> <ul style="list-style-type: none"> <li>• return of endometriosis</li> <li>• pelvic-abdominal pain</li> <li>• (pelvic floor condition (prolapse)</li> <li>• urinary incontinence</li> </ul> <p>-quality of life as defined by trial author</p> <p>-psychological or sexual functioning</p> <p>-patient satisfaction</p> <p>-menopausal symptoms</p>	<p>quality of life, defined as the total scores and items in the PGWB (Psychological General Well-Being) index and the MFSQ (McCoy's Female Sex Questionnaire).</p> <p>The results from both reports suggest that concomitant prophylactic oophorectomy at elective hysterectomy does not negatively affect sexual and psychological well-being in adequately oestrogenized premenopausal women. However, these findings should be taken in the context of the methodological limitations of the studies.</p> <ul style="list-style-type: none"> <li>• <b>Single study description</b></li> </ul>			





Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<ul style="list-style-type: none"> <li>• <b>Aziz 2005a, b</b></li> <li>• <i>Patients:</i> HYS only group: 217, HYS + BSO group: 106.</li> <li>• <i>Methods:</i> questionnaires</li> <li>• <i>Follow-up:</i> 14.2 ± 2.1 months in HYS only group, 13.8 ± 2.0 months in HYS +BSO group.</li> <li>• <i>Results:</i> No significant differences were found between the groups of women studied regarding any aspect of their sexuality</li> <li>• <i>Countries/centres:</i> Sweden/2</li> </ul>			



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
<b>Vergleich roboterassistierter Hysterektomie mit offener und laparoskopischer Hysterektomie</b>						
SR Tapper et al, 2014 (70)	See below	See below	<p>Total results see Below: here cost-effectiveness for benign HE: 4 studies</p> <p>The costs for robotic surgery were reported to be higher than for other techniques although some variation in the costs exists.</p> <p>No cost-effectiveness study was available</p>	Observational studies, retrospective	<p><b>1. Landeen L et al</b>, Clinical and cost comparisons for hysterectomy via abdominal, standard laparoscopic, vaginal and robot-assisted approaches. South Dakota Med 2011;64:197–9.</p> <p><b>2. Sarlos D et al</b>, Robotic hysterectomy versus conventional laparoscopic hysterectomy: outcome and cost analyses of a matched case-control</p>	3



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
					<p>study. Eur J Obstet Gynecol Reprod Biol 2010; 150:92–6.</p> <p><b>3. Wright JD et al</b>, Comparative effectiveness of robotic versus laparoscopic hysterectomy for endometrial cancer. J Clin Oncol 2012;30: 783–91.</p> <p><b>4. Wright KN et al</b>, Costs and outcomes of abdominal, vaginal, laparoscopic and robotic hysterectomies. JSLS 2012; 16:519–24.</p>	
<b>SR</b> Tapper et al, 2014 European Journal of	<b>Study Type :</b> No restriction: Randomized Controlled	P: Comparison of costs for hysterectomy and hospital stay	Search Results: 909hits; included: - clinical effectiveness on hysterectomy for	Information of original study reports Paraiso 2013 and Sarlos	Clinical effectiveness benign	1a



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
Obstetrics & Gynecology and Reproductive Biology (70)	Trials, Systematic Reviews, Health Technology Assessments, observational studies Search period: from inception to June 2013 Databases : PubMed/Medline, Cochrane Library), Centre for Reviews and Dissemination Databases (DARE, HTA and NHS EED) <b>In-/Exclusion criteria:</b> Comparison of patients with robotic assisted	(primary outcome) And duration of operation, length of hospital stay, short-term outcome (complications, oncologic variables) (secondary outcome) of robotassisted hysterectomy (RAH) versus other forms of hysterectomy (laparoscopic = LAH, abdominal hysterectomy = AH)	benign conditions: 1 systematic reviews, 4 HTA reports, 2 RCT, 4 comparative studies 1. Clinical effectiveness – only benign conditions reported: overall: no significant differences Results of observational studies not reported Results of RCT: a. Paraiso 2013 (patients blinded) 2 institutions, USA, 2007-2011, BMI max 44kg/m <sup>2</sup> , eligible patients for lap. HE, stratified per surgeon and uterus </>12week size, 5 surgeons, each trained for robot-assisted OP, at least 20 RAH done. Randomized: n=62; operated as	2012 included because of missing data in the review (drop outs not reported, conversions not reported)	condition RCT <b>1. Paraiso MFR, et al.</b> A randomized trial comparing conventional and robotically assisted total laparoscopic hysterectomy. Am J Obstet Gynecol 2013;208 (368):e1–7. <b>2. Sarlos D,et al.</b> Robotic compared with conventional laparoscopic hysterectomy. A randomized controlled trial. Obstet Gynecol 2012;120:604–11 Observational studies:	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	versus other forms of hysterectomy for malign and benign disease, RCT		<p>randomized: n=53 (no reasons given for all withdrawals, but for some stated in the text: conversions, see below)</p> <p><b>RAH</b> 26/31; <b>LH</b> 27/31</p> <p>Age, BMI, Parity n.s. between groups</p> <p>Loss to follow up: 0, missing data =1L</p> <p><b>per protocol analysis!</b></p> <p><b>Op time (min.):</b> RAH 172.8+/- 89.0, LH 102.7+/-63.7</p> <p>p=0,002, fastest surgeon +46 min. for RAH</p> <p>Op time associated with uterus weight (n.s. between groups: 293.9 +/- 299.9 g vs 282.9 +/- 214.7 g; range, 35–1242 g)</p> <p><b>Length of hosp.(days):</b> 1,4d</p>		<p><b>1. Gocemen AS et al,</b> Robot-assisted hysterectomy vs total laparoscopic hysterectomy: a comparison of short-term surgical outcomes. Int J Med Robotics Comput Assist Surg 2012;8:453–7.</p> <p><b>2. Orady M, et al,</b> Comparison of roboticassisted hysterectomy to other minimally invasive approaches. JSLS 2012; 16:542–8.</p> <p><b>3. Wright JD et al,</b> Robotically assisted vs laparoscopic</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>RAH <u>and</u> LH;  <b>Complications</b> (only major reported): both none  <b>Blood Loss</b>(ml): RAH 283, LH 294 n.s.  <b>Conversions:</b> 1 LH into laparotomy because of bleeding/inability of maintaining pneumoperitoneum, 1 LH received RAH because of error, 2 RAH into LH because of robot malfunction and inability to ventilate  <b>B.Sarlos 2012 (patients not blinded)</b>  1 institution, Aarau, Switzerland, 2008 to 2011, indication if no vaginal HE possible (nullipara, myoma), estimated uterusweight up to 500g. robotic and</p>		<p>hysterectomy among women with benign gynecologic disease. JAMA 2013; 309: 689–98.  <b>4. Landeen L et al</b>, Clinical and cost comparisons for hysterectomy via ab-dominal, standard laparoscopic, vaginal and robot-assisted approaches. South Dakota Med 2011; 64:197–9.  Health Technology Assessments:  <b>1. Camberlin C, Arnaud S, Leys M, De Laet C.</b> Robot-assisted</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>conventional laparoscopic hysterectomy were performed by two senior gynecologic surgeons, performing an average of 50 laparoscopic total hysterectomies per year for almost 10 years and had performed at least 30 robotic hysterectomies before begin of this study</p> <p>Randomized: n=100 patients, 80% power to detect difference of 15min total operating time. n=95 with operation</p> <p>Pat. Characteristics n.s.</p> <p>Missing values (no operation performed on two laparoscopic hysterectomy and</p>		<p>surgery: health technology assessment. Brussels: <b>Belgian Health Knowledge Centre (KCE)</b>. KCE Reports 104C; 2009.</p> <p>2. Ho C, Tsakonas E, Tran K, et al. Robot-assisted surgery compared with open surgery and laparoscopic surgery: clinical effectiveness and economic analyses. <b>Ottawa: Canadian Agency for Drugs and Technologies in Health</b></p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p><b>three robotic hysterectomy patients)</b> were replaced by the median of available measurements in the respective study arm, as well for QoL</p> <p><b>Primary outcome:</b> <b>Total Operating time</b> (first skin incision to last skin suture) robotic group: 106 min(+/-29) laparoscopic group: 75 min (+/-21) (median -29min. P &lt;.001) still significant without docking time</p> <p>Secondary outcome: Net operating time (without "docking time" of robot), 96 +/- 28 robot HE, 75+/-21 LAH diff. 20 (11-29) p&lt; 0,001</p> <p><b>Hospital Stay</b> n.s. (3,3 and 3,1 days)</p>		<p>(CADTH); 2011.</p> <p><b>3.</b> Thavaneswaran P. Robotic-assisted surgery for urological, cardiac and gynaecological procedures. ASERNIP-S Report No. 75. <b>Adelaide, South Australia: ASERNIP-S;</b> 2009, May.</p> <p><b>4.</b> Health technology assessment of robot-assisted surgery in selected surgical procedures. <b>Ireland: Health Information and Quality</b></p>	





Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p><b>- blood loss</b> 87 mL (+/-67) robotic HE, 79 (+/- 57) laparoscopic HE n.s.</p> <p><b>- QoL (before and twice after Op (2-3 and 6-8 weeks))</b> with validated EQ-5D questionnaire, n=75 with data robot group change +13+/-10 LAH: change +5+/-14 p&lt;0,001 Not blinded</p> <p><b>- Complications rates</b> No severe intraoperative complications occurred in either group (n.s.) Minor complications 15 robot 11 LAH n.s.</p> <p><b>-Conversion</b> robot group: 1x to LAH, 5x undocking and vaginal</p>		<p><b>Authority (HIQA);</b> 2012, January. Systematic Review:</p> <p><b>1.</b> Weinberg L, Rao S, Escobar PF. Robotic surgery in gynecology: an updated systematic review. Obstet Gynecol Int 2011;2011: 852061.</p> <p><b>2.</b> Liu H, Lu D, Wang L, Shi G, Song H, Clarke J. Robotic surgery for benign gynaecological disease. Cochrane Database Syst Rev 2012;2:CD0089</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			morcellement LAH: - - <b>Analgetics</b> n.s.		78.	
SR Liu H et al, 2012 Cochrane Collaboration (71)	<p>Studytype : Randomized Controlled Trials Search period : from inception to 21 November 2011 Databases : Cochrane Menstrual Disorders and Subfertility Group Trials Reg., Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, PsycINFO, Chinese Biomedical Lit. Database (CBM), Chinese Medical Current Contents(CMCC), CINAHL, Current Controlled Trials, ClinicalTrials.gov , World Health Organization International Trials Registry, Citation indexes, Conference abstracts on the ISI Web of Knowledge, LILACS (Latin American and Caribbean Health Science Lit. , Clinical StudyResults• OpenSIGLE (grey Literature in Europe), Ref. lists, Hand-searching in 2 chinese and 2 english gynecological journals</p>		<p>285 hits/9full texts/ • 2 RCT in 6 publications (Sarlos 2010, Paraiso 2011) included Not included: • 2 ongoing trials (Kho 2007b; Paraiso 2007) • 1 Metaanalysis of observational studies (Reza 2010) <b>Trial characteristics</b> <b>Sarlos et al 2010:</b> n=80, 40=conventional HE, 40=robotic HE, indication: when vaginal HE was not indicated because of nulliparity of large myoma. Swiss single center trial, conference abstract no further data available, incomplete outcome</p>	<p>• <b>Cochrane Risk of Bias Tool:</b> Blinding only judged for outcome assessors possible) • <b>Tests for heterogeneity</b> were carried out using the Chi2 test, with significance set at P &lt; 0.1. The I2 statistic was used to estimate the total variation across studies that was due to heterogeneity, where &lt; 25% was considered as low-level, 25% to 50% as moderatelevel, and &gt; 50% as high-level heterogeneity <b>Reporting Bias:</b> If</p>	<p>Only 1 trial identified: Sarlos et al, 2010: <b>Sarlos D</b>, Kots LV, Stevanovic N, Schar G. Robotic hysterectomy versus conventional laparoscopic hysterectomy: Costs and preliminary results of a randomized controlled trial. Archives of Gynecology and Obstetrics 2010; 282 Suppl:11–2. [58th Congress of the German</p>	1b-



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	<p>In &amp; Exclusion criteria :</p> <ul style="list-style-type: none"> <li>• Robotic surgery versus laparoscopic surgery</li> <li>• Robotic surgery versus open surgery</li> <li>• Comparison of different types of robot assistants for elective surgery in women with benign gynecological disease</li> </ul> <p>Primary outcomes</p> <ul style="list-style-type: none"> <li>• Intraoperative and postoperative complications</li> <li>• Quality of life (QoL)</li> </ul> <p>Secondary outcomes</p> <ul style="list-style-type: none"> <li>• Early and late mortality (early mortality: death within 30 days; late mortality: death within 3 months)</li> <li>• Total operating time</li> <li>• The instrument set-up time (robotic versus laparoscopic surgery)</li> <li>• Overall and postoperative hospital stay</li> <li>• Estimated blood loss, or transfusion</li> <li>• Cost (direct and indirect costs)</li> <li>• Rate of conversion (convert to open surgery)</li> <li>• Postoperative pain (pain scores, use</li> </ul>		<p>data reporting</p> <p>Risk of bias:</p> <ul style="list-style-type: none"> <li>- methods of sequence generation and allocation concealment were not reported</li> <li>- no information about blinding</li> <li>- No reporting of exclusions after randomisation</li> </ul> <p><b>Results Sarlos et al, 2010:</b></p> <ul style="list-style-type: none"> <li>- <b>no intraoperative complication</b> in either group</li> <li>- <b>no significant differences in the quality of life index</b> were found comparing robotic surgery to laparoscopic surgery. Tools for assessment were not reported.</li> <li>- total operating time for robotic surgery was significantly longer than for laparoscopic surgery (no detailed</li> </ul>	<p>there were 10 or more studies in an analysis, a funnel plot was used to explore the possibility of small study effects (a tendency for estimates of the intervention effect to be more beneficial in smaller studies). Within study reporting bias was detected by seeking published protocols and comparing the outcomes between the protocol and the final published study.</p> <ul style="list-style-type: none"> <li>• The data from primary studies were combined using the fixed effect model</li> </ul>	<p>Society for Gynecology and Obstetrics (Deutsche Gesellschaft für Gynäkologie und Geburtshilfe, D GGG) Munich Germany]</p> <p><b>Paraiso et al 2011:</b> no comparison for methods of hysterectomy</p> <p><b>Ongoing trials:</b></p> <p>Kho 2007b published data only: Laparoscopic Hysterectomy With and Without Robotic Assistance: a Randomized Prospective Trial. Ongoing study March</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	of pain killers)		<p>data)</p> <ul style="list-style-type: none"> <li>-no data on mortality</li> <li>-robotic surgery did not significantly shorten the overall hospital stay as compared to laparoscopic surgery (no detailed data)</li> <li>-robotic surgery failed to significantly reduce intraoperative blood loss as compared to laparoscopic surgery (no detailed data)</li> <li>- the average cost of laparoscopic surgery amounted to EUR1417 (821material, 596 personnel costs),while for robotic surgery was 3384 (2295material, 1088 personnel costs (no statistical result shown)</li> <li>- there was no conversion either in the robotic group or the laparoscopic group</li> </ul>		<p>2007.</p> <p>Paraiso 2007 published data only A</p> <p>Prospective Randomized Trial Comparing Conventional vs. Robotic Assisted Laparoscopic Hysterectomy. Ongoing study June 2007.</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
SR Iavazzo C, Gkegkes ID 2014 Single-Site port robotic-assisted hysterectomy: a systematic review (72)	<b>Search:</b> PubMed and Scopus, and reference lists (29.12.2012), last 10 years, english <b>Inclusion</b> of all studies/case reports for single-site port robot-assisted hysterectomy		6 Reports, 3 single case reports, 3 case series (2-7pat., retrospective, no comparisons), 16 patients altogether 2 cancer, 4 benign disease Age: 34-70 BMI: 15,8-35,8 kg/m <sup>2</sup> Duration: 105-311min, Median: 109,180 Blood Loss: 10-750ml, Median, 50 Uterus weight (2 reports) 40-310g Conversion: 1/16 No transfusion (4 reports) Hospital stay 2-6days No complications reported No follow up reported No results on cosmesis reported	Only very little published data! No comparative studies	<b>Escobar PF,</b> Fader AN, Paraiso MF, Kaouk JH, Falcone T (2009) Robotic-assisted laparoendoscopic single-site surgery in gynecology: initial report and technique. J Minim Invasive Gynecol 16:589–591 <b>Fader AN,</b> Escobar PF (2009) Laparoendoscopic single-site surgery (LESS) in gynecologic oncology : technique and initial report. Gynecol Oncol 114:157–	4



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
					<p>161</p> <p><b>Kane</b> S, S KJ (2010) Laparo-endoscopic single-site surgery hysterectomy using robotic lightweight endoscope assistants. J Robotic Surg 3:253–255</p> <p><b>Nam</b> EJ, Kim SW, Lee M et al (2011) Robotic single-port transumbilical total hysterectomy: a pilot study. J Gynecol Oncol 22:120–126</p> <p><b>Lue</b> JR, Murray B, Bush S (2012) Single port robotic hysterectomy technique</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
					improving on multiport procedure. J Minim Access Surg 8:156–157 <b>Mereu L, Carri G, Khalifa H (2012) Robotic single port total laparoscopic hysterectomy for endometrial cancer patients.</b> Gynecol Oncol 127:644	
<b>Cost-effectiveness hysterectomy for benign conditions</b>						
SR Pynnä et al, 2014 Cost-effectiveness of hysterectomy for benign gynecological conditions (146)	<b>Search:</b> Medline, Cochrane Library, PsycINFO, CINAHL, and Nursing databases, 28 December 2011 and 4 January 2012	<b>All published studies regarding the cost-effectiveness of hysterectomy performed for benign indications</b> - Inclusion criteria were the availability of pre- and post-intervention health-	Study selection and characteristics <b>24 studies included</b> out of 1666 hits 14(58%) from the UK, 3 each (12.5%) from the USA and Finland, two (8%) from China and one (4%) from the Netherlands. One	Study quality measured according to Drummond et al. – specific for cost effectiveness (values 1-10) See Appendix 1 Characteristics of included studies	Beinfeld et al 2004 USA Bhattacharya et al 2011 UK Clegg et al 2007 UK Edwards et al (the REST investigators) 2007 UK	1b Formally downgraded because of different study types and comparisons



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
	Searches were restricted to meta-analyses, systematic reviews, randomized controlled trials and observational studies. Ongoing studies were retrieved from the Clinical-Trials.gov registry	related quality of life measures (HRQoL) and data on costs - HRQoL, costs, and cost-effectiveness of treatment were the main outcome measures	article was authored by a research group partly from Canada and partly from the UK. All but three studies were from the 21st century (87.5%). The older studies were published in 1985 (11), 1993 (12) and 1998 (13). Eight studies (33.3%) were modeling studies, seven (29.2%) were randomized controlled trials, and seven were observational studies. Studies (n = 24) focused on treatment of symptomatic fibroids (n = 8), treatment of heavy menstrual bleeding (n = 10), various surgical techniques (n = 5) and the effect of various indications for hysterectomy (n = 2). Follow-up periods	see Appendix S3	Garry et al 2004 UK Garside et al 2004 UK Hirst et al 2008 UK Hurskainen et al 2001 Finland Hurskainen et al 2004 Finland Kennedy et al 2003 UK Lumsden et al 2000 UK Moss et al 2011 UK Roberts et al 2011 UK Sandberg et al 1985 USA Sculpher et al 1993 UK Schulper 1998 UK Sculpher et al 2004 UK	





Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>varied from 4 months to over 10 years. SF/RAND-36 or EQ-5D measures and societal cost perspective were most commonly used. Only 11 studies used individual patient data.</p> <p>Results</p> <p>HRQoL following hysterectomy was generally good but costs were high. The cost-effectiveness depended on indication, age, and duration of follow-up. The cost-effectiveness of hysterectomy has been surprisingly poorly studied. Conclusions are difficult to draw due to different study designs, indications, follow-up times, and HRQoL instruments used. Rates of</p>		<p>Showstack et al 2004 USA</p> <p>Taipale et al 2009 Finland</p> <p>Volkers et al 2008 The Netherlands</p> <p>Wu et al 2007 UK</p> <p>You et al 2006 China</p> <p>You et al 2009 China</p> <p>Zowall et al 2008 Canada/UK</p>	



Studientyp Quelle	Search/Included Studies	Patients/Intervention/ Comparison/Outcome	Ergebnisse	Methodische Studienqualität	Literaturbelege	Evidenz- niveau CEBM
			<p>hysterectomy have declined less than expected with the introduction of new treatment modalities. Costs of surgery are high. Laparoscopic hysterectomy seem to be the least cost-effective, although further data from original patient cohorts with long-term follow-up are needed.</p>			



### 5.11. Nicht eingeschlossene Publikationen zum Vergleich der Hysterektomieverfahren

Tabelle 16: Nicht eingeschlossene Publikationen zum Vergleich der Hysterektomieverfahren (nach Volltextscreening)

Author, Year, study- or publication typ	Subject/Topic	Reason for exclusion
Adelman JR, Bardsley TR, Sharp HT, 2014, Systematic Review(64) Urinary tract injuries in laparoscopic hysterectomy: a systematic review.	inclusion criteria : published articles in English (last 10 years) of original research referring to urologic injuries occurring during either laparoscopic or robotic surgery for gynecologic indications.  A primary search of the database yielded 104 articles + secondary cross-reference 6 articles, 40 articles met inclusion criteria, 3 were excluded because of an inability to extract urinary tract injuries from total injuries.  Statistical analysis was performed using a generalized linear mixed effects model.  The overall urinary tract injury rate for laparoscopic hysterectomy was 0.73%. The bladder injury rate ranged from 0.05% to 0.66% across procedure types, and the ureteral injury rate ranged from 0.02% to 0.4% across procedure type.	Full text not available , included studies not known incl. study design
Clarke-Pearson DL, Geller EJ, 2013 Complications of hysterectomy Obstet Gynecol. Mar;121(3):654-73	Overview of complications of HE :  Most Common complications of hysterectomy categorized as infectious, venous thromboembolic, genitourinary (GU) and gastrointestinal (GI) tract injury, bleeding, nerve injury, and vaginalcuff dehiscence. Infectious complications after hysterectomy are most common, ranging from 10.5% for abdominal hysterectomy to 13.0% for vaginal hysterectomy and 9.0% for laparoscopic hysterectomy.	No systematic search provided, most often Nieboer et al cited.

Author, Year, study- or publication typ	Subject/Topic	Reason for exclusion
	<p>Venous thromboembolism is less common, ranging from a clinical diagnosis rate of 1% to events detected by more sensitive laboratory methods of up to 12%. Injury to the GU tract is estimated to occur at a rate of 1–2% for all major gynecologic surgeries, with 75% of these injuries occurring during hysterectomy. Injury to the GI tract after hysterectomy is less common, with a range of 0.1–1%. Bleeding complications after hysterectomy also are rare, with a median range of estimated blood loss of 238–660.5 mL for abdominal hysterectomy, 156–568 mL for laparoscopic hysterectomy, and 215–287 mL for vaginal hysterectomy, with transfusion only being more likely after laparoscopic compared to vaginal hysterectomy (odds ratio 2.07, confidence interval 1.12–3.81). Neuropathy after hysterectomy is a rare but significant event, with a rate of 0.2–2% after major pelvic surgery. Vaginal cuff dehiscence is estimated at a rate of 0.39%, and it is more common after total laparoscopic hysterectomy (1.35%) compared with laparoscopic-assisted vaginal hysterectomy (0.28%), total abdominal hysterectomy (0.15%), and total vaginal hysterectomy (0.08%). With an emphasis on optimizing surgical technique, recognition of surgical complications, and timely management, we aim to minimize risk for women undergoing hysterectomy.</p>	
O'Neill M, Moran PS, Teljeur C et al, 2013(147) Robot-assisted hysterectomy compared to open and laparoscopic	To review the safety and effectiveness of robot-assisted hysterectomy compared to traditional open and conventional laparoscopic surgery, differentiating radical, simple total with node staging, and simple total hysterectomy.	Only indications for hysterectomy for cancer considered



Author, Year, study- or publication typ	Subject/Topic	Reason for exclusion
approaches: Systematic review and meta-analysis		
H. G. Kenngott, L. Fischer, F. Nickel et al(148), 2012  Systematic Review  Status of robotic assistance -a less traumatic and more accurate minimally invasive surgery?	Overview of development and actual practice of robotic surgery	No sepcific information on trials for benign gynecological conditions
Wu KY, Lertvikool S, Huang KG et al, 2011(149)  Laparoscopic hysterectomies for large uteri.  Review	Abstract : « we conducted a systematic review of laparoscopic hysterectomies for large uteri. »  Description of soup group analysis comparing complications and conversion rates of LH in uteri </> 500g  Conclusion : There are three key points of successful and efficient laparoscopic hysterectomies for large uteri. First is to insert the primary trocar at the Lee-Huang point and the ancillary trocars at the level of umbilicus at least. Second is to reduce blood loss by GnRH given preoperatively, oxytocin infused intraoperatively, and devascularization of the uterus completely. Third is to remove the specimen from the vagina if possible. According to recent studies, laparoscopic hysterectomies for large uteri by experienced laparoscopists is safe and feasible if the strategies mentioned	No systematic search provided



Author, Year, study- or publication typ	Subject/Topic	Reason for exclusion
	above were strictly followed.	
Niro J, Panel P,(150) 2011  Systematic Review [Management of symptomatic fibroids: role of supracervical hysterectomy and laparoscopy]	Management of symptomatic fibroids: role of supracervical hysterectomy and laparoscopy	No new information, other SR existing for this topic
Scandola M, Grespan L, Vicentini M, Fiorini P , 2011 (151)  Systematic Review and Metaanalysis  Robot-assisted laparoscopic hysterectomy vs traditional laparoscopic hysterectomy: five metaanalyses.	Metaanalysis for robotic surgery in gynecology for end-points :  Bloss loss, operative time, number of conversions to laparotomy, hospital length of stay (LOS), and number of postoperative complications	No differentiation of benign and malignant gynecological condition
Cannone F, Ladaique A, Lambaudie E et al, 2011	Robot-assisted laparoscopy in gynecologic surgery	No abstract available. Full text : no systematic search stated, narrative review



Author, Year, study- or publication typ	Subject/Topic	Reason for exclusion
Robot-assisted laparoscopy in gynecologic surgery.		
Forsgren C, Altman D 2010(152) Review	<p>Risk of pelvic organ fistula in patients undergoing hysterectomy The reported incidence of pelvic organ fistula after hysterectomy ranges from 0.1 to 4% in different studies, and a higher incidence is generally reported after radical hysterectomy compared with hysterectomy on benign indications.</p> <p>Evidence from observational studies suggests that hysterectomy increases the risk for pelvic organ fistula disease compared with women with an intact uterus and that risk factors include laparoscopic and total abdominal hysterectomy, increasing age, smoking, diverticulitis and pelvic adhesions</p>	No systematic search stated
Bijen CB1, Vermeulen KM, Mourits MJ, et al, 2009 (153)  Costs and effects of abdominal versus laparoscopic hysterectomy: systematic review of controlled trials.	<p>Analysis was performed on 2226 patients, of which 1013 (45.5%) in the LH group and 1213 (54.5%) in the AH group. Five studies scored \$10 points (out of 19) for methodological quality. The reported total direct costs in the LH group (\$63,997) were 6.1% higher than the AH group (\$60,114). The reported total indirect costs of the LH group (\$1,609) were half of the total indirect in the AH group (\$3,139). The estimated mean major complication rate in the LH group (14.3%) was lower than in the AH group (15.9%). The estimated total costs in the LH group were \$3,884 versus \$3,312 in the AH group. The incremental costs for reducing one patient with major complication(s) in the LH group compared to the AH group was \$35,750.</p> <p>Conclusions: The shorter hospital stay in the LH group compensates for the increased procedure costs, with less morbidity. LH points in the direction of cost</p>	Cost effectiveness not a primary outcome



Author, Year, study- or Subject/Topic publication typ	Reason for exclusion
	effectiveness, however further research is warranted with a broader costs perspective including long term effects as societal benefit, quality of life and survival.

## 5.12. Kosten-Effektivität von Hysterektomieverfahren: Systematischer Review

Tabelle 17: Kosten-Effektivität von Hysterektomieverfahren: Systematischer Review von Pynnä et al, 2014

Study Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations





Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
Beinfeld et al 2004 USA		To compare the cost-effectiveness (CE) of uterine artery embolization (UAE) with that of hysterectomy for women with symptomatic uterine fibroids	Hypothetical cohort of women aged 40 years with a diagnosis of uterine fibroids and no desire for future pregnancy	Monte Carlo Markov decision model	EQ-5D, RAND-36, QWB, TTO	Societal perspective  Costs computed from the 1999 Medicare Provider Analysis and Review database. Additional cost information retrieved from hospital accounting database  Total costs until menopause (\$) No treatment 4,949 Hysterectomy 7,847 UAE 6,916	QALYs No treatment 7,31 Hysterectomy 8,18 UAE 8,29  ICER (\$) No treatment 0 Hysterectomy, dominated by UAE UAE 2,007	UAE a cost-effective alternative to hysterectomy for management of symptomatic uterine fibroids. Results sensitive only to changes in the model parameters of costs and QoL.	10	Interventions after hysterectomy not modeled. Ovarian failure, which is an important complication associated with UAE, was not included in our model. Only costs of MR imaging performed after UAE were included.  Results of study apply only to women with no desire for future pregnancy  Limitations regarding the uncertainty surrounding several model parameters although taken into account by means of sensitivity analysis.
Bhattachar		To determine	2814 women	Systematic review and individual	EQ-5D,	UK NHS perspective	Total QALYs:	Hysterectomy	10	Individual



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
ya et al 2011 UK		the clinical effectiveness and CE of hysterectomy, first- and second-generation endometrial ablation (EA), and Mirena® for the treatment of heavy menstrual bleeding	treated for heavy menstrual bleeding in national and international trials.  Economic model: hypothetical cohort of 10,000 eligible women compared for each strategy (x4)	patient data meta-analysis, Markov model	RAND-36, TTO	Total costs (1000£): 1.gen. EA 23 590 2.gen. EA 19 470 hysterect. 23 000 Mirena 16 150	1) 1.gen EA 63 745 2) 2.gen EA 69 582 3) hysterect. 73 332 4) Mirena 68 566  ICER vs hysterectomy 1) hysterectomy dominates 2) 970 £/add. QALY 4) 1440 £/add. QALY	is the most cost-effective treatment strategy for heavy menstrual bleeding.  EA satisfactory for a very high proportion of women, but it doesn't yield complete cessation of bleeding. Mirena should be offered before more invasive procedures although relatively few trials have yet evaluated the effectiveness of Mirena.		patient data (IPD) from at least 35% of randomised women were unavailable. The outcome measures used across trials inconsistent; studies involving EA and Mirena focused on comparing reduction in bleeding, while hysterectomy trials focused on patient satisfaction, QoL and resource usage. Available long-term follow-up data on Mirena use are so inconsistent that interpretation of this data must be cautious.  In addition, the fact that the



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
										complexity of the model contributed to a long running time has some effect on the extent of sensitivity analyses that were undertaken.
Clegg et al 2007 UK		To estimate the cost-utility (CU) of levonorgestrel intrauterine system (LNG-IUS; Mirena) compared to second generation endometrial ablative techniques [i.e. microwave endometrial ablation (MEA) and thermal balloon endometrial ablation (TBEA)) and hysterectomy in the treatment of menorrhagia in the UK.	Five hypothetical cohorts of women with heavy menstrual bleeding	State-transition Markov-model	EQ-5D	NHS UK perspective  Costs/patient over 5years (£) IUS+abl 828 IUS+hyst 1355 TBEA 1679 MEA 1812 Hysterect. 2983  Online-survey in UK: IUS £328	QALYs gained/patient IUS+abl 4.14 IUS+hyst 4.12 TBEA 4.13 MEA 4.13 Hysterect. 4.01  Online-survey: IUS 4.12  For cost/QALY to exceed £30000 threshold in IUS+abl, would the failure rate of IUS have to augment from used 42.6%	IUS followed by ablation when needed offers a cost-effective treatment of menorrhagia over a 5year time period. The health-benefits of the treatments measured as QALYs were not substantially different between groups. Thus individual preferences and circumstances essential.	10	Finnish patient cohort may differ from UK patients, utility values may vary, the probabilities of outcomes and resource use for the model were extrapolated from different sources rather than directly observed. Model time period 5years since IUS must be replaced after that time, the other treatments are, however, permanent. Thus the



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							(Hurskainen data) to 85.5% compared to MEA alone and 90.3% to TBEA as primary treatment. Thus IUS followed by ablation if needed seems to dominate CUA			model may overstate the long-term health economic benefits of IUS. Nevertheless, the cost of replacing an IUS is small compared to total cost of therapy of menorrhagia. Only direct healthcare costs. Utility values and resource use estimates of "an average patient", thus does not take into account individual factors or circumstances.
Edwards et al (the REST investigators) 2007 UK		To assess the safety and efficacy of uterine artery embolization (UAE) versus surgery in the treatment of	157 patients undergoing treatment for symptomatic uterine fibroids (106 UAE, 51 surgery (43 hysterectomy	Randomized trial. Primary outcome: SF-36 at 1mo and 1y after treatment. Secondary outcomes: EQ-5D, 11-point symptom score, time to recovery of normal activities, satisfaction score, complications, adverse events, need for further	SF-36, EQ-5D	NHS UK perspective  Mean cost/patient over one year (£)  UAE 1727	No significant difference between the groups in any of the 8 components of the SF-36 at 12 months. At 1mo	No significant difference between the groups in QoL at 1y. Both groups had significant improvement	9	The surgery group had patients treated with myomectomy or hysterectomy, though the



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
		symptomatic uterine fibroids at 1 year after treatment	s, 8 myomectomies)	intervention for treatment failure.		Surgery 2673	embolization group had a significantly greater improvement in scores than the surgery group for physical function (85 vs 57), social function (64 vs 44) and physical-role (37 vs 11) components. EQ-5D scores do not differ significantly (1mo UAE 74 vs surgery 67, 1y UAE 82 vs surgery 83)	in each component of the SF-36 score relative to baseline. Surgery associated with acute morbidity but only one major adverse effect. Embolization associated with significantly faster recovery. At one year 10 of 106 women of the embolization group had required a secondary intervention to treat persistent or recurrent symptoms. The CMA shows that embolization is more cost-effective than surgery at 1 year.		myomectomy group was small.  Time until resumption of usual activities must be viewed cautiously since it can be biased by the patients' expectations (or caregivers' guidance).  Lacks long-term follow-up.



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
Garry et al 2004	UK	To test the null hypothesis of no significant difference between laparoscopic hysterectomy (LH), abdominal hysterectomy (AH) and vaginal hysterectomy (VH) with regard to death, major or minor complication rates, blood loss (intraoperatively), pain assessment, sexual activity, body image, health status, QoL and resource use, and also to assess the CE of the alternatives	1380 women in the UK or South Africa undergoing hysterectomy	Patient records, questionnaires at 6 weeks, 4 months and 1 year after hospital discharge	EQ-5D for CEA. Also SF-12	UK NHS perspective  Total costs (£) LAVH 1654,00 VH 1253,20 LAH 1705,72 AH 1519.64	Mean QALYs over one year adjusted for baseline utility LAVH 0,899 VH 0,897 LAH 0,870 AH 0,862  ICER LAVH compared to VH, 267333 £/QALY LAH compared to AH, 26 571 £/QALY	LAH associated with higher risk of major complications and takes longer to perform than AH. LAH is, however, associated with less pain, quicker recovery and better short-term QoL after surgery than AH. CE of LAH depends on the threshold value the NHS attaches to an additional QALY. CE is also influenced by the use of reusable vs disposable surgical equipment. Individual factors must be balanced. Results from the vaginal	10	Exclusion of patients having an indication for hysterectomy of fibroids of >12 weeks in size. In some patients, resource use data and EQ-5D responses were wholly or partially missing. Missing data were imputed using a multivariate multiple imputation procedure assuming data were missing at random.  The trials not blinded.  Baseline characteristics of patients treated with vaginal or abdominal hysterectomy differ which is why these



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
								trial were inconclusive as the study was under-powered. LAVH was not cost effective relative to VH.		groups are analysed separately and the groups cannot be compared with each other.  No data on patients who fitted inclusion criteria but did not decide to participate in the trial is recorded.  Financial constraints particularly near the end of the financial year which impacted on ability to perform laparoscopic surgery.
Garside et al 2004 UK		To estimate the clinical effectiveness and CE of microwave endometrial ablation (MEA) and thermal balloon endometrial	Hypothetical cohort of 1000 women/treatment group, starting age 42years	Systematic review and Markov model	TTO	NHS perspective  Total costs at 10 years (£) Hysterect. 2320512 TCRE 1731734	Total QALYs Hysterect. 8774,34 TCRE 8357,03 TCRE+RB 8357,99 RB 8359,92	Second-generation techniques more cost-effective than first-generation techniques. Both TBEA and MEA less	10	Costs of managing complications not included. Economic model very sensitive to the utility values used, especially the



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
		ablation (TBEA) for heavy menstrual bleeding, compared with the existing (first-generation) endometrial ablation (EA) techniques of transcervical resection (TCRE) and rollerball (RB) ablation, and hysterectomy.				TCRE+RB 1785045 RB 1752359 MEA 1448470 TBEA 1323925	MEA 8360,70 TBEA 8360,77  ICER (£/QALY)  TBEA dominates all other options except hysterectomy, for which ICER 2410 £/QALY. MEA dominates all other except TBEA and hysterectomy, for hysterectomy ICER 2108 £/QALY.	costly than hysterectomy. Hysterectomy results in more QALYs but may result in more serious complications. Balance of guarantee of amenorrhoea vs risks and recovery time of major surgery and loss of womb. Thus, new minimally invasive surgical techniques have been developed.		value for women who are 'well' following recovery from an EA procedure or hysterectomy. Little published evidence is available for this, leaving the results of the cost-effectiveness model uncertain.  Of included studies only Cooper et al. 1986 used a recognized QoL measure (SF-36), no trials used a condition-specific measure of QoL. In the economic modeling, Scuppher's patient data of 60 patients were used. QALY results may highly be





Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
										influenced by personal preferences of treatment options of these 60 women.  Little published data on long-term follow-up of women undergone MEA or TBEA for heavy menstrual bleeding.
Hirst et al 2008 UK		To examine and compare the medium term (min 2years) results of hysterectomy and uterine artery embolization (UAE) as a treatment for symptomatic uterine fibroids with regard to safety, efficacy, special issues in the	1734 women treated for symptomatic uterine fibroids in UK	Multi-centre retrospective cohort study. Data from hospital records and patients themselves by postal questionnaire.  Questionnaire data included free-text comment, this qualitative material analysed using constant comparison. A two-stage probabilistic decision model to assess CE.	SF-36, EQ-5D	NHS UK perspective  Overall costs UAE £ 2676 Hysterectomy £ 3462	Overall QALYs UAE 8.203 Hysterectomy 8.241,  When conservation of uterus given a utility value of 0.01, UAE QALY-score higher than for hysterectomy group  Overall with probabilistic analyses the	UAE less expensive even after repeat procedures. Better QoL results for UAE  in the short term. This advantage may be eroded over time. Sizes of the differences in costs and QoL between UAE and	10	The limitations of an observational retrospective cohort study design, no pretreatment measures.



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
		UAE group, CE, and women's own perspectives on the treatments.					probability of CE is greater with UAE than hysterectomy when the maximum willingness to pay is less than £30,000.	hysterectomy small. Woman's subjective attitude towards resolution of symptoms and preservation of uterus essential. UAE likely to be highly cost-effective for those women who prefer womb conserving treatment.		
Hurskainen et al 2001	Finland	To compare QoL and CE results of levonorgestrel-releasing intrauterine system versus hysterectomy for treatment of menorrhagia	236 women with menorrhagia who were referred to five university hospitals in Finland	Randomly assigned treatment, Outcome measures: menstrual blood loss, HRQoL at 12-month follow-up, costs.	EQ-5D, RAND-36	Societal perspective  Total cost per woman IUS \$1530 Hysterectomy \$4222	EQ-5D score in both groups 0,1 higher than pretreatment, no difference between groups, RAND-36 only difference in pain, hysterectomy dominating with change of 21.2 vs IUS 11.8	Hysterectomy is successful but has a risk of complications, IUS usually diminishes bleeding, a third of devices were removed, and 20% underwent hysterectomy	10	Long-term follow-up needed since costs for IUS may occur later, hysterectomy costs and complications occur soon after the operation.



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							<p>ICER done for pain, (only measure showing better outcome in the hysterectomy group): 1% improvement in the RAND-36 pain score cost about \$270 in the hysterectomy group.</p>	<p>during 1y. HRQoL and other measures of psychosocial wellbeing improved in both groups, no significant differences between groups, except for pain. Hysterectomy about three times more expensive than IUS.</p>		
Hurskainen et al 2004	Finland	To compare outcomes, QoL, and costs of the LNG-IUS vs hysterectomy in the treatment of menorrhagia in a randomized study with a 5-year follow up	236 women with menorrhagia who were referred to five university hospitals in Finland	Randomly assigned treatment, Outcome measures: menstrual blood loss, HRQoL, other measures of psychosocial wellbeing (anxiety, depression, sexual function), costs	EQ-5D, RAND-36	<p>Societal perspective</p> <p>Discounted total costs/patient (\$)</p> <p>IUS 2817</p> <p>Hysterectomy 4660</p>	<p>All HRQoL scores improved (EQ-5D change +0,10 for hyst, +0,08 for IUS), no substantial difference between the groups except the general health status measured by VAS, which improved only</p>	<p>HRQoL outcomes of LNG-IUS and hysterectomy similar. 42% of the women assigned to the LNG-IUS group subsequently underwent hysterectomy, still overall direct and indirect costs</p>	10	Findings may be typical for the Finnish healthcare system and thus differ from other countries.



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							<p>in the hysterectomy group (change in hyst. group 4.4, IUS 0.4) and the physical functioning in RAND-36 which deteriorated in both groups equally. Baseline scores for IUS group were lower than for the hysterectomy group but these subanalyses were not based on intention to treat and thus evidence is not robust.</p> <p>Because the difference in QALYs showed no statistical difference between the groups, no ICER was calculated.</p>	after 5 years were approximately 40% lower in the LNG-IUS group. In general, women were equally satisfied with LNG-IUS and with hysterectomy.		



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
Kennedy et al 2003 UK		A multicentre RCT assessing the costs and benefits of using structured information and analysis of women's preferences in the management of menorrhagia	894 women treated for heavy menstrual bleeding in six UK hospitals	<p>3 groups</p> <p>1)control: no intervention, standard practice</p> <p>2)information: informative video and booklet sent home 6 weeks before appointment</p> <p>3)interview: in addition to receiving the information (booklet+video), women also attended a structured interview immediately before their consultation. Questionnaire of satisfaction of the information tools, satisfaction of interview before appointment at baseline, 6, 12 and 24 mos. Resource use diary.</p>	SF-36, EQ-5D	<p>UK NHS perspective</p> <p>Total costs after 2 years follow-up (£)</p> <p>Control 1810</p> <p>Info 1333</p> <p>Info+interview 1030</p>	<p>QALYs over 2 years</p> <p>Control 1,574</p> <p>Info 1,567</p> <p>Info+interview 1,582</p> <p>Info+interview dominates over information alone and control group. Compared with information, control has an incremental QALY of £79,500 (control more expensive but slightly higher QALY).</p>	<p>Neither intervention had a major impact on health status. Evidence-based information was neither effective nor cost-effective. Addition of a structured interview helped women to use the information to clarify their values and preferences and had a significant effect on treatment preferences, subsequent management and long-term satisfaction. It also had a high probability of being cost-effective.</p>	10	<p>Possibility of contamination bias: clinicians could have applied experience gained from consultations with the intervention groups in their consultations with the control group. This bias would have the effect of reducing the differences between the groups.</p> <p>Possibility of clustering bias in terms of the consultation style of particular consultants or the types of patient referred to them. Thus 'consultant' incorporated as a random effect in the statistical analysis.</p>



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
										Possible inability to ensure that clinicians were blind to the allocation group.
Lumsden et al 2000 UK		To determine the safety, CE and effect on QoL of laparoscopic-assisted vaginal hysterectomy (LAVH) compared with total abdominal hysterectomy (TAH) in the management of benign gynaecological disease.	200 women scheduled for abdominal hysterectomy for a benign gynaecological disease	Patient records during hospital stay, costs, EQ-5D VAS at baseline, 1, 6, 12 mos, Patient diary of the dates when simple 'milestones' to recovery were achieved.	EQ-5D VAS	NHS perspective  Total costs (£) TAH 1667 LAVH 2112	QoL measures: VAS score – preoperative VAS score  At 1month: TAH 6.8, LAVH 7  At 6mo: TAH 14.9, LAVH 11.3  At 12mo: TAH 15.9, LAVH 12.6	LAVH was significantly more expensive than TAH due to the longer operating time and the use of disposable equipment. No difference in patient satisfaction or recovery time. Inhospital stay shorter for LAVH but recovery milestones reached after a similar length of time. Both routes equally safe and the overall complication rate was low. The results fail	9	Follow-up patient cohort diminished to half of original cohort in both groups.

Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
								to suggest a need for all gynaecologists to develop the skills to perform LAVH.		
Moss et al 2011 UK		To compare the long-term (5-year) results of uterine artery embolisation (UAE) with surgery for women with symptomatic uterine fibroids	157 women suffering from symptomatic uterine fibroids	Primary outcome: SF-36. Secondary outcomes: EQ-5D, an 11-point symptom score, a satisfaction score, complications, adverse events, need for further intervention for treatment failure. Baseline, 1mo, 6mo, 12mo, 2year, 3y, 4y, 5y follow-up questionnaires, costs	SF-36, EQ-5D	NHS perspective  Total costs (£) 0-1year UAE 1727 surgery 2673  1-5year UAE 671 surgery 318 (UAE more further interventions)  0-5year UAE 2398 surgery 2991, calculated. Given difference in costs 524pounds	Little difference in QALYs between the UAE group and surgery group for the 5-year period (difference of -0.02 QALYs)  No significant differences between groups in any of the components of the QoL measures. Both arms showed a gain in QoL, reaching levels comparable with age-matched normative QoL SF-36 data. EQ-5D 5year score for UAE 85, for surgery	The improvement in QoL seen at 1y was maintained and equal in both groups at 5y. UAE is a safe and effective technique for women with symptomatic fibroids who wish to avoid hysterectomy. Its safety profile is similar to surgery: most complications occurring within the first 12 mos. Symptomatic relief and satisfaction excellent in both groups.	10	Uncertainty of the estimates of costs and treatment effects.  The number of women undergoing myomectomy too small to draw any meaningful conclusions.



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							80, SF-36 general health UAE 78, surgery 76.	Almost 1/3 in UAE group required further invasive treatment. Thus costs augment and are ultimately similar at 5y in both groups.		
Roberts et al 2011 UK		To undertake CEA comparing 1)first and 2)second generation endometrial ablative techniques, 3)hysterectomy, and the 4)levonorgestrel releasing intrauterine system (Mirena) for treating heavy menstrual bleeding.	Hypothetical cohorts of 10 000 women x4 suffering from menorrhagia.  Utility values obtained from 2814-woman cohort from different trials	Patient meta-analysis, state transition (Markov) model	TTO, EQ-5D, RAND 36-SF	NHS perspective  Total costs (1000£): 1) 23 590 2) 19 470 3) 23 000 4) 16 150	Total QALYs: 1)63 745 2)69 582 3)73 332 4)68 566  ICER vs hysterectomy 1)dominated 2)970 pounds/add. QALY 4)1440 pounds/add. QALY	Hysterectomy is the preferred strategy as the first intervention for heavy menstrual bleeding.	10	Utilities used reflect only the satisfaction of the outcomes, doesn't take into notice pre-treatment anxiety, which can lead to decisions to avoid treatment.  Doesn't include costs to women on the 6-8 -week convalescence period after hysterectomy.  Lack of long term data exclude





Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
										possible effects of long term complications such as urinary stress incontinence for which surgery is required.  Results are highly sensitive to utility values used in the analysis.
Sandberg et al 1985 USA		To evaluate the effect of hysterectomy or hysterectomy and salpingo-oophorectomy versus alternative medical management on life expectancy, QoL and direct medical costs.	Women attending hysterectomy due to benign neoplasm, disorders of menstruation, acquired abdominal anatomy, cervical disease, endometriosis	Analysis of data from medical literature and public health reports to assess the risks, benefits and costs of hysterectomy. QoL data gathered from responses of interviewed physicians.	QoL measure between 0 and 1	<p>Perspective of healthcare provider</p> <p>Cost vary depending on age and indication between 1200-3400 USD in the hysterectomy group and between 1900-3800 USD in the hysterectomy+oophorectomy group, the latter group nearly always being more expensive</p> <p>Net costs (1000\$)</p> <p>Benign neoplasm 30y h: 1,2 h+o 1,9</p>	<p>Total QALYs gained, group A: benign neoplasm, menstrual disorders, cervical disease, endometriosis. Group B: acquired abnormal anatomy</p> <p>30y hyst: A 0,35, B 0,60</p> <p>hyst+ooph A 0,70, B 0,90</p>	Hysterectomy an effective treatment for most indications and age groups. Women under 35y who do not take replacement estrogens after hysterectomy plus oophorectomy will have a shorter life expectancy due to a markedly	6	QoL data gathered from responses of interviewed physicians regarding loss of QoL from the symptoms associated with the conditions at hand and not from randomly selected women suffering from the conditions



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
						40y h: 2,3 h+o 2,7 50y h: 3,2 h+o 3,3  Disorders of menstruation 30y: h 1,6 h+o 2,4 40y: h 2,3 h+o 2,6  Acquired abnormal anatomy 30y: h 1,3 h+o 2,0 40y: h 1,7 h+o 2,0 50y: h 2,2 h+o 2,3 60y: h 2,7 h+o 2,6  Cervical disease 30y: h 3,0 h+o 3,7 40y: h 3,4 h+o 3,8  Endometriosis 30y: h+o 3,4 40y: h+o 3,5	40y hyst: A 0,30, B 0,55 hyst+ooph A 0,60, B 0,80  50y hyst A 0,25, B 0,45 hyst+ooph A 0,50, B 0,65  60y hyst B 0,25 hyst+ooph B 0,40  CE (1000\$/QALY) Benign neoplasm 30y h: 11,0 h+o 12,0 40y h: 29,0 h+o 18,0 50y h: 40,0 h+o 33,0	higher rate of coronary heart disease. Other groups that would have net declines in life expectancy are women whose risks of reproductive tract cancer are markedly lower than average and women who have high operative risk. Cost/QALYs for hysterectomy fall between 10 000- 40 000 \$/QALY gained.		



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							Disorders of menstruation 30y: h 15,0 h+o 15,0 40y: h 28,0 h+o 17,0  Acquired abnormal anatomy 30y: h 7,9 h+o 10,0 40y: h 11,0 h+o 9,0 50y: h 13,0 h+o 13,0 60y: h 25,0 h+o 14,0  Cervical disease 30y: h 27,0 h+o 23,0 40y: h 43,0 h+o 25,0			



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							Endometriosis 30y: h+o 21,0 40y: h+o 23,0			
Sculpher et al 1993 UK		To evaluate the relative health service cost of endometrial resection versus abdominal hysterectomy for the treatment of menorrhagia during a 4mo follow-up and the value women attach to their health state before and after surgery.	200 women requiring surgical treatment for heavy menstrual bleeding; after withdrawals, hysterectomy n=97, endometrial resection n=99.	Resource use from cost data routinely generated for Bristol General Hospital. If not available, this data from a variety of published sources. Questionnaire sent home at 4mo after surgery: patients asked to assess QoL 1mo before surgery, 2weeks and 4mo after surgery. Also use of GP services.	EQ-VAS	Health service costs, NHS perspective?  Total mean costs/patient (£) Endometrial resection 560,05 Hysterect. 1059,73	EQ-VAS change in comparison to 1mo before operation  At 2weeks Endometr. Resection 19.5 Hysterectomy 8.3  At 4mo Endometr. Resection 36.9 Hysterectomy 43.9	In short term endometrial resection is associated with less post operative morbidity and lower costs. In the long run hysterectomy may be more effective in relieving menstrual symptoms.	8	Short follow-up, exclusively health service costs, health state valuation retrospectively.
Schulper 1998 UK		A CUA to assess whether abdominal hysterectomy (AH) or transcervical resection of the	A target sample of 60 women suffering from heavy menstrual bleeding out of	Decision tree, interview of health state valuation, economic modelling. Costs and utility values largely from Sculphur 1993 data.	TTO	Health service resource use  Total expected costs at 2y (£)	Expected QALYs TCRE 1,363 AH 1,593	23% retreatment rate for TCRE. Still AH remains more costly than TCRE.	10	Health state valuation of a sample of 60 women. ICER is particularly sensitive to variation in the



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		endometrial (TCRE) is more cost-effective over a 2y perspective.	175 possible candidates from the Bristol trial			TCRE 794 AH 1 139	ICER of AH 1 500 £/QALY gained	However, AH is more effective. Each additional QALY generated by AH has an incremental cost of £1500.		unit cost of a day at the ward and to the values of post-TCRE and post-AH health states, varying these parameters do not however reverse the conclusion that AH is more cost-effective.  Uncertainty of long term costs and benefits.
Sculpher et al 2004 UK		To assess the CE of laparoscopic hysterectomy compared with conventional hysterectomy (abdominal or vaginal)	1346 women requiring a hysterectomy for reasons other than malignancy	Two separate randomized comparisons: laparoscopic hysterectomy (ALH) versus abdominal (AH) and laparoscopic hysterectomy (VLH) versus vaginal hysterectomy (VH). Case record forms to assess costs, unit costs from the health service database. QoL questionnaire at baseline, 6weeks, 4mo, 1y.	EQ-5D	NHS perspective  Total costs/patient (£) ALH 1706 AH 1520  VLH 1654 VH 1253	QALYs over 1y adjusted for baseline EQ-5D utility ALH 0,870 AH 0,862  VLH 0,899 VH 0,897  ICER £/QALY ALH vs AH: 26 571	Generally LH more costly than standard hysterectomy due to disposable equipment. QALY differences small. VLH unlikely to be cost effective when compared to VH. CE of ALH compared with AH more finely	10	Health outcomes first measured at six weeks postintervention. This may have missed some of the health gains associated with quicker recovery of the laparoscopic procedures.  Productivity costs were not taken into account.



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							VLH vs VH: 267 333  The probability of laparoscopy being more cost effective than abdominal hysterectomy is 56% if the NHS is willing to pay up to £30 000 for an additional QALY	balanced, mainly due to shorter inpatient stay. With reusable equipment use (without affect on outcomes), the additional cost of ALH compared with AH would fall to £74 and ICER £10 571.		
Showstack et al 2004 USA		To address economic questions concerning total (TAH) or supracervical (SCH) hysterectomy (the "TOSH" trial) in a randomized trial during a 24-month follow-up	125 premenopausal women aged 30-50 attending hysterectomy	Structured interviews at 0,12 and 24 mos, telephone interviews at 3, 6, 9, 15, 18, and 21 mos. Resource use from inpatient and outpatient data. Analyses using multiple linear regression models.	SF-36 physical component summary, mental component summary	Relative resource use (not "costs" or "charges" to insurers, providers, or individual patients)  Total resource use TAH \$6,448 SCH \$7,479	Higher scores on baseline SF-36 physical component summary predicted lower subsequent resource use; a 1-point increase in baseline physical component summary associated with a decrease of \$107 in 24-month resource use. No association of	Total resource use of TAH and SCH comparable, especially in the first year, during the second year resource use augments in SCH group due to rehospitalization. BMI >35 and heavy or very heavy menstrual bleeding associated with higher	7	Neither subjects nor clinicians were blinded  Lack of statistical power to rule out differences in total resource as large as \$2,616 over 2 years; however, there were no rehospitalizations resulting from hysterectomy



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							mental health component summary with resource use.	resource use		<p>complications and any potential difference appears to be associated with hospitalizations in the SCH group during the second year, most of which were unlikely to be related to the study hysterectomy.</p> <p>Lack of measurement of the number of in-hospital medical consultations or the use of pharmaceuticals.</p> <p>Findings for the associations of BMI and heavy bleeding history with resource use based on exploratory analysis and</p>



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
										should be interpreted with caution.
Taipale et al 2009	Finland	To gain knowledge about the utility of hysterectomy in a real-world setting and to relate the utility of the intervention to its costs.	337 women entering for routine hysterectomy due to a benign disease (210 benign uterine or ovarian cause, 20 endometriosis, 51 uterovaginal prolapse, 56 menorrhagia).	15D-HRQoL questionnaires at baseline and 6mo follow-up, compared with that of the general female population at baseline. Direct hospital costs from Ecomed clinical patient administration system	15D	<p>Perspective of secondary care provider</p> <p>Costs at 6mo/patient (€)</p> <p>Whole group 3 138</p> <p>Under 50y 2 835</p> <p>50-60y 3 202</p> <p>over 60y 3 556</p> <p>Benign uterine or ovarian cause 3 157</p> <p>Endometriosis 3 114</p> <p>Prolapse 2 607</p> <p>Menorrhagia 3 553</p>	<p>QALYs gained</p> <p>Whole group 0,222</p> <p>Under 50y (discounted by 5%) 0,277</p> <p>50-60y (discounted) 0,063</p> <p>over 60y (discounted) 0,069</p> <p>Benign uterine or ovarian cause 0,100</p> <p>Endometriosis 0,837 (only group in which a clinically significant amount of 55% of patients had an HRQoL improvement of <math>\geq 0.03</math>)</p> <p>Prolapse 0,523</p> <p>Menorrhagia</p>	Hysterectomy improves HRQoL in women with benign gynecological problems. However, clinically important HRQoL improvement was seen in the majority of patients only in the endometriosis group and in younger patients. Best results in dimensions of elimination and sexual activity. Cost/QALY gained for hysterectomy for benign uterine disorders higher than that observed for many other	9	<p>Only direct hospital costs included.</p> <p>Operative treatment results compared to hypothetical situation where the HRQoL would remain constant at the baseline level over time. This is not always true as symptoms can often be relieved, and HRQoL improved, by conservative treatment. Patient groups varied in size (n=20 for endometriosis, n=210 for benign uterine and ovarian causes).</p>





Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							0,183  Cost/QALY gained (€) Whole group 14 135 Under 50y (discounted by 5%) 10 235 50-60y (discounted) 50 825 over 60y (discounted) 51 536  Benign uterine or ovarian cause 31 570 Endometriosis 3 720 Prolapse 4 985 Menorrhagia 19 415	surgical interventions. Thus, more cost-effective treatments options should be considered especially in older patients.		
Volkers et al 2008		To investigate whether uterine	177 patients undergoing	RCT, clinical follow-up after treatment, self-report	MOS-SF-36, EQ-	Societal perspective	No significant differences in	24-month mean costs	10	Findings may be typical for



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
The Netherlands		artery embolization (UAE) is a cost-effective alternative to hysterectomy for patients with symptomatic uterine fibroids	treatment for symptomatic uterine fibroids (UAE n=88, hysterectomy n=89)	questionnaire and an out-of-hospital resource use survey at 6 weeks and 6, 12, 18, and 24 mos.	5D-3L, HUI-3	Total costs/patient at 2-year follow-up (\$) UAE 11 626 Hysterect. 18 563	QoL measures  SF-36 (mental/physical component summary) MCS UAE 5.80, Hyst. 7.26 PCS UAE 9.42, Hyst. 9.32  EQ-5D UAE 0.086, Hyst. 0.102  HUI-3 UAE 0.068, Hyst. 0.094	lower for UAE than hysterectomy. Overall cost differences relatively insensitive to variations in four important cost parameters. No difference in clinical effectiveness and QoL between the treatment strategies.		the Dutch healthcare system and insurance legislation and thus differ from other countries.  UAE was performed according to the state of the art at the onset of the study. Since then, the technique of UAE has developed (e.g. more expensive spherical particles used instead of polyvinyl alcohol particles), and, in some institutions, postprocedural MR imaging is being performed to detect the fibroid infarction rate, thus indicating the need for



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
										any repeat embolizations in case of unsatisfactory technical or clinical. These developments increase costs but may also increase the clinical success rate of UAE.  Relief of symptoms related to fibroids usually occurs after menopause. Hence, longer follow-up needed (e.g. until menopause).
Wu et al 2007 UK		To evaluate the relative CE of uterine artery embolisation (UAE) and hysterectomy in women with symptomatic uterine fibroids	A total of 1108 women who underwent UAE (n = 649; average follow up of 8.6y) or hysterectomy (n = 459; average follow up of 4.6y) for the treatments of	Probabilistic decision model based on data from a large comparative cohort (HOPEFUL study) and literature. Direct health service costs related to the interventions and complications included in the model.	EQ-5D	NHS UK perspective  Costs/patient during first year (£) UAE 1677 Hysterect. 3282  During rest of the life	QALYs/patient during first year UAE 0.820 Hysterect. 0.815  During rest of the life until menopause in	UAE is less expensive than hysterectomy. Short term QoL results favour UAE. This advantage may be eroded over time	10	Utility decrements based on expert opinion.



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
			symptomatic fibroids			<p>until menopause in women with average age of 44y</p> <p>UAE + £860</p> <p>Hysterectomy + £0</p> <p>Women with average age of 35y</p> <p>UAE + £1735</p> <p>Hysterectomy + £0</p> <p>Overall (£)</p> <p>44y: UAE 2536</p> <p>hysterect. 3282</p> <p>35y: UAE 3411</p> <p>Hysterectomy 3282</p>	<p>women with average age of 44y</p> <p>UAE 7.384</p> <p>Hysterectomy 7.426</p> <p>Women with average age of 35y</p> <p>UAE 11.639</p> <p>Hysterectomy 11.725</p> <p>Overall</p> <p>44y: UAE 8.203</p> <p>hysterect. 8.241</p> <p>35y: UAE 12.459</p> <p>Hysterectomy 12.540</p> <p>If utility value for conservation of the uterus =0.01, QALYs</p>	<p>especially in young patients due to additional procedures to deal with recurrent symptoms. However, important to consider young patients' desire for future family. Overall differences in costs and QoL between UAE and hysterectomy are small. Thus, subjective factors essential on treatment choice.</p>		



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							<p>of UAE will increase and overtake QALYs of hysterectomy with an overall difference of 0.050 and 0.057 in the older and younger group in favour of UAE. If the utility value for conservation of the uterus is assumed to be higher, e.g. 0.5, will the QALY difference in favour of UAE amplify.</p> <p>In the older age group UAE dominates after taking uterus conservation into account. In the younger age group ICER 2263€/QALY gained (utility value of 0.01 for uterus</p>			



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							conservation) and 211 £/QALY gained (utility value of 0.05)			
You et al 2006 China		To compare the cost and QALYs gained by hysterectomy, endometrial resection/ablation, levonorgestrel-releasing intrauterine system (LNG-IUS) and oral medical therapy for management of menorrhagia over 5y.	Hypothetical cohort of patients suffering from heavy menstrual bleeding	Markov model. Clinical inputs estimated from literature. Charges of healthcare services of public hospitals and clinics as posted in the Hong Kong Gazette.	TTO	<p>Perspective of healthcare provider in Hong Kong</p> <p>Costs/patient (\$)</p> <p>IUS 4 528</p> <p>Oral medical treatment 5508</p> <p>Endometrial resection/ablation 6185</p> <p>Hysterectomy 6878</p>	<p>QALYs gained</p> <p>IUS 4.625</p> <p>Oral medical treatment 4.575</p> <p>Endometrial resection/ablation 4.624</p> <p>Hysterectomy 4.725</p> <p>Cost/QALY gained (\$)</p> <p>IUS 979</p> <p>Oral medical treatment 1204</p> <p>Endometrial resection/ablation 1338</p> <p>Hysterectomy 1456</p> <p>ICER</p>	CUA shows that hysterectomy, with an ICER less than \$50 000, appears to be a cost-effective treatment of menorrhagia over a 5y period. LNG-IUS least costly and most effective alternative when non-surgical intervention is the patient's preference. Individual factors should be taken into account.	10	<p>Clinical probabilities and utility scores derived from overseas studies.</p> <p>Mortality rates of endometrial resection/ablation and hysterectomy and re-insertion rate of LNG-IUS extremely low and thus not included in CUA.</p> <p>Time frame limited to 5y. The analysis would result in higher uncertainty over a longer time frame because the need for treatment of</p>



Study	Country of Origin	Aim of the study	Subjects	Methods	QALY Instrument	Perspective and Costs	QALYs and/or Cost/QALY	Authors' conclusions	Quality of Study	Limitations
							<p>compared to IUS</p> <p>Oral medical treatment: dominated by IUS</p> <p>Endometrial resection/ablation: dominated by IUS</p> <p>Hysterectomy 23 500 \$/QALY gained</p>			<p>menorrhagia might decline as women reach menopause.</p> <p>Indirect costs not included.</p>
You et al 2009 China		To compare the cost and QALYs of hysterectomy, myomectomy, and uterine artery embolization (UAE) for symptomatic control of uterine fibroids over 5y among patients who do not have a preference for uterus-conserving treatments	Hypothetical cohort of patients with symptomatic uterine fibroids	Markov model, direct medical costs and indirect costs (charges of health-care services of public hospitals and clinics posted in the Hong Kong Gazette)	TTO	<p>Perspective of Hong Kong society</p> <p>Total costs over 5years (\$)</p> <p>UAE 8847</p> <p>Myomectomy 9036</p> <p>Hysterectomy 8418</p> <p>After the first year</p> <p>UAE 6755</p> <p>Myomect. 7593</p> <p>Hysterectomy 8418</p>	<p>QALYs over 5 years</p> <p>UAE 4.245</p> <p>Myomectomy 4.273</p> <p>Hysterectomy 4.368</p> <p>UAE dominates the two other options at year one.</p> <p>Hysterectomy dominates from year 3 onward.</p> <p>ICER</p>	CUA shows all three treatments to achieve high QALYs with minimal difference between treatment arms. For the first year of follow-up, UAE dominates other treatment options. Over 5 years, hysterectomy appears to be the least costly and	10	<p>Clinical probabilities, resources used and utility scores derived from overseas studies. Utility values assumed to be the same as in women suffering from menorrhagia, other symptoms of uterine fibroids not taken into account.</p> <p>QALYs related to individual surgical complications</p>



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						UAE cheapest at one year, after the third year hysterectomy becomes the cheapest	myomectomy vs UAE at year five: 6750 \$/QALY gained	most effective treatment option.		<p>were not estimated because of the relatively brief duration of the complications. A lower utility score was instead assigned to the convalescence period of surgery interventions to reflect the higher rates of complications compared with UAE.</p> <p>Total costs sensitive to probability of need for reintervention in the myomectomy group, relative cost of UAE compared with hysterectomy, duration of convalescence in the hysterectomy group, and cost of procedure and</p>





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										duration of hospitalization in the hysterectomy and myomectomy groups.  Time frame limited to 5 years. Over a longer time frame, the analysis would result in higher uncertainty because of the limited long-term data on UAE and myomectomy.
Zowall et al 2008 Canada/UK		To estimate the CE of a treatment strategy for symptomatic uterine fibroids, which starts with Magnetic Resonance-guided Focused Ultrasound Surgery (MRgFUS) as compared with current practice	Hypothetic cohort of women for whom surgical treatment for uterine fibroids is being considered.	Markov model	Conversion of SF-36 data to SF-6D, TTO	NHS UK perspective  Total discounted direct medical costs of 1000 women at the age 39 followed until menopause or age 56 (£)  MRgFUS 3 101 644  Currently available procedures 3 396 913	QALYs MRgFUS 10 793.874  Current practice 10 783.216  MRgFUS dominates current practice	A treatment strategy starting with MRgFUS is potentially more effective and less costly than current practice. However, uncertainty of this conclusion reflecting quality of	10	Despite extensive sensitivity analyses, there remains some inherent uncertainty regarding the model's parameters.  Cost/QALY gained is sensitive to the cost of MRgFUS relative to



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		(25% UAE, 25% myomectomy, 50% hysterectomy)						underlying data should be emphasised.		<p>other treatments, the age of the woman and the NPV (nonperfused volume) relative to the total fibroids volume.</p> <p>Reproductive implications not taken into account. However, MRgFUS is believed to offer a way to preserve fertility, thus additional QoL gains may be associated to it.</p> <p>Indirect costs not taken into account.</p> <p>Limitations in the availability of cost data of MRgFUS.</p>

List of abbreviations. CE= cost-effectiveness, QALY= quality adjusted life years, (HR)QoL= (health related) quality of life, QWB= quality-of-well-being-scale, TTo= time trade-off, CU= cost-utility, NHS= national health service, CUA= cost-utility analysis, CEA= cost-effectiveness analysis, CMA= cost-minimization analysis, UAE= uterine artery embolization, ICER= incremental cost-effectiveness ratio, MRgFUS= magnetic resonance-guided focused ultrasound surgery, 1. gen EA= first generation endometrial ablation (TCRE= transcervical resection of the endometrium, RB= rollerball ablation), 2. gen EA= second generation endometrial ablation (MEA= microwave endometrial ablation, TBEA= thermal balloon



andometrial ablation), (LNG-)IUS= levonorgestrel-releasing intra-uterine system, LAVH= laparoscopically assisted vaginal hysterectomy, VH= vaginal hysterectomy, LAH= laparoscopic abdominal hysterectomy, (T)AH= (total) abdominal hysterectomy, SCH= supracervical hysterectomy,



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