Systematic Reviews in Gynecologic Surgery: Introduction

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On behalf of Systematic Review Group

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Promoting the Highest Standards for Gynecologic Surgical Care

Disclosures

- Urinary Incontinence, Mobility, and Muscle Function in Older Women, National Institute on Aging 1R03AG053281-01
- I am not a systematic review methodologist

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Objectives

- Understand the Hierarchy of Evidence in Scientific Literature
- Approach to Systematic Reviews
- How to Conduct a Good Quality Systematic Review

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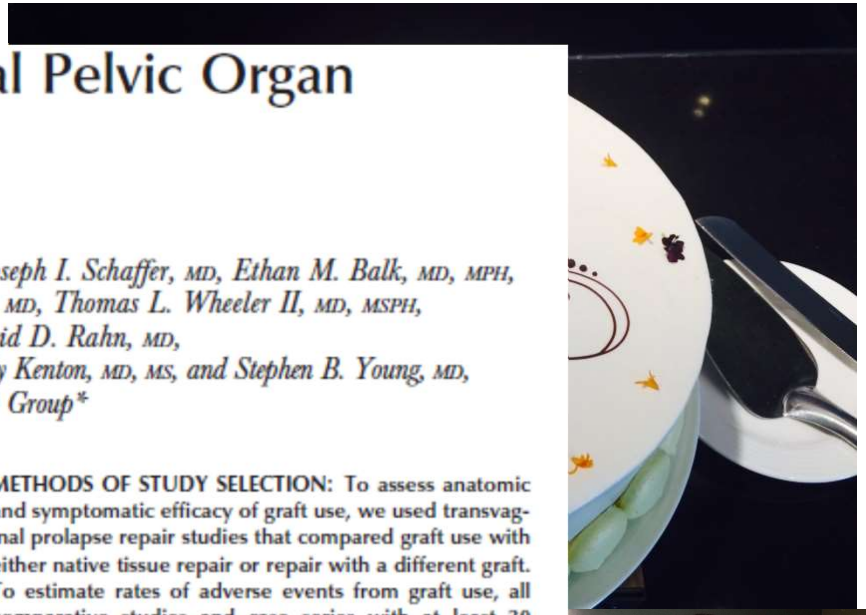
SGS Systematic Review Group (SRG)



Graft Use in Transvaginal Pelvic Organ Prolapse Repair

A Systematic Review

*Vivian W. Sung, MD, MPH, Rebecca G. Rogers, MD, Joseph I. Schaffer, MD, Ethan M. Balk, MD, MPH, Katrin Uhlig, MD, MS, Joseph Lau, MD, Husam Abed, MD, Thomas L. Wheeler II, MD, MSPH, Michelle Y. Morrill, MD, Jeffrey L. Clemons, MD, David D. Rahn, MD, James C. Lukban, DO, Lior Lowenstein, MD, MS, Kimberly Kenton, MD, MS, and Stephen B. Young, MD, for the Society of Gynecologic Surgeons Systematic Review Group**

OBJECTIVE: To estimate the anatomic and symptomatic efficacy of graft use in transvaginal prolapse repair and to estimate the rates and describe the spectrum of adverse events associated with graft use.

DATA SOURCES: Eligible studies, published between 1950 and November 27, 2007, were retrieved through Medline and bibliography searches.

METHODS OF STUDY SELECTION: To assess anatomic and symptomatic efficacy of graft use, we used transvaginal prolapse repair studies that compared graft use with either native tissue repair or repair with a different graft. To estimate rates of adverse events from graft use, all comparative studies and case series with at least 30 participants were included. For spectrum of adverse events, all study designs were included.

GYN (Aug)

Comparison of vaginal hysterectomy techniques and interventions for benign indications: A systematic review. Jeppson PC, Balgobin S, Rahn DD, et al.

Obstet Gynecol 2017 May;129(5):877-886.

GYN (Aug)

Treatment of Endometriosis-Associated Pain with Elagolix, an Oral GnRH Antagonist. Taylor HS, Giudice LC, Lessey BA, et al.

N Engl J Med. 2017 May 19. [Epub ahead of print]

select article)

Print FPM Articles

FPMRS (Jan) 4 questions **Correct: 4 of 4**

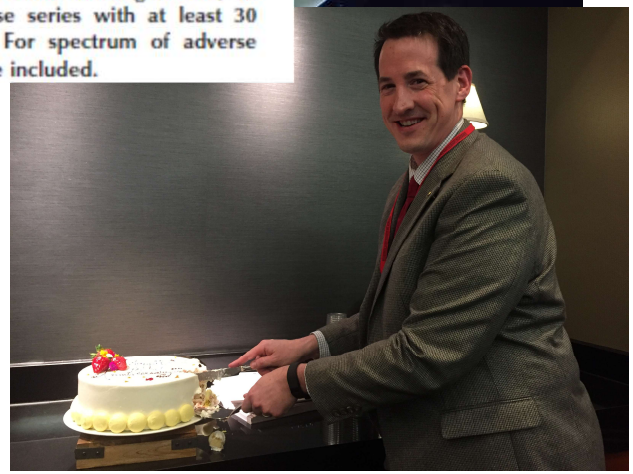
Graft and mesh use in transvaginal prolapse repair: A systematic review. Schimpf MO, Abed H, Sanses T, et al.

Obstet Gynecol 2016;128:81-91

FPMRS (Jan) 4 questions **Article Selected**

Inferior gluteal and other nerves associated with sacrospinous ligament: A cadaver study. Florian-Rodriquez ME, Hare A, Chin K, et al.

Am J Obstet Gynecol 2016;215:646.e1-6 Web Version



SGS SRG

- Evaluate literature effectively
- Apply EBM in your practice
- Manuscript reviewer skills
- High impact publications
- Develop excellent writing skills
- Become an expert in the area

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Evolution of Scientific Method

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Hierarchy of Evidence

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Systematic Review
– Why, What, and How –

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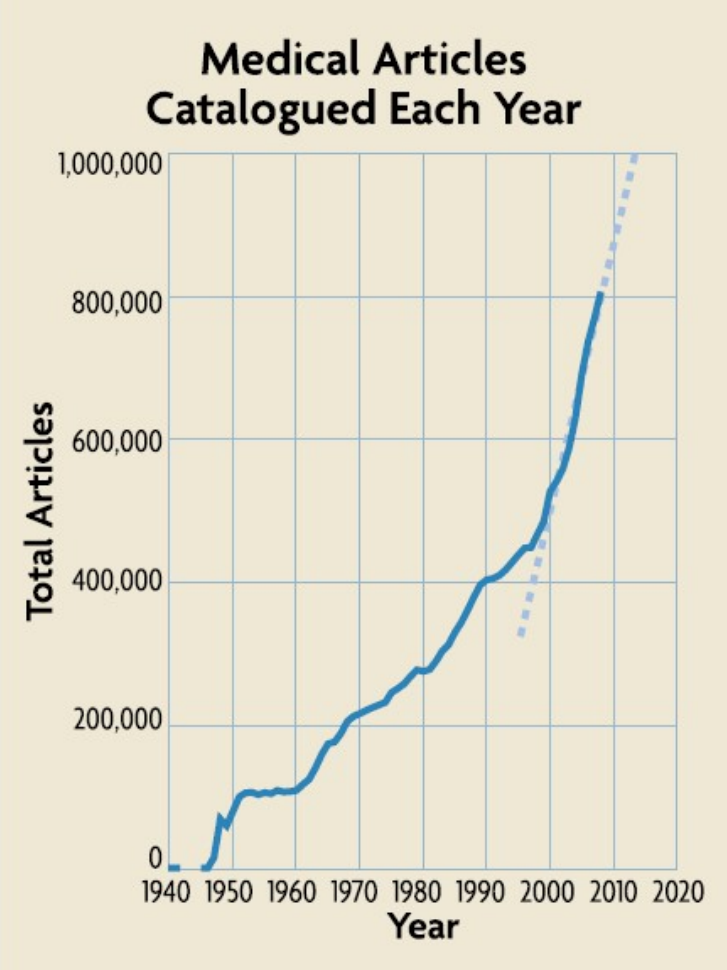
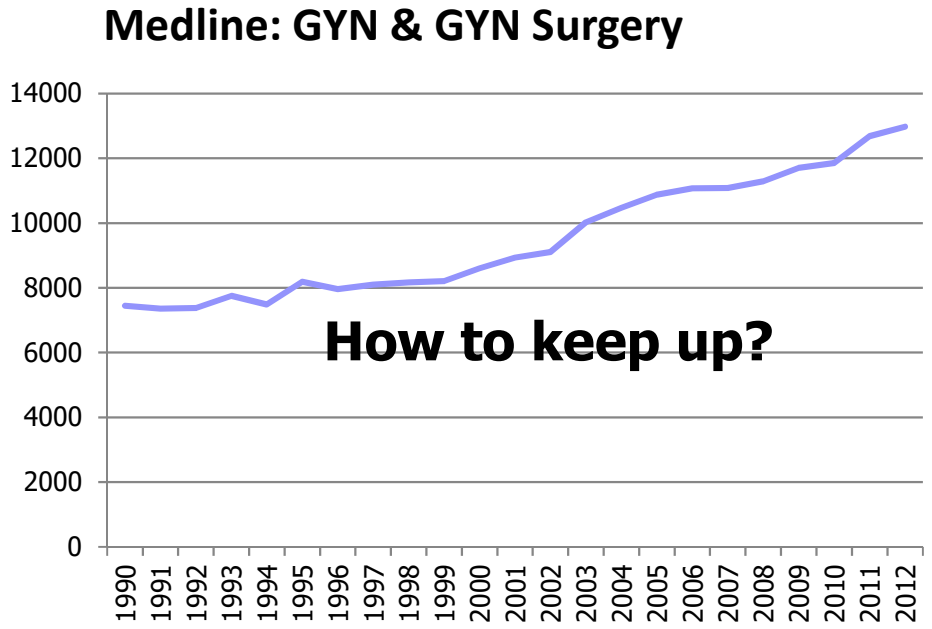
Exponential Growth of the Medical Literature



Gillam M et al. The Healthcare Singularity and the Age of Semantic Medicine. Health and Wellbeing.

- >20 million articles in biomedical literature
- ~1 million articles/year added
- Require ~21 hr/day of study to stay current



Institute of Medicine (IOM)

- Congress directed the IOM to develop standards for conducting SR's and CPG's
- Medicare Improvement for Patients and Providers Act of 2008

Value of Systematic Reviews

- Clinicians need unbiased information
- Too much information for practitioners to keep up with and synthesize
- Information of variable quality and reliability
- Studies examined individually offer only partial answers
- Identify research gaps

Systematic Review

- Application of a protocol to critically evaluate the evidence and rigorously combine the results
- Provides qualitative and quantitative summaries of the overall effect
- Aims to
  - Explain differences across studies
    - Based on populations, intervention details, outcome measurements, other factors
  - Evaluate the reliability and strength of the evidence
  - Guide future research

Basic Steps

- Formulate research question
- Determine study eligibility criteria
- Systematically search for all eligible studies
- Systematically extract all relevant data from each study
- Evaluate the quality (risk of bias) of each study
- Summarize the studies
  - Who included, what evaluated, results, quality
- Evaluate the heterogeneity across studies

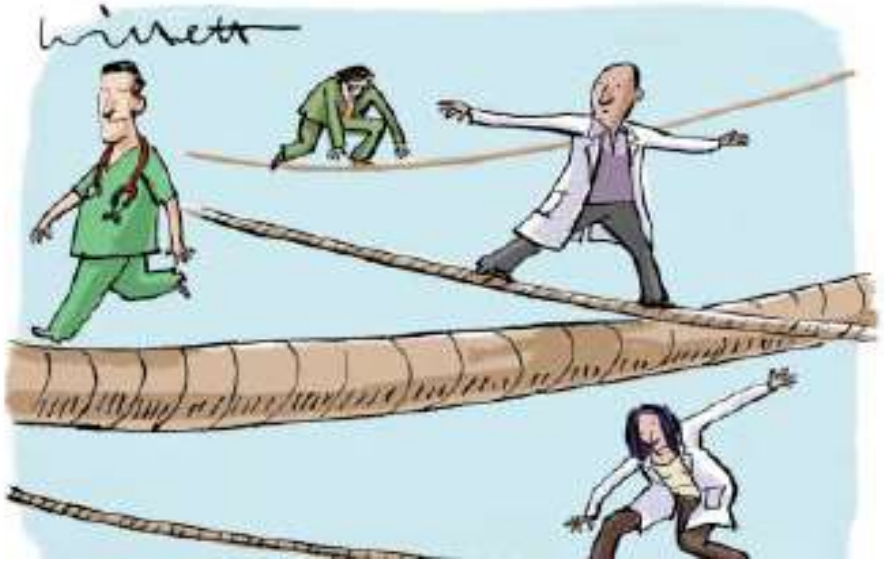
Grading quality of evidence and strength of recommendations

Grading quality of evidence and strength of recommendations

Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group

Clinical guidelines are only as good as the evidence and judgments they are based on. The GRADE approach aims to make it easier for users to assess the judgments behind recommendations

Healthcare workers using clinical practice guidelines and other recommendations need to know how much confidence they can place in the recommendations. Systematic and explicit methods of making judgments can reduce errors and improve communication. We have developed a system for grading the quality of evidence and the strength of recommendations that can be applied across a wide range of interventions and contexts. In this article we present a summary of our approach from the perspective of users of guidelines.



What makes a good guideline?

BMJ 2004

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GRADE approach

- "**Quality of a body of evidence**" refers to the extent to which our confidence in an estimate of effect is sufficient to support a particular recommendation

- "**Strength of a recommendation**" indicates the extent to which one can be confident that adherence to the recommendation will do more good than harm

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Quality Assessment Criteria

Study Design	Evidence Quality
Randomized trials	**High**
	Moderate
Observational studies	**Low**
Any other evidence	**Very Low**

Lower if

Study limitations
- 1 Serious
- 2 Very serious

Inconsistency
- 1 Important inconsistency

Indirectness
- 1 Some uncertainty
- 2 Major uncertainty

Sparseness
- 1 Sparse data

Imprecision
- 1 Imprecise data

Publication bias
- 1 High probability of reporting bias

Raise if

Large effect
+1 Large
+2 Very Large

Dose response
+1 Large
+2 Very Large

All plausible confounding
+1 Would reduce a demonstrated effect
+1 Would suggest a spurious effect when results show no effect

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Quality of Evidence

A	High	We are confident that the true effect lies close to that of the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very Low	Any estimate of effect is very uncertain, and often will be far from the truth.

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Strength of recommendation

Grade*	Implications		
	Patients	Clinicians	Policy
Level 1 'We recommend'	Most people in your situation would want the recommended course of action and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be adopted as a policy in most situations.
Level 2 'We suggest'	The majority of people in your situation would want the recommended course of action, but many would not	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require debate and involvement of stakeholders, before policy can be determined

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Linking the Quality of Evidence and the Strength of Recommendation

Strength of Recom-mendation	1	"Strong"
	2	"Weak"

Quality of Evidence	A	High
	B	Moderate
	C	Low
	D	Very low

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Linking the Quality of Evidence and the Strength of Recommendation

Table 2. Clinical Practice Guidelines for Treating Genitourinary Syndrome of Menopause

Presuming No Contraindication to Vaginal Estrogen, in Postmenopausal Women...	Guideline		Grade
1. with a single urogenital atrophy complaint of vaginal dryness, dyspareunia, itching or burning, dysuria, or urinary urgency	we suggest	application of either nonhormonal agents (moisturizers, lubricants) or vaginal estrogen.	2C
2. with a composite of multiple urogenital atrophy complaints (vaginal dryness, dyspareunia, itching or burning, dysuria, or urinary urgency)	we suggest	application of vaginal estrogen instead of nonhormonal agents.	2C
3a. presenting with urogenital atrophy complaints (eg, vaginal dryness, dyspareunia, itching or burning, dysuria, or urinary urgency) also reporting UUI	we recommend	application of vaginal estrogen (agents studied: estradiol vaginal ring and tablet).	1B
3b. for those women whose additional urinary complaints are frequency or nocturia or SUI	we suggest	application of vaginal estrogen.	2C

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Linking the Quality of Evidence and the Strength of Recommendation

Table 2. Clinical Practice Guidelines for Venous Thromboembolism Prophylaxis in Gynecologic Surgery

Gynecologic Surgery Type	Gynecologic Malignancy	Prior VTE	Other Risk Factors for VTE*	Age	We Suggest	Grade
Minor	No	No	No	Any	Early and frequent mobilization with or without perioperative IPC rather than pharmacologic prophylaxis	2C
Major	No	No	No	Any	Using IPC applied before induction of anesthesia and continued until time of discharge for the prevention of VTE	2C
Any	No	Yes	Yes or no	60 y or older	Using IPC applied before induction of anesthesia and continued until time of discharge and either LMWH† or UFH‡ for prevention of VTE; the decision between types of heparin therapies may be directed by physician preference, cost, ease of administration, or all of these	2C

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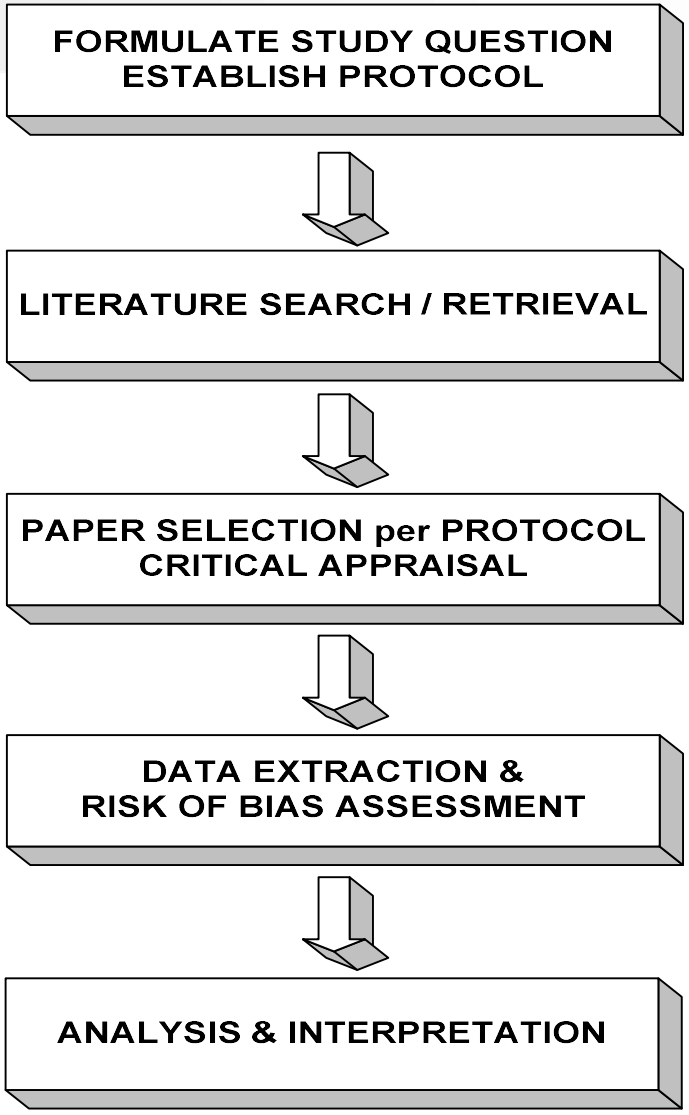
Steps to Conduct a Systematic Review



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Systematic Review: How

Venous Thromboembolism Prophylaxis in Gynecologic Surgery

A Systematic Review

David D. Rahn, MD, Mamta M. Mamik, MD, Tatiana V. D. Sanses, MD, Kristen A. Matteson, MD, MPH, Sarit O. Aschkenazi, MD, MS, Blair B. Washington, MD, Adam C. Steinberg, DO, Heidi S. Harvie, MD, MBA, MSCE, James C. Lukban, DO, Katrin Uhlig, MD, MS, Ethan M. Balk, MD, MPH, and Vivian W. Sung, MD, MPH, for the Society of Gynecologic Surgeons Systematic Review Group

OBJECTIVE: To comprehensively review and critically assess the available gynecologic surgery venous thromboembolism prophylaxis literature and provide clinical practice guidelines.

DATA SOURCES: MEDLINE and Cochrane databases from inception to July 2010. We included randomized controlled trials in gynecologic surgery populations. Interventions and comparators included graduated compression stockings, intermittent pneumatic compression, unfractionated heparin, and low molecular weight heparin; placebo and routine postoperative care were allowed as comparators.

METHODS OF STUDY SELECTION: One thousand two hundred sixty-six articles were screened, and 14 randomized controlled trials (five benign gynecologic, nine gynecologic oncology) met eligibility criteria. In addition, nine prospective or retrospective studies with at least 150 women were identified and provided data on venous thromboembolism risk stratification, gynecologic laparoscopy, and urogynecologic populations

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Systematic Review: VTE prophylaxis

- Literature review: inception to 2010
- 14 RCT
- 9 prospective/retrospective studies for (MIGS and UROGYN)
- Prevalence
  - 0-2% in benign GYN population without VTE prophylaxis
  - 1% with VTE prophylaxis
  - 0-14.8% vs 34.6% in GYNONC, respectively
- Identified Risk Factors,: age >60, prior DVT, h/o cancer Systematically extract all relevant data from each study
- Intermittent Pneumatic Compression (IPC) sufficient in preventing DVT in majority of benign GYN patients

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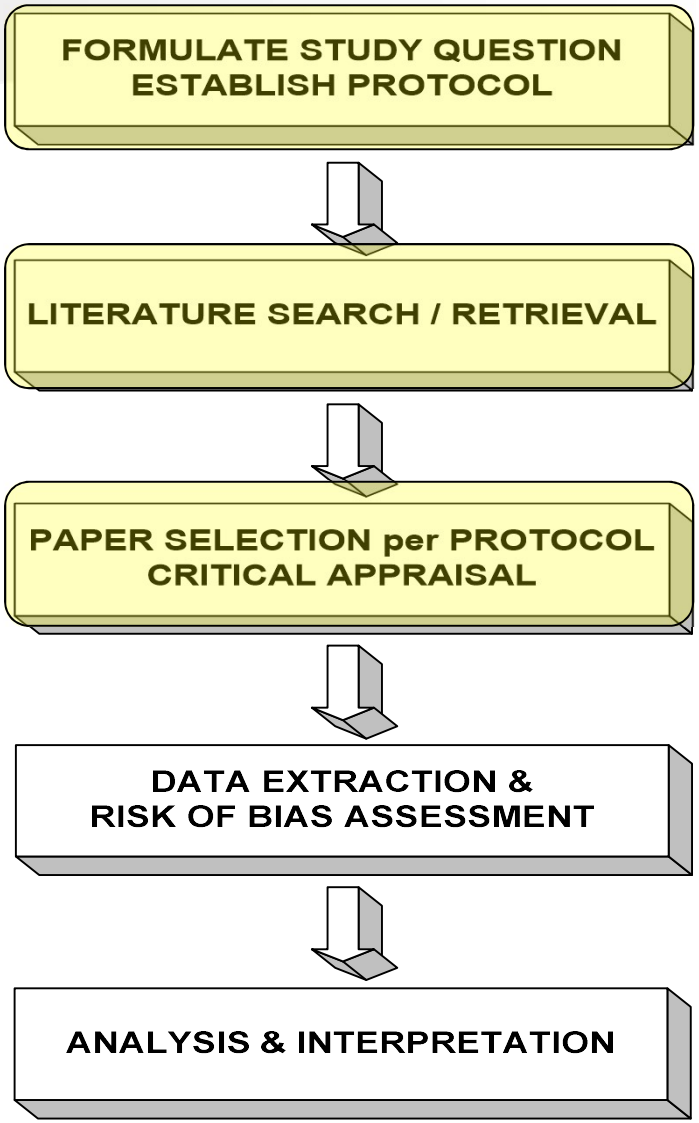
Systematic Review: Question, Literature, Selection



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Well-Formulated Research Question (PICO-D)

- **P** Population (eg, diagnosis, condition, risk status)
- **I** Intervention or exposure (eg, new surgical technique)
- **C** Comparator (eg, standard of care, no surgery)
- **O** Outcomes
  - Critical (most important, patient-centered)
  - Important (preferentially patient-centered)
  - *Not important (exclude from review)*
  - Adverse events, harms, complications
- **D** Study Design
  - Randomized, comparative, prospective, etc.
  - Study duration (dependent on critical outcomes)
  - Sample size (if a lot of evidence, maybe just harms)

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Research Questions

Poorly formulated research question:

- What's the best VTE prophylaxis in women undergoing benign gynecologic surgeries?

Well-formulated research question:

- In women undergoing surgery for presumed benign gynecologic conditions (and/or those with known gynecologic malignancy), how do women using prophylactic unfractionated heparin (UFH) or low molecular weight heparin (LMWH) compare with those using other active comparators in the prevention of perioperative symptomatic and asymptomatic venous thromboembolism (VTE) in light of potentially increased bleeding complications?

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Well-Formulated Research Question (PICO-D)

- **P** Population

Stratify:

- 1) women undergoing surgery for presumed *benign gynecologic conditions*
- 2) women undergoing surgery for *gynecologic malignancies*

Stratify:

- 1) laparoscopic and robot; 2) laparotomy; 3) vaginal surgery *OR*
- 1) minor vs. 2) major surgery

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Well-Formulated Research Question (PICO-D)

- **P** **Population**
- **I** **Intervention**
  - Graduated compression stockings (GCS)
  - Sequential compression devices (SCDs)
  - Heparin (UFH or low dose unfractionated heparin, LDUH)
  - LMWH

Well-Formulated Research Question (PICO)

- **P** Population
- **I** Intervention or exposure
- **C** Comparator
  - Graduated compression stockings (GCS)
  - Sequential compression devices (SCDs)
  - Heparin (UFH or low dose unfractionated heparin, LDUH)
  - LMWH
  - Placebo (? Reasonable to include placebo in today's era?)

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Well-Formulated Research Question (PICO)

- **P** Population
- **I** Intervention or exposure
- **C** Comparator
- **O** Outcomes
  - Confirmed DVT by Doppler / angiogram
  - Confirmed PE by CT angiogram
  - Bleeding complications: need for blood transfusion, EBL, return to OR for bleeding, hematoma
  - Death

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Systematic Review: Literature Search

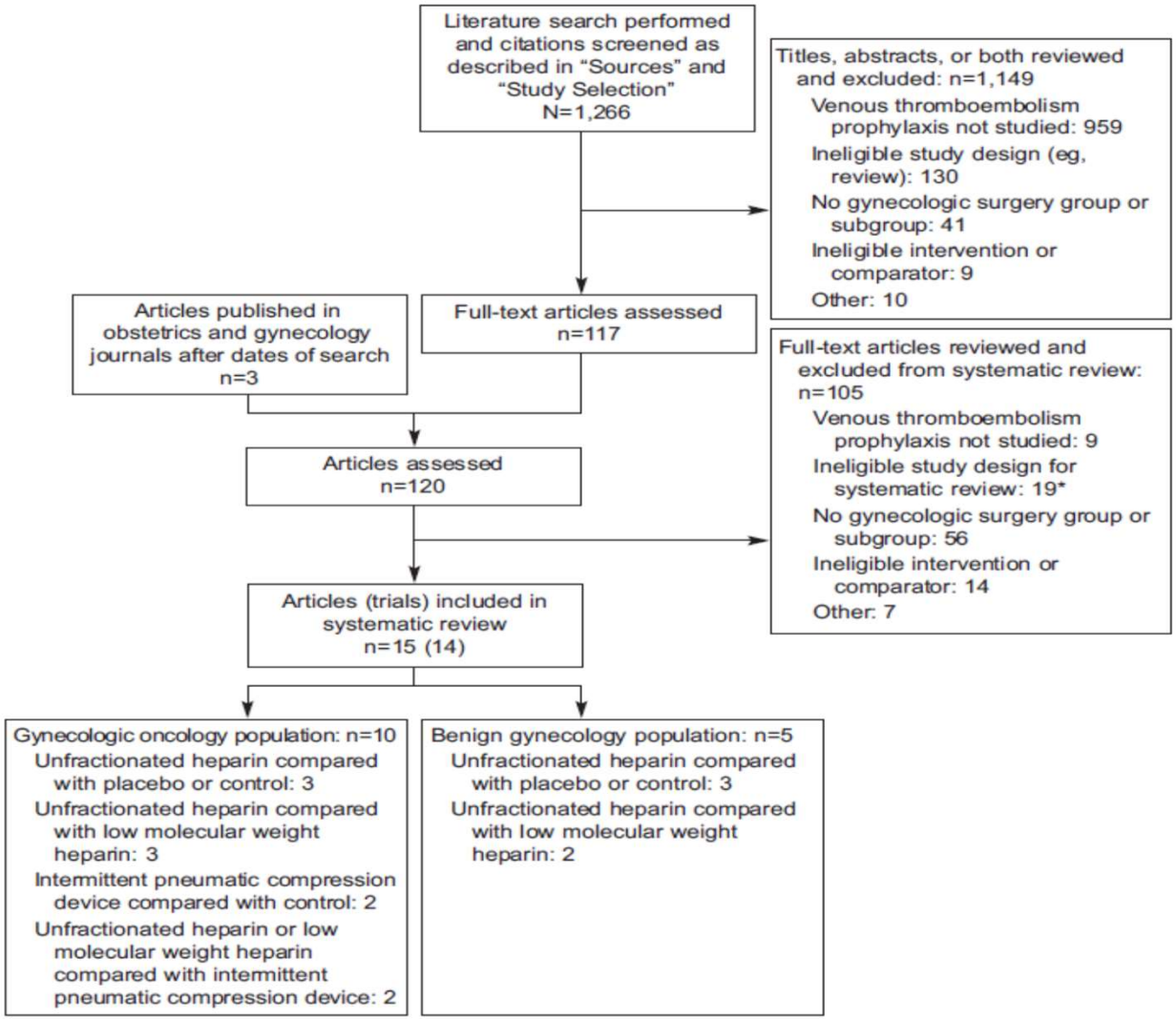
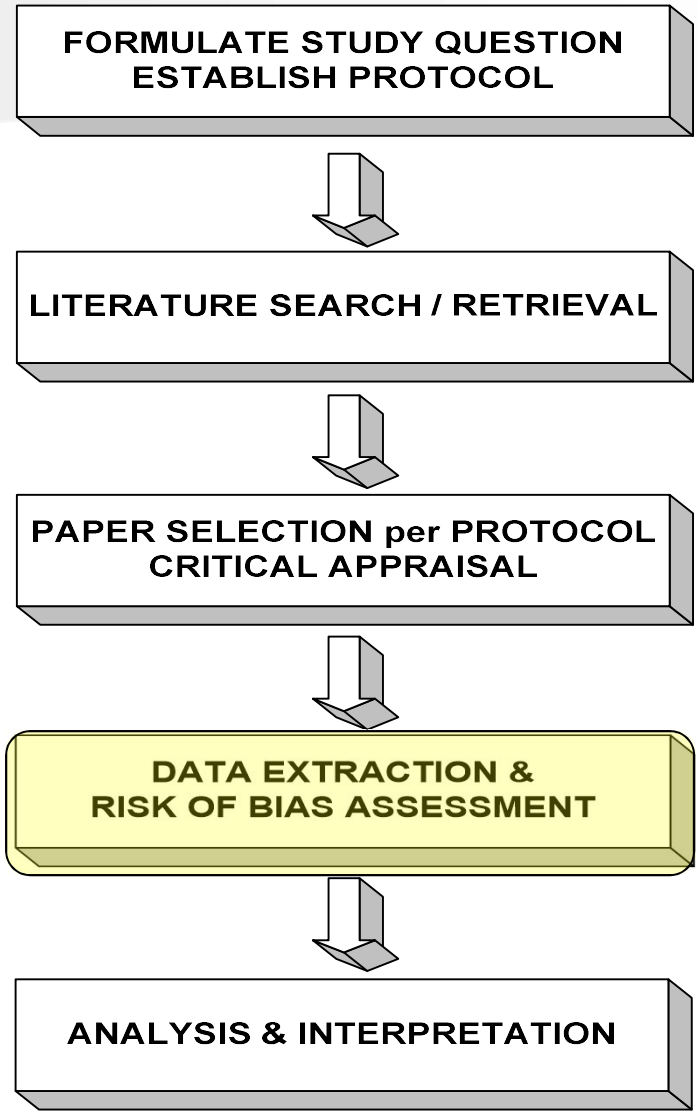


Fig. 1. Flow diagram of study search and systematic review. *After full-text review, 19 articles were ineligible for inclusion in the primary systematic review because they were not randomized controlled trials; 14 of these studies were either prospective or large retrospective studies in gynecologic surgery populations, nine of which were helpful in guideline formation.

Rahn. Surgical Venous Thromboembolism Prophylaxis. Obstet Gynecol 2011.

Systematic Review: Evidence Profile



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Systematic Review: Evidence Profile

Evidence Profile for Benign Major Gynecologic Surgeries: Unfractionated Heparin (UFH) vs. Placebo or Control									
							Summary of Findings		
Outcome	No. Studies	Total N	Methodological Quality	Consistency	Directness	Other Considerations	Evidence Quality	Effect	Outcome Importance
VTE Occurrence: clincally overt VTE or PE	2	1691	1B (-2), 1C (-4)	0	0	0	Very low	No difference	Critical
Bleeding: Transfusions	3	203	1A (0), 2B (-1)	0	0	0	Moderate	No difference	Critical
Bleeding: EBL	2	134	1A (-1), 1B (-2)	-1	0	0	Very low	Favor Placebo	High
Bleeding Complications: re-operation, wound hematoma, stopping ppx	3	1760	2B (-1,-2), 1C(-3)	0	0	0	Low	No difference	High
Laboratory Value Changes	2	161	2B (-1)	0	0	0	Moderate	No difference	Moderate
Wound, injection site complications, other	2	161	2B (-2)	0	0	0	Low	No difference	Moderate
Total	4	1802							
Balance of benefits and harms: comparing UFH (5000 units preop and bid postoperatively) to placebo or control for prophylaxis against VTE in a bengin gynecologic population, it is uncertain whether UFH is preferable to early ambulation. Use of UFH at these doses may result in greater EBL but no other differences in bleeding complication rates (weak evidence). Data are insufficient to compare differences in rate of VTE occurence.							Quality of overall evidence: C		

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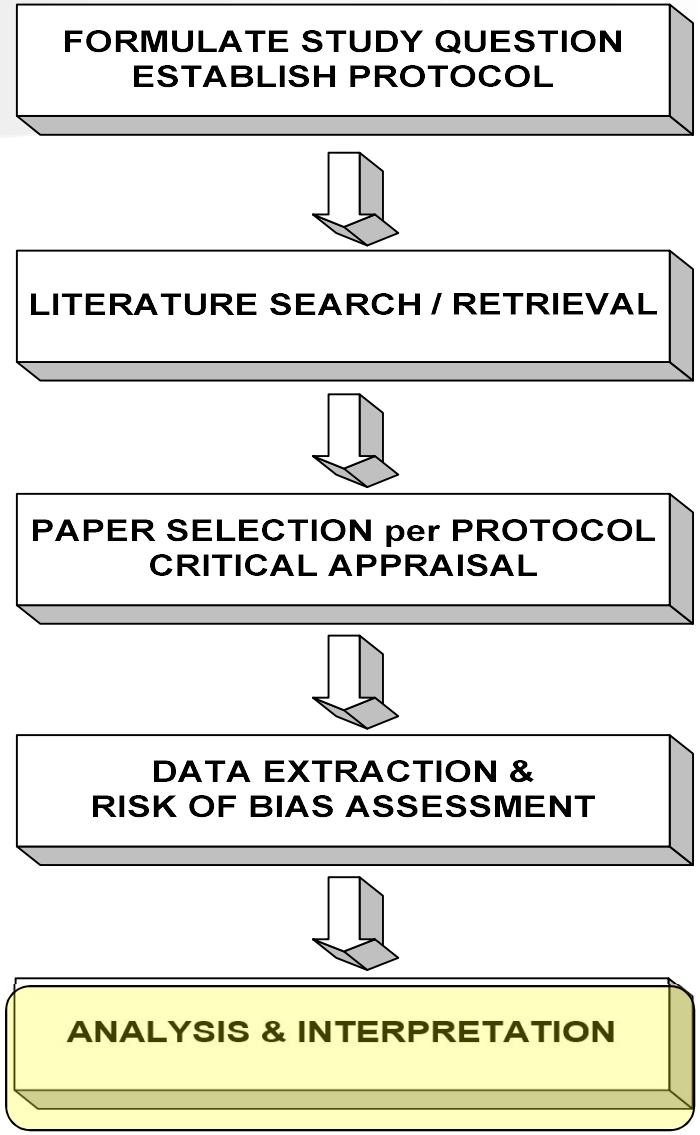
Systematic Review: Analysis, Interpretation, Clinical Practice Guidelines



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Systematic Review: Analysis, Interpretation, Clinical Practice Guidelines

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Any	Yes (or suspected)	No	Yes or no	Younger than 60 y	Using IPC applied before induction of anesthesia and continued until time of discharge for the prevention of VTE; using perioperative LMWH§ or UFH‖ in addition to IPC if there is otherwise a perceived high risk for VTE*	2C
Any	Yes (or suspected)	Either a history of VTE or age 60 y or older			Using IPC applied before induction of anesthesia and continued until time of discharge and either LMWH‡ or UFH§ for prevention of VTE and continuation of postoperative therapy for 2–4 wk after discharge[30,40] with the same doses of LMWH or UFH in this highest-risk population; the decision between types of heparin therapies may be directed by physician preference, cost, ease of administration, or all of these	2C

How to Use a Clinical Practice Guideline

- Use in the context of your practice (surgical variation) and patient population
- May open your eyes to new info – VTE RF
- May contradict what you believe – go to SR
- Most likely confirms what you already know
- Discuss with/give to your patients
- Use it as one tool in your toolbox

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- **Thank you**
- **Questions?**

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