CEU Quick Guide on Conducting Systematic Reviews

Below is a summary of the steps in the process of conducting a systematic review. Fuller information and working examples can be found in the subsequent pages.

Step 1 – Formulate an 'answerable' research question (page 2)

- Consider whether your question can be answered by research evidence.
- Note: research evidence is usually unavailable to answer specific questions relating to complex clinical cases, service management and audit/standards and would require your clinical judgement and/or expert opinion.

Step 2 – Conducting a systematic review of literature (page 3)

- Check if existing guidelines answer your question.
- Identify appropriate search terms – ensure it is broad enough to capture all relevant articles, however you also want it to be specific enough so you don't end up with a lot of irrelevant hits from your search.
- Use an appropriate literature database for your search (PubMED/Medline is a good starting point for articles in field of natural science and medicine).

Step 3 – Accessing and assessing the articles (page 4)

- Review the abstracts of the articles identified to check if they are relevant.
- Access, read and critically appraise the full article available to you.
- You can apply for an Open Athens log-in for access.
- Note that different study designs yield different types/quality of data so it is important that you assess the appropriateness and quality of evidence that you identified to inform your answer.
- The hierarchy of evidence (see page 4) should inform the weighting that you give to the findings of different studies to inform your answer.

- Step 4 – Concluding/answering the clinical question (page 5)
- Consolidate your findings and understanding to reach a conclusion/answer.
- It may be the case that the conclusion is that no evidence exists and therefore the question is unanswerable by evidence; expert opinion and clinical judgement is required in such a situation.
- This involves weighing up the evidence and considering how it helps in your clinical decisions.
- Where appropriate, broader clinical issues should also be considered (particularly where the question relates to a real-life case).
- See an example of an evidence-based response by the CEU to a member's enquiry in appendix 1 (page 6).

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Step 1 – Formulating an 'answerable' clinical question

Before conducting a systematic literature search, it is important to consider whether the clinical question can be answered with an evidence-based response.

A clinical question that is 'answerable' with an evidenced-based response typically includes the following (PICO/PEO) elements:

- Population (e.g. women with type 1 diabetes)
- Intervention/Exposure (e.g. contraceptive methods/IUS)
- Comparator (e.g. control group of women not using contraception)
- Outcome (e.g. safety/efficacy)

A clinical question that is unsuitable for an evidence-based response typically relates to:

- complex clinical cases
- clinical management or audit/standards

Consider the 2 examples below received by the CEU via the enquiry service:

Example 1
A 20-year-old woman requests IUS insertion. She gives a history of sporadic intermenstrual bleeding since menarche at age 12 years, approximately 5 episodes per year. K=7/31. Swabs are negative and the cervix appears normal. I have requested an USS. **Assuming this is normal are there any further investigations (gynae or endocrine) that I should request before it would be appropriate to fit the IUS?**

- This query requires clinical judgement and cannot be answered by an evidence-based scientific review of the literature.
- The enquiry was responded to with an email stating that: CEU is not able to give advice regarding individual clinical cases; our role is to provide evidence-based general guidance for contraceptive use on which individual clinical judgement can be based.
- In such instances, the CEU recommends seeking advice from a local specialist.

Example 2
I have a 20-year-old patient with past history of ileocolic intussusception, requiring an ile-ectomy and ileal-ileal anastomoses in 1995. She only finds oral contraception acceptable. Combined contraception is contraindicated on account of migraine with aura. She had a previous failure on COCP with unplanned pregnancy aged 16yrs and describes good adherence at this time. **Is there any evidence that the previous bowel resection could reduce the efficacy of a POP?**

- The clinician have provided the woman's medical history, known contraindication to specific methods (COC) and information about acceptability of contraceptive methods ("only oral contraception").
- The question being asked is unambiguous. The concern here relates to **efficacy** of using the **progestogen-only pills** given that the woman had a **small bowel (ileal-ileal) resection**. This is helpful in terms of refining the search strategy which will be discussed in step 2.

The "PICO" elements for this example are:

Population	Women who had a small bowel (ileal-ileal) resection
Intervention	Progestogen-only pills
Comparator	Women without a history of small bowel resection
Outcome	Efficacy of contraceptive method

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Step 2 – Conducting a systematic review

After establishing that the clinical question can be answered with an evidence-based scientific/systematic review of the literature, a preliminary search is conducted to identify whether existing clinical guidance is available and sufficient in answering the enquiry. The following checks should be conducted to identify existing Clinical Guidelines that answer the question:

- Existing FSRH guidance including the UKMEC, clinical guidance and statements
  - (http://www.fsrh.org/pages/clinical_guidance.asp)
- Guidance from other organisations including:
  - RCOG (https://www.rcog.org.uk/en/guidelines-research-services/)
  - BASHH (https://www.bashh.org/about-bashh/publications/)
  - NICE (http://www.nice.org.uk/Guidance)
  - SIGN (http://www.sign.ac.uk/our-guidelines.html)

If no guidance exists or if the guidance is judged to be insufficient (or likely to be outdated due to new evidence), a systematic literature search should be conducted.

Electronic bibliographic databases

The following electronic bibliographic databases are useful for your literature search:

- The Cochrane Library (http://onlinelibrary.wiley.com/cochranelibrary/search) for published Cochrane Systematic Reviews.
- PubMed/MEDLINE (http://www.ncbi.nlm.nih.gov/pubmed/)
- EMBASE (http://www.elsevier.com/online-tools/embase)
- Google scholar can be a good resource to look for additional articles or citations.

Search terms and strategy

The goal of the systematic literature search is to achieve a balance between ***sensitivity*** (capturing all relevant articles) and ***precision*** (eliminating irrelevant hits). As a general rule, you want to aim for high sensitivity so you do not miss out relevant articles which can bias your conclusions (or cause it to be misinformed or wrong).

Search ***sensitivity*** is achieved by searching for all possible variations/permutations of a search term. A **search string** can be constructed by joining together the different terms using the Boolean operator 'OR.'

- You can simply type in the term that you want the search engine to use. This will give you a starting point for your search to see what kind of literature exists.
- You can broaden your scope using OR to ensure you don't miss out how different authors may use similar terms (e.g. oral OR pills), different forms of the same word (e.g. quickstart OR quickstarting OR quick-start) or spelling (e.g. sterilisation OR sterilization).

You can improve the ***precision*** of your search by using different symbols (including "" and *) in PubMed search. However, please note that these symbols may not work for other databases – see help menu in individual databases for more information:

- Encasing term within a double quotation mark ("xxx xxx" will perform a search of literature with the specific term(s) indicated (e.g. "contraceptive pill" will only bring up articles containing the term 'contraceptive pill' but not pick up articles on 'contraceptives' or 'contraception').
- Adding an asterisk after a term (xxx*) will perform a truncation search which means that it will search for words used in the literature that starts with the root (e.g. Contracept* will include a search for contraceptives and contraception).

It is recommended that a search string should be constructed separately for each element (population, intervention or outcome) of your clinical question. These can then be joined using Boolean operator 'AND' to identify the articles that met the criteria for each of the search strings. Typically 2 strings (population/condition) AND (intervention) are combined.

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Step 3 – Accessing and assessing the articles

Now that a list of articles has been identified, the next step is to select the articles that are relevant in answering your question. The following filters will help narrow the pool of articles to include only the relevant articles:

- screening the title/abstract for duplicates and articles clearly not relevant (eg animal studies, patents)
- Exclude articles which you have no access to the abstract/full text, or non-English
- Articles which do not directly address the clinical question (eg a narrative review of a condition or contraceptive method or molecular studies) may be kept/used to provide useful background information.

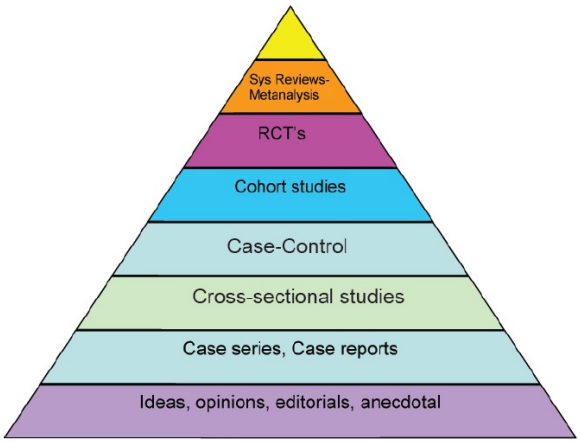
Access to articles

You may have free access to articles based on the institution you are affiliated with including universities and professional organisations (e.g. FSRH, RCOG, RCGP) or the health board you work in.

- You can apply for an Open Athens log-in. Access to different journals vary according to the subscription that our organisation has as part of their Open Athens arrangements.
- For more information, see Open Athens website (http://www.Open Athens.net/).

Types of literature/level of evidence

- Full articles deemed to be potentially suitable should be obtained for review.
- Personal review articles ideally should not be used within the guidance documents but can be used to find relevant papers and for background.
- Below is the hierarchy of evidence with the peak (systematic review/meta-analysis) being judged the highest level.
- Accordingly, the findings of well-conducted studies higher on in the hierarchy will be judged as being more robust and hence should be considered as giving more weight to the conclusions reached in a review.



Aslam S, Georgiev H, Mehta K, Kumar A. Matching research design to clinical research questions. Indian J Sex Transm Dis [serial online] 2012;33:49-53. Available from: http://www.ijstd.org/text.asp?2012/33/1/49/93829 [Accessed 18 July 2017]

Critical appraisal of the literature

The quality of the studies included in a systematic review should be considered at every step of the process. In the context of conducting a systematic literature search and review to answer a member's enquiry, the CEU do not use critical assessment tools to examine the risk of biases; the CEU adopts the GRADE approach to evaluation of evidence quality when developing FSRH clinical guidance. You may wish to use particular critical appraisal tools to facilitate an assessment of the risk of biases at this point.

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Step 4 – Concluding/answering the clinical question

The conclusion that you reach at the end of this process should be based on weighing up the strength and weakness of the studies and evidence that you have found, assessed and collated. This should help inform your clinical judgement and be a core step in your decision-making process.

It is important to acknowledge that, especially in relation to rare conditions, often there may be no study/evidence available to inform your answer. In such situations, expert opinion and clinical judgement is required.

The CEU response to example 2 can be found in appendix 1.

References and further reading:

Aslam S, Georgiev H, Mehta K, Kumar A. Matching research design to clinical research questions. *Indian J Sex Transm Dis [serial online] 2012*; **33:** 49-53. Available from: http://www.ijstd.org/text.asp?2012/33/1/49/93829 [Accessed 16 October 2015]

Khan KS , Kunz R, Kleijnen J and Antes G. *Systematic reviews to support evidence based medicine. How to Review and Apply Findings of Health Care Research (Second Edition).* London: CRC Press, 2011. Online version can be found at: http://sgh.org.sa/Portals/0/Articles/Systematic%20reviews%20to%20support%20evidence-based%20medicine%20%282nd%20edition%29.pdf [Accessed 16 October 2015]

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Appendix 1: Example of evidence based response to member's enquiry

I have a 20 year patient with past history of ileocolic intussusception, requiring an ileectomy and ileal-ileal anastomoses in 1995. She only finds oral contraception acceptable. Combined contraception is contraindicated on account of migraine with aura. She had a previous failure on COCP with unplanned pregnancy aged 16yrs and describes good adherence at this time. Is there any evidence that the previous bowel resection could reduce the efficacy of a POP?

Response

[Introduction regarding the condition] Ileocolic intussusception is a process in which a segment of intestine invaginates into the adjoining intestinal lumen, causing bowel obstruction. Treatment options include the resectioning (e.g. ileal-ileal anastomoses) of the intussuscepted bowel loops.

[Outcome of systematic literature search] The CEU conducted a systematic literature search and did not find any study looking at effectiveness of oral contraception with a specific history of intussusception or following ileal-ileal anastomoses or a history of ileectomy.

[Summary of evidence/helpful information which may be directly or indirectly relevant to the question that should be considered] Oral contraceptives (OC) are mainly absorbed from the small intestine, and contraceptive efficacy depends on adequate absorptive capacity. Ileal or ileocecal resection results in more rapid intestinal transit and less time for absorption which may affect bioavailability of OC. Fat malabsorption as a result of extensive resectioning of the small intestine may also contribute to the decreased absorption of fat-soluble OC. [1]

The FSRH guidance on Inflammatory Bowel Disease noted that oral contraception may be less reliable in women with IBD who have malabsorption due to small bowel resection. [2] No evidence was identified to suggest any reduction in the efficacy of the combined patch, progestogen-only injectables, progestogen-only implants or intrauterine methods in this situation.

We found one systematic review looking at contraceptive use amongst women with a history of bariatric surgery. [3] The systematic review identified two pharmacokinetic studies which reported on contraceptive hormone levels and absorption following a single dose of contraceptive hormone after jejunoileal bypass surgery [4,5]. Based on the limited evidence regarding the effectiveness of oral contraceptives following jejunoileal bypass, the authors of the systematic review concluded that there is no substantial evidence of decreased contraceptive effects due to a bypass procedure.

[Conclusion and recommendation] The CEU concludes that there is inadequate information in the literature to confirm effectiveness of any OC following intussusception surgery of the small bowel. Bearing this in mind, if an individual woman has had a documented failure of combined oral contraception, it would seem sensible to avoid the oral route and promote non-oral methods.

References

1. Titus R, Kastenmeier A, Otterson MF. *Consequences of gastrointestinal surgery on drug absorption.* Nutrition in Clinical Practice 2013; **28**: 429-436

2. Faculty of Sexual & Reproductive Healthcare (FSRH). Sexual and Reproductive Health for Individuals with Inflammatory Bowel Disease. 2016. http://www.fsrh.org/documents/ceu-clinical-guidance-srh-ibd/

3. Paulen ME, Zapata LB, Cansino C, et al. *Contraceptive use among women with a history of bariatric surgery: a systematic review.* Contraception 2010; **82**: 86-94.

4. Victor A, Odlind V, Kral JG. *Oral contraceptive absorption and sex hormone binding globulins in obese women: effects of jejunoileal bypass.* Gastroenterology Clinics of North America 1987; 1**6**: 483-491.

5. Andersen AN, Lebech PE, Sørensen TI, et al. *Sex hormone levels and intestinal absorption of estradiol and D-norgestrel in women following bypass surgery for morbid obesity.* International journal of obesity 1981; **6**: 91-96.

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