Using evidence reviews to develop focused systematic review questions

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Introduction

Systematic literature reviews (SLRs) have a number of important functions, but are essential for supporting Health Technology Assessments.

SLR questions are based on PICO elements which specify types of participants (P), interventions (I) comparators (C), and outcomes (O) of interest.

Evidence reviews (ERs) can act as stand-alone data sources and allow the researcher to acquire a detailed understanding of a disease area and literature base, in order to develop robust PICO elements. These PICO elements are then used to develop focused SLR questions.

ERs are also useful for determining if the proposed SLR question has been previously answered within the literature.

What is an evidence review?

An ER is a type of rapid review (Tricco et al., 2015), which provides a comprehensive overview of a variety of different aspects of a disease area. This may include biological, clinical, health-related quality of life (HRQL) or economic aspects of the disease and is intended to be the starting point for any individual who wishes to obtain an overall understanding of a disease area.

In many circumstances, ERs are useful stand-alone sources of information. However, they can be used to support a variety of projects, for example network meta-analyses, economic models, value proposition and global value dossier development, as well as informing product strategy.

If being used to develop PICO, ERs initially involve understanding the overall objective of the SLR. Once the end purpose of the SLR is understood, researchers can agree contents of the ER within a cross-functional team including scientists, medical writers, research analysts, health economists, editors and consultant clinicians.

ERs provide the reader with an overall understanding of the disease area, which enables easier focusing of systematic review questions and population of PICO with relevant search terms.

Examples of sections that may be included within an ER, depending on the end-purpose of the SLR, are summarised in Table 1.

Table 1: Examples of ER section headings that can be included based on the long term aims of a project

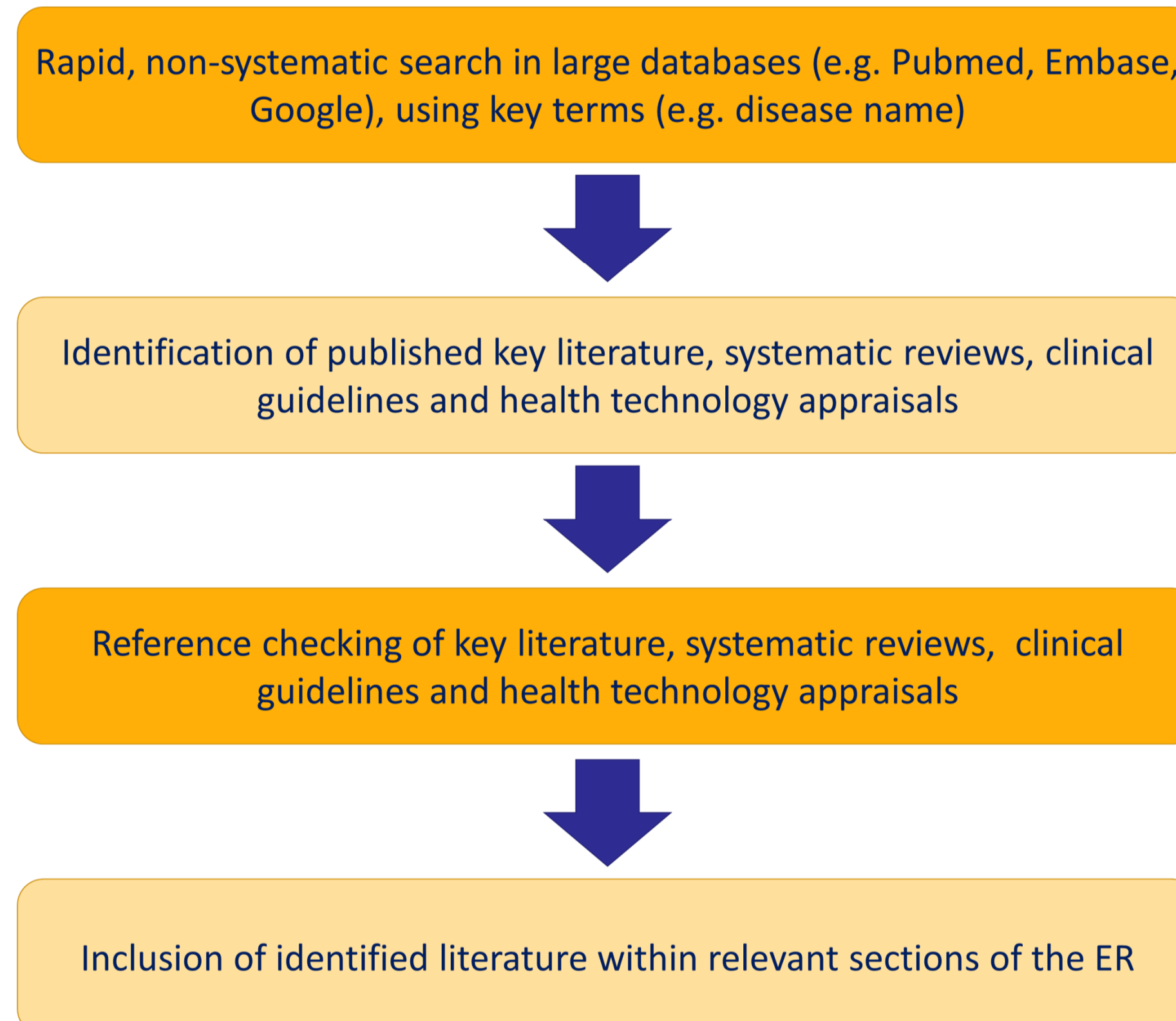| Suggested ER sections for inclusion:	What will the ER be used for?		
	Stand-alone data source	Select comparators for a Network meta-analysis (NMA)	Influence economic model design
Definitions and diagnosis	✓	✓	✓
Epidemiology	✓	✓	✓
Treatments	✓	✓	✓
Clinical guidelines and treatment pathways	✓	✓	✓
Key clinical trials	✓	✓	✗
Published systematic reviews	✓	✓	✓
Health-related quality of life and health-state utility values	✓	✗	✓
Costs/ economic evaluations	✓	✗	✓
HTA decisions	✓	✓	✓
Real-world evidence and registries	✓	✗	✓

*Note: These section headings are examples. Table is non-exhaustive and ERs can be individually tailored to support the needs of a variety of different projects

Methods involved in developing evidence reviews and systematic reviews

The process used to identify literature for inclusion within an ER is summarised in Figure 1. Literature which is used to write an ER is searched for using a targeted, iterative process, beginning with identification of key publications, systematic reviews, clinical guidelines and health technology assessments. The reference lists from the key literature are then checked, to identify additional important sources, such as key clinical trials, HRQL studies and cost/ economic evaluations.
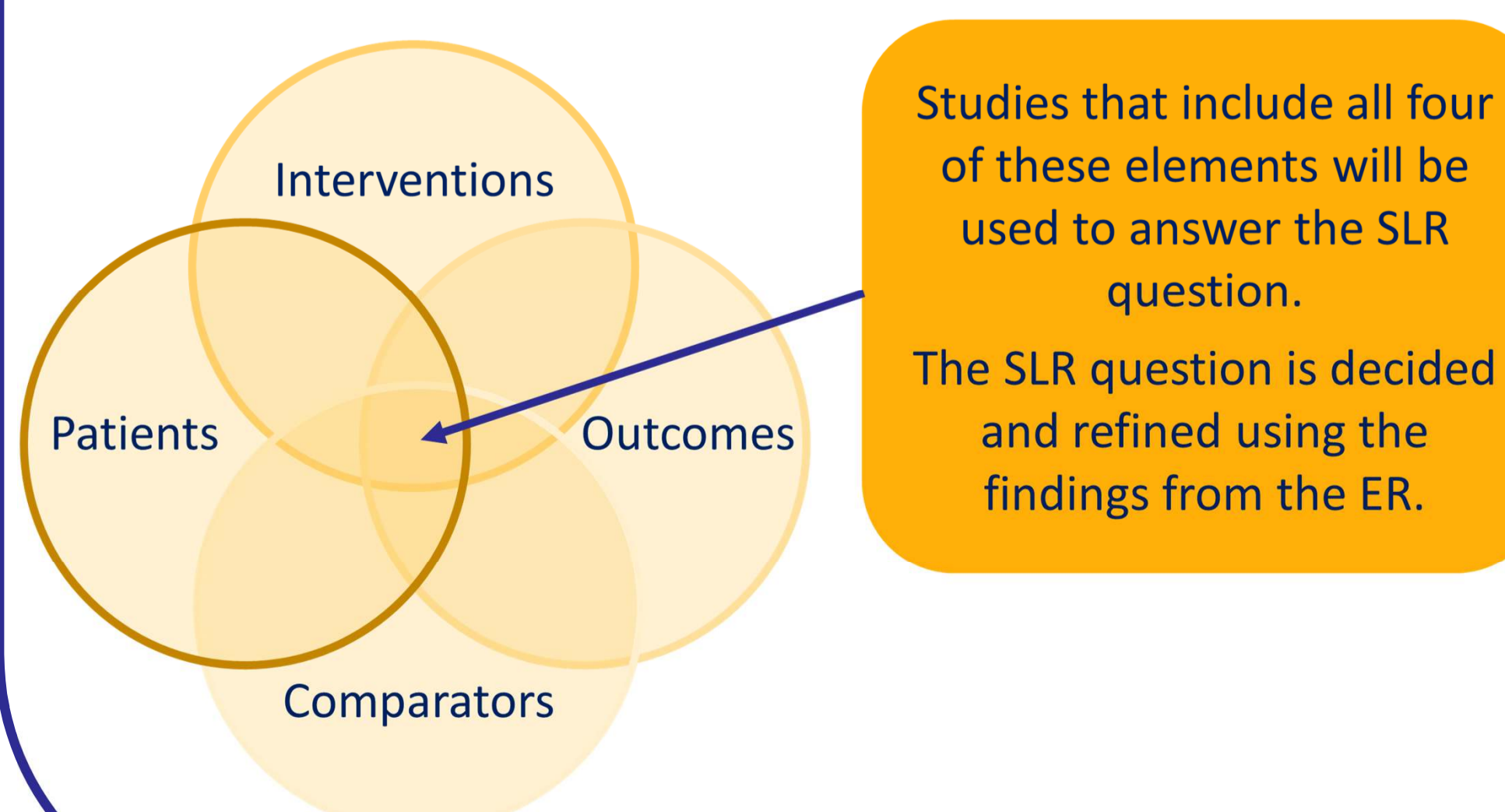
Relevant literature which provides information pertaining to the agreed ER sections is detailed within the review and used to form overarching summaries. Data gaps are easily identified which can inform strategic development of projects.

Figure 1: The process involved in identifying literature for inclusion within an evidence review

Rapid, non-systematic search in large databases (e.g. Pubmed, Embase, Google), using key terms (e.g. disease name)

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Identification of published key literature, systematic reviews, clinical guidelines and health technology appraisals

↓

Reference checking of key literature, systematic reviews, clinical guidelines and health technology appraisals

↓

Inclusion of identified literature within relevant sections of the ER

The literature used to write an SLR is searched for by first agreeing the SLR question which is focused using the findings from the ER. The PICO elements are populated with relevant search terms which are used to construct a robust search strategy. The search strategy should be used to obtain literature from a number of large databases (e.g. Embase, MEDLINE and Econlit), and hand-searching of relevant congresses and conference abstracts should also be carried out in order to identify the most recent data which may not have yet been published in peer-reviewed manuscripts. This entire process often yields a high volume of references which are screened to identify only those adhering to the previously agreed PICO (Figure 2). Those which qualify for inclusion are then data extracted and written up into the SLR, which then answers the original question in a focused manner.

Figure 2: The target literature that will be included in the SLR in order to answer the focused question developed from the ER

Interventions

Patients

Outcomes

Comparators

Studies that include all four of these elements will be used to answer the SLR question.

The SLR question is decided and refined using the findings from the ER.

Typical timelines and expected results for evidence reviews and systematic reviews

Timelines for developing ERs and SLRs are shown in Figure 3. ERs typically take up to 12 weeks to produce, after which the SLR development process can begin immediately. The development of PICO can begin towards the end of the ER write-up as it is generally the case that by this point, the writer has developed a thorough understanding of the disease area and can begin to refine the SLR question in collaboration with the cross-functional group.

Figure 3: Timelines for the process involved in developing an ER, PICO elements and an SLR

Evidence review

PICO development

Systematic review

Month: 1 2 3 4 5 6 7 8 9
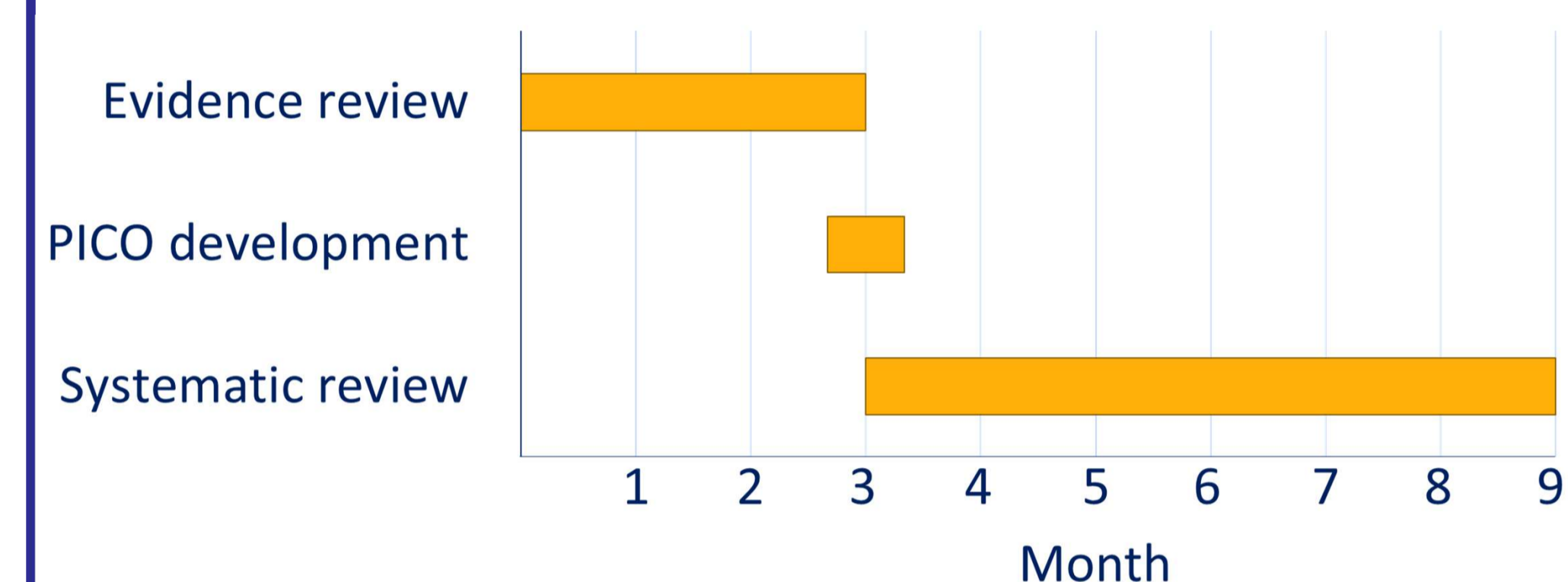
Note: timelines can vary, depending on the scope of the ER and SR

Due to the iterative nature of the searching process involved in identifying literature for ERs, different writers may find different sources which can be included in the review. However, as sections are based on key published literature and provide a general understanding of different aspects of the disease area, the findings are likely to be the same.

SLRs in contrast answer highly-focused questions. In order to answer these questions, methods have to be clearly defined within a protocol, with a robust rationale to justify them. This allows multiple researchers to follow the same methods, identify the same publications which are eligible for inclusion, extract the same data from the resulting publications and use them to develop the same conclusions which are able to answer the systematic review question. The highest quality SLRs begin with the most appropriate, focused SLR questions and these are refined by first obtaining a general but thorough understanding of the disease area, which can be developed using the findings of an ER.

Conclusions

- An ER is a type of rapid review which can be used to support a number of different projects, and develop questions to be answered by SLRs.
- An ER is a rapid way of providing an overall, detailed understanding of different aspects of a disease area.
- ERs help us to understand disease classification, subtypes, and line of treatment, which justifies the selection of participants for an SLR.
- Knowing which treatments are available, whether they are recommended in clinical guidelines and HTAs, and relevant treatment stratification factors for target participants justifies interventions and comparator selection for SLRs.
- Methods for reporting efficacy in clinical trials informs the outcomes element of an SLR.
- ERs allow researchers to determine if the SLR question has been previously answered and published.
- ERs are a useful way of informing the framing of PICO elements and refining search questions for SLRs.

References
Tricco, A. C., J. Antony, W. Zarin, et al. (2015). A scoping review of rapid review methods. BMC Medicine 13(1) 1-15.

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