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Knowledge Synthesis in Evidence-Based Medicine

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Systematic reviews are the most common form of knowledge synthesis and remain a cornerstone of the practice of evidence-based medicine. They offer enhanced rigor and validity relative to traditional narrative review articles by reducing bias and increasing objectivity. In answering focused research questions, systematic reviews are directly applicable to clinical practice as well as the development of clinical guidelines and the identification of knowledge gaps, which may drive future primary research directions. Typically, such a rigorous process necessarily requires substantive time to carefully and systematically identify, screen, and synthesize all relevant available primary research on a topic. Further, other knowledge synthesis methods have emerged to address the varying needs of decision makers with respect to condensed timelines and more diverse research questions, as well as to allow incorporation of already synthesized evidence into reviews. These alternative methods include rapid reviews, scoping reviews, and overviews of systematic reviews, which are being used with increasing frequency by clinicians, decision-makers, and researchers. We encourage clinicians and researchers in nuclear medicine and other imaging sciences to acquire a greater familiarity with these methods and to consider them in clinical decision making, the development of clinical guidelines, and the planning of future research activities.

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A quarter of a century ago, the evidence-based medicine (EBM) movement promised to transform clinical practice from one entrenched in opinion, tradition, and anecdote into one integrating empirical evidence, clinical judgement, and patient values.[1,2] In the ensuing period, a quagmire of research evidence has been published in the effort to guide clinical practice.[2] Increased adoption of EBM principles will allow clinicians and policy makers to summarize vast quantities of evidence in a way that will produce reliable and unbiased conclusions to guide clinical decisions.

Health care providers often lack the time to appraise the many sources of sometimes conflicting evidence available to them.[3,4] Traditionally, an authoritative expert in a field would write a narrative review to provide recommendations for practice supported by subjectively chosen evidence, publishing the review as a book chapter or journal article. However, regardless of intention, these narrative reviews are prone to bias: some studies are undoubtedly missed and not consulted, justification for inclusion of some studies and exclusion of others is not provided, the quality of the included studies is generally not assessed, an objective quantitative synthesis of the evidence is not conducted, and conclusions may be developed first and the evidence supporting them found later.[4,5] *Systematic review* (SR) methods address the limitations of such narrative reviews. However, a SR is not simply an inflated narrative review, in which more databases are searched and more literature included.[5] What fundamentally sets SRs apart from narrative reviews are the formal methods employed throughout the review process to minimize bias and increase the reliability of the conclusions

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Table 1 Differences Between Narrative and Systematic Reviews (Adapted From Petticrew, 2001[5], Cook et al., 1997[4], and Sargeant and O'Connor, 2014[8])

Review Element	Traditional Narrative Reviews	High-Quality Systematic Reviews
Review question	Often a general discussion of a potentially broad subject with no stated hypothesis	Focused on clear question(s) to be answered or hypotheses to be tested
Searching for relevant studies	Data sources and search methods not usually specified; do not usually attempt to locate all relevant literature	Comprehensive: provide explicit strategies to locate all relevant published and unpublished studies; selection bias reduced
Inclusion and exclusion of studies	Usually do not describe or justify why certain studies are included and others excluded	Have explicit criteria that studies must meet for inclusion; selection bias reduced
Quality assessment of the included studies	Often do not critically appraise study methods or quality or consider differences between the included studies	Systematically examine the methods of the included studies, investigating potential biases in the studies that may cause differences in study results (heterogeneity)
Synthesizing study results	Usually a qualitative summary that does not differentiate between findings of studies that may have differing methods or higher risk of bias	May be quantitative or qualitative; heterogeneity of study results is considered and described; statistical pooling (meta-analysis) possible where data and study methods are similar
Conclusions derived	Usually not based on the totality of the evidence	Based on the totality of the evidence, with consideration of the risk of bias in the included studies

drawn.[5,6] The major differences between narrative and SRs are summarized in Table 1.

High-quality SRs are the highest form of evidence upon which clinical decisions can be based[7]; however, not all practitioners are well-versed in this methodology. The objectives of this article are to provide specialists in the field with an introduction to SRs (including their utility in clinical practice), and to describe considerations for nuclear medicine specialists who may wish to conduct a SR but are unclear where to start. In addition, we introduce readers to other knowledge synthesis methods—*rapid reviews, scoping reviews,* and *overviews of reviews*—summarizing the contexts for their use and how they may inform clinical decision making; prominent resources worthy of consultation for the latter approaches are provided for interested readers. All of the aforementioned knowledge synthesis methodologies can offer considerable value in synthesizing existing research to inform clinical practice and/or guide future directions for specialists in the field of nuclear medicine.

What is Knowledge Synthesis?

Medical research evolves over time, with early publications often reporting more extreme positive or negative results than subsequent publications.[9] Additionally, findings from highly cited publications in prestigious journals may be challenged or even overturned by less-prominent later publications.[10,11] Thus, individual clinical studies are not reliable sources of evidence upon which to base clinical decisions. *Knowledge syntheses* are scientific studies that derive data from primary studies. They then use reliable, reproducible, and explicit methods to amalgamate and summarize that data in a way that minimizes bias and improves the reliability and accuracy of conclusions.[12] A variety of approaches and methods to conduct knowledge syntheses exist, with the most common one being a SR. More recently, a broader range of synthesis methods have developed based upon the generic SR approach including *rapid reviews*, *scoping review*, and *overviews of reviews*. Regardless of the method, knowledge syntheses generally involve the same steps, which are outlined in Figure 1. The similarities and differences between the knowledge synthesis methods have been highlighted in Table 2.

Systematic Reviews

Fundamental Concepts of Systematic Reviews

If methodologically sound, a SR establishes the most accurate, precise, and minimally biased answer possible to a refined clinical question through assembly and distillation of all available empirical evidence.[13] SRs of intervention studies can provide valuable information to clinicians regarding the efficacy and safety of a treatment compared to one or multiple alternative treatments. For example, a recent SR found ^{177}Lu-prostate-specific membrane antigen radioligand therapy was significantly more efficacious and had fewer adverse effects causing discontinuation of treatment than third-line therapy in cases of metastatic castration-resistant prostate cancer.[14] The findings of high-quality SRs of interventions can be used to develop clinical practice guidelines and can contribute data for input into health economic evaluations. In addition to applications for the evaluation of medical interventions, SRs are also used for questions related to the evaluation of diagnostic tests,[15] with methodological advances that allow comparisons and ranking of multiple diagnostic tests based on their accuracy.[16] Recent SRs have found that Fluor-18-fluorodeoxyglucose positron emission tomography and computed tomography (^{18}F-FDG-PET/CT), with adequate patient preparation for suppression of physiological myocardial FDG uptake, is useful for the

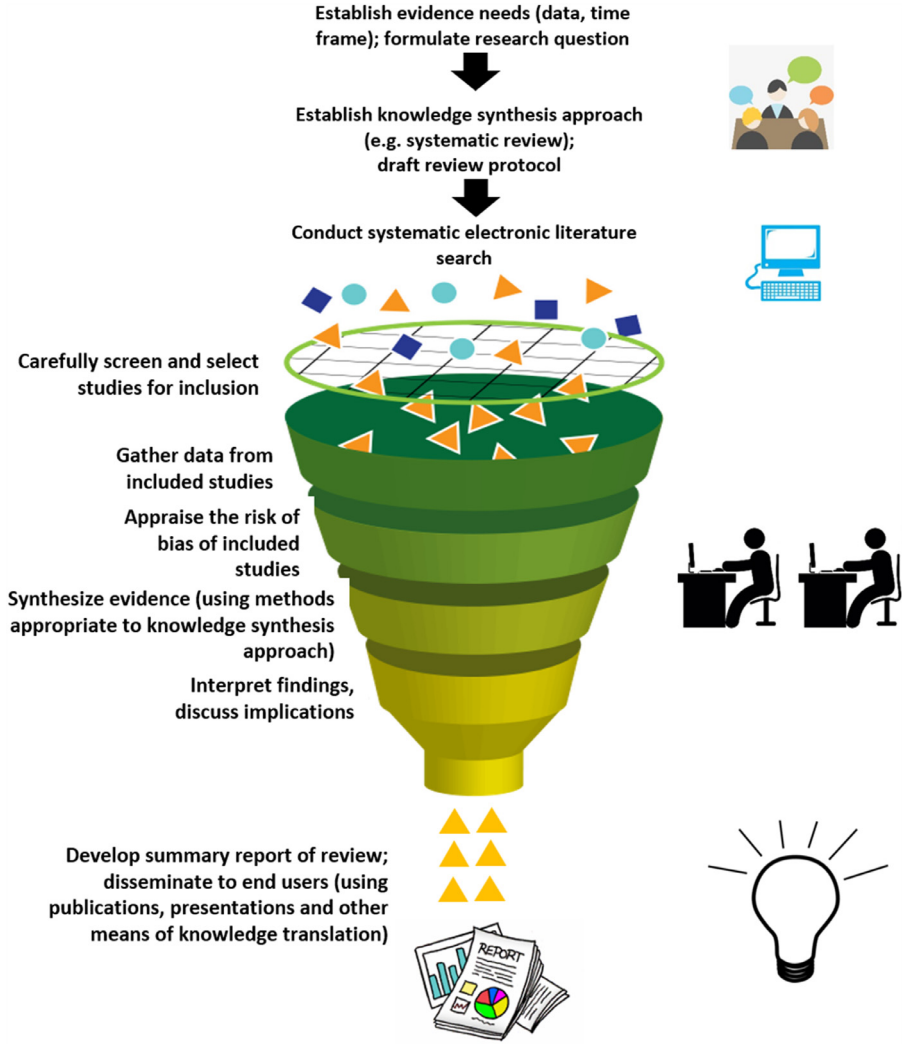

Figure 1 Stages of the knowledge synthesis process.

diagnosis of infection in cardiac implantable electronic devices (CIED) and infectious endocarditis, based on pooled estimates of sensitivity, specificity, and accuracy.[17-19] The findings from these reviews have been used to support position papers in the field[20,21] and may contribute to future clinical practice guidelines.

SRs may also identify existing knowledge gaps in a field, an equally important finding which may drive future primary research. The aforementioned recent SR of ^{18}F-FDG-PET/CT, labeled leukocyte scintigraphy, and ^{67}Ga citrate scintigraphy for the diagnosis of CIED infection found only two studies that met the review inclusion criteria for leukocyte scintigraphy, and none were identified for ^{67}Ga citrate.[17] For inclusion in the SR, studies of LS and ^{67}Ga citrate were required to have used single-photon emission computer tomography (SPECT) or SPECT-CT imaging methods, reflecting current technology; earlier studies using planar imaging methods were therefore excluded. While the findings of the two LS studies provide preliminary evidence that the test may be useful, a knowledge gap has been highlighted for both LS and ^{67}Ga citrate modalities in the evaluation of CIED infection.

Knowledge gaps have also been demonstrated by SRs of nuclear medicine interventions. For example, two SRs of the efficacy of ^{177}Lu-prostate-specific membrane antigen radioligand therapy for metastatic castration-resistant prostate cancer have highlighted a lack of randomized controlled trials (RCTs)—all included studies were observational in design (eg, retrospective cohort, case series).[14,22] Well-designed RCTs reduce bias by randomizing the allocation of treatments, thereby balancing patient characteristics across treatment groups. As such, they are preferred for inclusion in SRs.[13] Further, important consideration needs to be given to epidemiological principles in the proper design of those RCTs, an example of which is provided in the literature.[23] When RCTs are not available for the question of interest, it is valid to include observational studies in a SR; however, these reviews are more prone to bias.[7]

The risk of bias (ROB) within each included study should be assessed in a SR to identify studies that may have more or less reliable findings. The impact of studies with a high ROB on a review's findings can be determined by sensitivity analyses, in which quantitative analyses are performed with and

Table 2 Overview of Distinctions Between Knowledge Synthesis Methodologies [13,29–47,76]

	Systematic Reviews	Rapid Reviews	Scoping Reviews	Overview of Reviews
Timeframe	6 months to 2 years	Usually 4 to 16 weeks, but may be up to a maximum of 6 months	6 to 12 months	6 months to 18 months
Protocol	Developed *a priori* with little adjustment. Deviations reported in review.	Defined *a priori*, with flexibility. Deviations reported in the protocol.	Developed *a priori* with flexibility. Deviations reported in review.	Developed *a priori* with little adjustment. Deviations reported in review.
Question	Focused clinical question, narrow parameters	Focused to broader questions; applicable to various types of questions	Broad question	Broad question, with breadth related to scope of population, intervention, or outcomes.
Sources & Searches	Comprehensive sources, explicit strategies	Sources may be limited but sources/strategies made explicit	Comprehensive sources, explicit strategies, with possible modifications, may include research in progress	Comprehensive sources, explicit strategies
Inclusion/exclusion	Defined *a priori*	Defined *a priori* and post hoc; refined as appropriate	Defined *a priori*, with flexibility	Defined *a priori*
Primary study designs	Typically RCTs, but may include observational studies	Emphasis on a staged approach starting with evidence from SRs moving stepwise to include primary studies if needed	All publication types may be considered. Feasibility may add constraints.	Systematic reviews
Study selection/ data extraction	Independently, in duplicate	One reviewer, with verification	Independently, in duplicate	Independently, in duplicate
Appraisal	Rigorous; critical appraisal*	Rigorous; critical appraisal* for both the SRs and/or the primary study evidence contained within	None	Rigorous; Critical appraisal* for both the SRs and the primary study evidence contained within
Synthesis	Narrative +/- quantitative	Narrative +/- quantitative (if appropriate and time permits)	Narrative, with graphical representation	Narrative +/- quantitative; caution required with use of indirect comparisons across reviews
Inferences	Evidence-based – generates a conclusion to answer the research question	Limited, cautious interpretation of the findings to answer the research question	Presents existing knowledge, knowledge gaps, and may help determine the need and focus of a systematic review	Evidence-based collates and distils existing synthesized evidence from the body of review literature to answer the research question
Limitations	RCTs not always possible, bias in observational studies	RRs may be prone to biases; impact of specific shortcuts on results and conclusions requires further research	Limited depth of data collection; No evaluation of the quality of the information or the risk of bias	Not all reviews may be up-to-date; potential variation in quality; gaps in synthesized evidence to answer the question.
Reporting guidelines	PRISMA [29]	PRISMA extension for RRs (under development; Stevens 2018 [76])	PRISMA extension for scoping reviews [30]	Preferred Reporting Items for Overviews of SRs including harms [31]; Hartling 2016 [32]
Resources	Cochrane Handbook [13], AHRQ [33], JBI [34], CRD [35]	WHO [36], Dobbins 2017 [37], Garritty [38]	Arksey & O'Malley 2005 [39], Levac 2010 [40], Colquhoun 2014 [41], Peters 2015 [42]	Cochrane Handbook: Chapter 22 [43]; Ballard 2017 [44]; Pieper 2014 [45]; Pollock 2016 [46]; Cochrane Comparing Multiple Interventions Group [47]

*Critical appraisal could include risk of bias and/or quality assessment.

without the studies in question, and the findings compared. Minimal change suggests the review findings are robust. Tools to appraise ROB have been developed for most study designs, including RCTs,[24] nonrandomized studies,[25-27] and diagnostic test accuracy (DTA) evaluations.[28] A common issue that increases ROB in DTA evaluations in nuclear medicine and other disciplines is the lack of a gold standard reference test that correctly classifies the target condition (ie, has 100% sensitivity and specificity).

Beyond traditional journal publication, several databases of existing SRs of relevance to medical fields including nuclear medicine are available, including the Cochrane Library,[48] the Centre for Reviews and Dissemination (CRD) at the University of York,[49] the Agency for Healthcare Research and Quality (AHRQ),[50] and others.

Conducting Systematic Reviews

The aim of this section is to serve as a summary of considerations for investigators wishing to embark upon a SR, not as a guide for conduct. There are several online resources available that provide guidance for conduct. The *Cochrane Handbook for Systematic Reviews of Interventions* is considered one of the leading guidance documents for SRs of interventions.[13] The Cochrane Screening and Diagnostic Tests Methods Group is in the process of developing a handbook for DTA reviews, of which several chapters can currently be accessed (https://methods.cochrane.org/sdt/handbook-dta-reviews). We also refer readers to guidance provided by CRD[35] and The Joanna Briggs Institute,[34] the latter being specific to the SR of DTA studies.

Many SRs are commissioned to fill known knowledge gaps; however, investigator-led reviews are also common. Given the high requirement of resources and funding to conduct a rigorous SR, the need for the review should be firmly established.[35] Comprehensive searches of bibliographic databases (eg, MEDLINE) and SR libraries should be performed. The CRD maintains a database of protocols of SRs that should also be searched to identify any that may be in process (PROSPERO, accessible at https://www.crd.york.ac.uk/prospero/). Should an existing SR addressing the question of interest be identified, its recency and quality should be assessed. Given that many SRs are considered out of date by the time they are published,[51] a review update may be necessary to incorporate recent literature. To assess review quality, simplified[35] and complex[52] critical appraisal frameworks are available.

Once the need for a SR is established, a review team should be assembled.[35] Members of the review team should have expertise in knowledge synthesis methods, library science, clinical expertise relevant to the topic, epidemiology, and statistical methods. This group will develop the review protocol and undertake the review. The inclusion of clinical experts in the research team is important, as they will be consulted during the review process for content expertise and to ensure the scope of the review is relevant to stakeholders. Uptake of review findings by the target audience is enhanced if knowledge users are included at all stages of the review process,[53] and some funding bodies make their inclusion a requirement in funding applications.[54]

A comprehensive review protocol developed *a priori* is key to minimizing bias and ensuring reproducible methods. Protocols should be registered in the PROSPERO database and, preferably, be published in a peer-reviewed journal to increase transparency of methods and reduce duplication.[55] Reporting of protocols should be guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) guidelines.[56] Components of the review protocol include clinical background and rationale for the review, the review question, methods to search the literature, criteria and methods for relevance screening of citations, methods for data extraction, methods for assessment of ROB, analytical methods, and plans for reporting of findings and knowledge translation.

In protocol development, formulation and refinement of the review question is critical to focusing the review on a clear, precise, and answerable research question that will inform clinical decision making. A review objective may be specific (ie, of limited breadth) or broad; as the breadth of the objective increases, the resources and time required for the review also increase. A poorly worded or defined review question may complicate subsequent stages of the review process, leading to wasted efforts collecting extraneous data that may ultimately not be useful in analyses. Thus, the review objective and question(s) should be as focused and defined as possible.

Framing the review question by the criteria that will define relevant studies for the review is recommended. For reviews of DTA studies, the acronym PIRD specifies the key review elements: *Population* of interest, *Index* test (test being evaluated), *Reference* test, *Diagnosis* of interest.[34] For example, a recent Cochrane review[57] aimed to "determine the diagnostic accuracy of regional cerebral blood flow single-photon emission computed tomography [index test] for diagnosing frontotemporal dementia (FTD) [diagnosis] in populations with suspected dementia in secondary/tertiary healthcare settings [population]," with several reference standards for diagnosis defined within the methods section. For reviews of interventions, the acronym PICOS is generally applied: *Population* of interest, *Intervention* of interest, *Comparator(s)*, *Outcome(s)*, and *Study design*.[35]

Setting the PIRD or PICOS criteria for inclusion of studies in the review is a key component of the review protocol. These criteria should capture all studies of interest and be practical to apply while screening studies for relevance. If criteria are too narrow, they may miss relevant studies and limit generalizability of the findings; if too broad, the data extracted may be voluminous and difficult to synthesize. If exclusions are to be made based on patient population, clear justification should be provided (eg, a test is known to perform differently in pediatrics and adults). Inclusion of all patient populations and analysis of data within subgroups (eg, pediatrics vs adults, male vs female), is often a better approach. Index test(s) of interest may have evolved over time and whether all or some of the iterations of the index test will be included should be defined in the protocol. Cut-off values defining positive and negative results should also be specified, as well as details of conduct that determine what is an acceptable test (eg, conducted/interpreted by laboratory vs clinical context). The reference test should reflect the currently accepted gold standard for diagnosis and its description should be similar to that of the index test, with respect to cut-off values, etc. Multiple reference standards may be identified; for example, five reference standards were acceptable for diagnosis of FTD in the earlier noted Cochrane review.[57] The diagnosis of interest should be explicitly stated (eg, FTD). One can also state the types of studies to be considered for inclusion; generally, for DTA assessment, cross-sectional and case-control designs are used, although longitudinal and cohort studies in which diagnoses are made over time may also prove useful. Setting PICOS criteria for reviews of intervention studies follows similar logic. Descriptions of the interventions and comparators of interest should be based upon the review question. Outcomes of interest should be defined to guide data collection; however, studies are generally not included or excluded based upon the outcomes they report. For intervention reviews, RCTs are the preferred study design for inclusion; however, as mentioned above, concessions can be made in the presence of sparse evidence.

The review protocol should set the search methods that will be used to identify studies of potential interest. The search strategy, the databases to be searched, and other means of study identification (eg, scanning of bibliographies, contacting experts, hand searching journals, and searching grey literature databases) should be defined. Date and language restrictions, and filters used should be documented and justified. The drafted search strategies should be peer reviewed[58] and run to obtain a sense of the breadth of literature available on the topic.

Relevance screening of references identified by the searches should be conducted in duplicate by two reviewers in two stages: (1) screening by title and abstract and (2) screening of full texts identified as potentially relevant at the first stage. Disagreements between reviewers should be resolved, with consultation with a third reviewer in cases of nonconsensus. Specialized SR software is available which can be used to facilitate reference screening and management. Data extraction from included studies is also generally performed in duplicate by two reviewers, with conflict resolution as described for relevance screening. All included studies should be appraised for ROB using the assessment tool appropriate to their study designs (eg, the Cochrane ROB tool for RCTs,[24] the Newcastle Ottawa tool[26] for observational studies, and the QUADAS-2 tool for DTA studies[28]). All screening questions, data extraction forms, and ROB assessment questions should be piloted by reviewers to ensure consistency amongst reviewers.

Synthesis of data in SRs can take several forms, including narrative summary, meta-analysis,[13] and network meta-analysis.[16,59,60] Some reviews may compile all narrative information on a specific subject and consequently report only a narrative summary of the evidence found. For example, one past review aimed to provide a narrative overview of studies investigating the role of ^{18}F-FDG-PET scanning in patients with aortic aneurysms, with a focus on molecular characteristics of the aneurysm wall.[61] Narrative syntheses may also prove to be the only recourse in SRs of quantitative evidence, when the available data are sparse or the heterogeneity of studies is too high to justify pooling. After an extensive search of the literature, a review of the diagnostic accuracy of functional imaging in histologically proven pediatric rhabdomyosarcoma found only eight relevant studies that were ultimately summarized narratively due to insufficient data.[62]

SRs are often paired with quantitative methods to synthesize data, including meta-analyses and network meta-analyses. A meta-analysis is a statistical method in which outcome data from multiple similar studies are pooled to estimate an overall effect of one intervention (or test) compared to another. Most quantitative data in nuclear medicine studies can be pooled, including comparative effects of interventions (eg, odds ratios, risk ratios, and mean differences) and measures of DTA (eg, sensitivity and specificity). Studies included in a meta-analysis are weighted based on precision and sample size, giving larger studies more of an impact on the pooled estimate. While traditional meta-analyses compare two interventions (or tests), network meta-analyses can compare multiple interventions.

Understanding the quality (or strength) of evidence obtained from SRs is important to inform its use in clinical decision-making. The GRADE framework is considered a best practice, as it provides a structured approach that encourages transparency in how the quality of the evidence is interpreted. GRADE is comprised of five main domains: study limitations, indirectness of evidence, inconsistency of evidence, imprecision, and publication/other related bias.[63-65]

Rapid Reviews

The vital role of SRs in healthcare is undeniable. However, they are not without their challenges; they require 6-24 months to complete,[66,67] can be costly to produce, and are operationally challenging to conduct (Table 2). A *rapid review* (RR) streamlines the SR process to inform more urgent decision-making.[68] RRs are usually completed between 1 and 6 months and are a time and resource-efficient way to identify and summarize an evidence base. The exponential growth of published health research is a large-scale problem facing SRs, and there is a pressure to complete SRs more efficiently and for less cost, while maintaining scientific rigor. RRs offer an alternative approach that balances reductions in time with increases in bias.

RRs aim to be rigorous and transparent in methods and reporting, but are less robust than well-conducted SRs given their concessions in methodology to improve timeliness. SRs have methodological features to minimize bias; however, it is currently unknown how susceptible RRs are to bias. *Therefore, it is important to consider the need for and appropriateness of undertaking a RR vs a traditional SR, in light of the potential limitations of this approach*. Additionally, clinicians should keep in mind these potential limitations when considering the conclusions drawn by a RR in the context of their own clinical decision-making. A RR conducted for the purposes of another group's decision-making may not be appropriate for the decision at hand. Restrictions placed on the review question, searches, and eligibility criteria in the interests of expediting the RR process may have resulted in evidence not being included that could be critically relevant to the decision at hand. Using a RR in which the scope does not align with the decision at hand may not be worth the potential risks of incomplete or biased evidence.

To illustrate the use of RRs in nuclear medicine, Madsen et al applied a RR approach to identify and describe clinically relevant evidence for the use of ^{18}F-FDG-PET/CT in the evaluation of lung cancer.[69] Several abbreviated SR methods were used, including the use of only one reviewer to screen and extract data, excluding studies that were published in languages other than English, excluding non-Scandinavian studies, and only doing a cursory assessment of study quality. Importantly, the authors acknowledged these limitations, and despite them, the RR served to inform the standardization of the use of PET/CT in lung cancer in the Region of Southern Denmark. Additional considerations and resources regarding the conduct of RRs are outlined in Table 2.

Scoping Reviews

As mentioned earlier, SRs are typically carried out to address *what* works through a well-defined question, with a specific population, intervention, comparator, and outcomes. However, not all research questions are of this nature. *Scoping reviews* first emerged in the social sciences, where protocol-driven SR methods were deemed too narrow and prescriptive. Scoping reviews address exploratory research questions aimed at mapping key concepts or types of evidence, or at identifying gaps in research related to a defined area.[41] Specifically, a scoping review might (1) examine the extent, range, and nature of research activity; (2) identify research gaps in the existing literature; (3) help determine the value of undertaking or the focus of a full SR; or (4) clarify key concepts, summarize, and disseminate research findings.[39,70] Conversely, they are not appropriate for clinical decision-making, which requires a more in-depth appraisal of research studies.

Scoping reviews are a newer approach to knowledge synthesis that have gained popularity in the last decade, with methods outlined in several key articles.[39,40,70] The process of conducting a scoping review includes rigorous and transparent methods comparable to those for SRs (Table 2)[71]; however, literature suggests that scoping reviews remain poorly understood[72] and poorly conducted when evaluated against the available scoping review methodology guidance documents.[66] The majority of scoping reviews have been performed in the health sector.[71]

Overviews of Systematic Reviews

As SRs have become recognized as the methodologically robust vehicle to synthesize primary literature; their presence in the biomedical field has greatly increased over time.[73,74] There can be circumstances in which synthesizing the findings of several SRs may be insightful. *Overviews of SRs* offer an opportunity to collate broad bodies of related evidence, serving as an efficient means for the busy clinician to examine all synthesized evidence in one document.[75] Overviews can provide an examination of differences that may exist between SRs and the potential causes of discordance among reviews, thereby guiding clinical decisions. Overviews can synthesize different interventions for the same condition, different indications for the same intervention, multiple outcomes for the same intervention and condition, adverse effects of an intervention across various conditions, or multiple reviews on the same topic where conflicting results and conclusions are known.[43,45] For example, multiple SRs may evaluate various combinations of PET, PET/CT, MRI, and PET/MRI, and the various radiotracers for biochemical recurrence of prostate cancer; an overview could collate and synthesize that body of evidence. Alternatively, multiple SRs may examine the utility of an imaging modality across the stages of patient care in one document, from disease detection, staging, and prognosis development, through to providing guidance for (re)treatment and response evaluation. To guide clinicians, the overview should highlight to whom the evidence is applicable and should report any surrounding uncertainties, including gaps in the synthesized evidence. As well, it should indicate where future research efforts should be focused and whether more research is likely to change the conclusions of the overview.[46]

Overviews have some challenges, including the potential for missing data from the included primary research, data extraction errors that are carried over to the overview, datedness in relation to more newly published evidence, reliance on the decision and methods used in the included SRs, inconsistencies in outcomes and methods across reviews, and the loss of details of the primary studies.[75] Yet, despite these challenges, overviews have an important role to play in synthesizing outcomes of multiple SRs including those in imaging and nuclear medicine.

In contrast to traditional narrative reviews, SRs provide an objective summary of all available evidence, with minimal bias, making them robust tools to aid clinical decision-making. SRs and other forms of knowledge synthesis facilitate the practice of EBM and optimize patient outcomes.

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