

FILTERING OUT THE NOISE

Uncovering the “pearls” in clinical literature that have immediate impact on patient care.

The High Volume of Clinical Research

The practice of evidence-based medicine, emphasizing scientific inquiry into diagnosis, treatment, and prognosis, dates at least back to the eighteenth century.¹ However, the logistics of practicing evidence-based medicine have become increasingly daunting. In 2015, over 1 million scientific articles were newly indexed in PubMed. Despite this high volume of potentially clinically relevant publications, adoption of innovative treatments is far from immediate. Estimates of the time from publication to adoption in medical practice vary, but many studies have converged upon about 17 years as the average time.²

The Agency for Healthcare Research and Quality describes the problem well: “Primary care professionals must maintain their proficiency in a range of medical knowledge that spans nearly every area of medicine. And new medical knowledge continues to expand and change at an ever-increasing rate. The challenge for primary care has quickly become: how can we keep pace with new information, learn how to best implement it in our practices, while also continuing to serve a full schedule of patients?”³

Considering both the high volume of literature and the variable quality of what is published, one group of distinguished scholars has asserted that “finding the high-quality evidence is like trying to sip pure water from a hose pumping dirty water, or looking for ‘rare pearls.’”⁴ In order for clinicians to find the best, most current evidence to treat their patients, they need a source that both filters for clinical relevance and evaluates the quality of the evidence.

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An Urgent Need for Fundamental Change

In order to facilitate the best possible treatment, clinicians need immediate access to research results from the medical literature, provided in a context that takes into account the current state of knowledge in the field. This current knowledge can vary widely and, depending on the area of medicine, may include evidence at a variety of levels, ranging from those offering a relatively low level of certainty (e.g., case reports and observational studies) to those with greater certainty (e.g., randomized controlled trials and systematic literature reviews) to those that integrate several of these types of evidence with expert opinion to arrive at more nuanced conclusions (e.g., expert syntheses, such as those found in many guidelines).⁵ Ideally, a clinician should be able to obtain a summary that incorporates all of these types of information, making the best information available to the clinician at each decision point in the course of evaluating, treating, and following a patient.

Both complicating and enhancing the clinician’s work is the increasing ability of patients to read and research their own conditions using publicly available resources. Patients come to the doctor’s office armed with information from many sources – advice from friends and family, websites, and advertisements from television and periodicals. In order to address patients’

concerns sensitively and helpfully, clinicians need to be well-versed in the data, especially in areas where subtle misunderstandings can make a big difference in treatment.

In the words of Paul Glasziou, professor of evidence-based medicine at Oxford, “If today’s practitioners are to retain their professionalism, clinicians’ information and research appraisal skills need to be improved urgently. Otherwise they risk being rapidly overtaken by administrators and patients who may not be able to use a stethoscope but are comfortable using Google, Wikipedia, and the internet.”⁶

An innovative approach is required that will enable clinicians to keep up with current medical knowledge and answer both their own and their patients’ questions. One promising new process called Systematic Literature Surveillance may be the solution that health care providers are looking for. Developed by a physician and refined by a team of physicians and scientists at EBSCO Health, Systematic Literature Surveillance is a process that enables prompt translation from clinical research to practice by scanning the literature and critically appraising the best available clinical evidence across numerous medical disciplines.

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The Distinction Between Systematic Literature Surveillance and Systematic Reviews

Systematic Literature Surveillance is different from a Systematic Review. One major difference is that while Systematic Reviews focus on evidence that meets certain minimum quality thresholds, sometimes high-quality evidence is not available to inform a particular decision. There are many potential reasons for a lack of high-quality evidence: for example, a nascent field in which advanced research has not yet been done, a rare disease for which it is difficult to accrue enough cases to do large trials, or an area in which controlled trials are ethically problematic. Rather than fail to draw a conclusion, the Systematic Literature Surveillance process comes down on the side of using the best available evidence while acknowledging potential biases, thus giving clinicians access to the largest volume of potentially helpful (though imperfect) data. A former Medicare Chief Medical Officer points out that “The quality of evidence is continuous, with confidence in the evidence ranging from low to high, and a clear inflection point at which the evidence changes from insufficient to sufficient is lacking. Adequacy is a judgment about the evidence rather than a characteristic of the evidence itself.”⁷

In addition to the emphasis on quality standards, which may limit the volume of literature available to inform a Systematic Review, a Systematic Review is typically a systematic effort to find evidence pertinent to a specific clinical question, proceeding via a series of sequential steps: first filtering and evaluation of the literature, then data extraction, followed by summarization, interpretation, journal submission with peer review, and finally publication.^{8,9,10} This sequential focus on multiple aspects of a single clinical question leads to a long time lag between posing the initial question and providing an answer. In contrast, in Systematic Literature Surveillance, these same systematic functions are applied across the literature in real time, so that the different stages

may be going on simultaneously for multiple individual studies within multiple areas of clinical interest. By performing this sequential process across multiple clinical questions at once, rather than for a single clinical question at a time, it is possible to increment the database of clinically important research more quickly across a wide range of topic areas.

Yet another difference between Systematic Literature Surveillance and Systematic Review is that Systematic Literature Surveillance categorizes the available evidence rather than looking for evidence in a specific area. For example, while a Systematic Review might focus on a particular type of treatment for a disease, Systematic Literature Surveillance provides information about a wide range of treatments, of varying types and with varying levels of supporting evidence, to support the conversation between clinician and patient about the best approach.

Having highlighted these differences, it is important to emphasize that Systematic Literature Surveillance does not compete with Systematic Reviews, but rather complements them. Not only do both processes use the same toolkit, but Systematic Reviews frequently form part of the evidence base for Systematic Literature Surveillance.

The Systematic Literature Surveillance Process

The process of using Systematic Literature Surveillance to inform a clinical reference tool was developed by Brian Alper, MD, in 1997.^{11,12,13} The steps of the Systematic Literature process are shown in the figure below:



STEP 1: IDENTIFY THE EVIDENCE

The surveillance process starts with a comprehensive, systematic identification of all published content potentially relevant to clinical practice. To identify this content, an exhaustive list of vetted sources is constructed, including peer-reviewed journals, organizations that produce evidence-based guidelines and recommendations, and organizations that produce evidence-based syntheses of data.

For peer-reviewed journals, the list covers all journals identified by specialists across all fields of medical practice and in all areas of the globe as key sources of literature in their areas of practice; these include both general practice and specialty journals. For example, *DynaMed Plus* currently maintains a list of over 500 journals meeting these criteria, all of which are searched daily for new articles.

Likewise, a comprehensive list of international organizations that produce evidence-based guidelines and recommendations is constructed, and websites for each of these organizations are checked regularly for new or updated documents. For instance, the organizations that *DynaMed Plus* surveys for guidelines and recommendations include specialty societies (such as the American Heart Association), international organizations and collaborative efforts (such as the World Health Organization and Choosing Wisely), and government agencies (such as the Centers

for Disease Control). Sources surveyed for Systematic Reviews include the Cochrane Collaboration and several sources that produce evidence-based health technology assessments.

The intent of developing this list is to cast a broad net for sources of pre-screened evidence that are relevant to clinical practice. The initial layer of scrutiny provided by these entities ensures a minimum baseline level of quality, which will be refined later in the process by further selection and critical appraisal of the individual articles. Each source is either searched in full (i.e., “cover-to-cover”) or filtered using a set of evidence-based clinical queries to identify clinically relevant studies.¹⁴

STEP 2. SELECT THE BEST

In order to select the best evidence for clinical practice, it is necessary to establish both the relevance of a study to clinical practice and how it adds to the existing literature. This combined consideration of clinical relevance and clinical validity ensures systematic selection of the best studies to inform clinical practice. Practically speaking, these judgements are best made by clinical specialists, who methodically evaluate each item using pre-defined criteria, as well as their knowledge of the existing literature. For instance, sometimes a new study may add one specific piece of information, like the efficacy of a treatment within a particular subpopulation of patients. Other times, a study may describe a new method of diagnosis or treatment that changes the clinical approach entirely. The clinical specialist tags the item with specific information about how it is clinically relevant for use in steps 3-5: critical appraisal, objective reporting, and synthesis.

STEP 3. CRITICAL APPRAISAL

An important component of the Systematic Literature Surveillance process is appraising the quality of the best available evidence in order to guide the clinician to the best possible evidence-based decision. The scientists performing the critical appraisal typically train in this method for several months, with oversight from more experienced raters, and then undergo ongoing reviews by peers and more experienced raters to ensure consistency of the appraisals. One potential system for addressing quality is summarized as follows:

- Level 1 (likely reliable) evidence addresses clinical (i.e., patient-oriented) outcomes and meets quality criteria which minimize bias.
- Level 2 (mid-level) evidence also addresses clinical outcomes, but does not meet the quality criteria to achieve Level 1 evidence labeling.
- Level 3 (lacking direct) evidence either is not based solely on scientific analysis (e.g., expert opinion) or is based on non-clinical outcomes such as laboratory values.

Quality criteria for an individual study to be considered Level 1 might include the following:

- Clinical or patient-oriented outcome
- Population, intervention, comparison and outcome in the study is representative of expected clinical practice
- Appropriate random allocation method
- Appropriate blinding of all persons (patient, treating clinician, outcome assessor) if possible
- Adequate follow up (endpoint assessment)
- Accounting for dropouts (even if not included in analysis)
- Adequate precision of effect estimate based on confidence intervals and statistical power
- Consistency of findings across measures of similar outcomes

STEP 4. OBJECTIVELY REPORT

Once an item has been critically appraised, it must be reported accurately and without distortions. The systematic approach to objective reporting includes expressing results consistently in ways that are comparable. The use, when possible, of absolute risk reduction and number needed to treat ensures comprehensibility for physicians and patients and allows the direct comparison of different treatments.^{15, 16, 17} Likewise, the use of confidence intervals, when available, demonstrates the potential range of interpretations of the results and prevents reliance on a simple yes/no answer suggested by a p value. The systematic approach also includes consistency in wording – for example, the use of definitive wording for level 1 evidence (e.g., “esomeprazole reduces heartburn”) vs. the use of “may” for level 2 evidence (e.g., “zinc supplementation may reduce pneumonia”).

Another way to ensure objectivity is to have precise definitions of types of potential study bias, which are consistently expressed and presented with explanations of the findings leading to the conclusion of potential bias, allowing transparency for the reader. Some examples are shown below.

Description of bias	Additional information presented
Low adherence	Adherence rate
Baseline differences	Characteristics that were unbalanced at baseline
High crossover rate	Crossover rate
High dropout rate	Dropout rate
High loss to follow-up	Proportion lost to follow-up
Methodologic limitations	Description of methodologic limitations
Without intention-to-treat analysis	Number analyzed or analysis method
Inadequate statistical power	Number needed for adequately powered comparison

As another way to ensure accurate reporting, a summary may be checked by several people – for example, written initially by one individual skilled in critical appraisal, reviewed by a second such person, further reviewed by a clinician to ensure that the study findings are correctly placed within the overall context of patient care, and then copy-edited as a final error-checking step.

STEP 5. SYNTHESIZE THE EVIDENCE

To provide useful information for making evidence-based clinical decisions, it is important to incorporate the potentially disparate conclusions from a variety of sources into a summary that presents a comprehensive view of the evidence and highlights or explains areas where evidence is conflicting. This synthesis process may include grouping studies according to similarities or differences, as well as reanalyzing the evidence as researchers’ understanding of an area evolves. Once a need for synthesis (represented by the existence of 2 or more primary studies in a common area) is identified, the steps of synthesis include searching for additional evidence (e.g., other studies in the same or a similar area), determining the appropriate focus of the summary

(for example, specific patients, interventions, comparators, and/or outcomes), and either consolidating the results if possible or explaining where there are differences and the potential reasons for inconsistency.

STEP 6. USING EVIDENCE TO MAKE RECOMMENDATIONS

For clinical recommendations to be most useful, they should be based on the body of synthesized evidence and informed by clinical needs. The process of making recommendations therefore should integrate synthesis of the evidence with clinical perspective. A systematic methodology for generating recommendations includes multiple steps to ensure transparency and consistency:¹⁸

- a. Recommendations are initially drafted by clinical editors (including ≥ 1 with methodological expertise and ≥ 1 with content domain expertise) aware of the best current evidence for benefits and harms, and the recommendations from guidelines.
- b. Recommendations are phrased to match the strength of recommendation. Strong recommendations use “should do” phrasing, or phrasing implying an expectation to perform the recommended action for most patients. Weak recommendations use “consider” or “suggested” phrasing.
- c. Recommendations are explicitly labeled as Strong recommendations or Weak recommendations when a qualified group has explicitly deliberated on making such a recommendation.
- d. Recommendations are verified by ≥ 1 editor with methodological expertise, not involved in recommendation drafting or development, with explicit confirmation that Strong recommendations are adequately supported.
- e. Recommendations are published only after consensus is established with agreement in phrasing and strength of recommendation by all editors.
- f. If consensus cannot be reached then the recommendation can be published with a notation of “dissenting commentary” and the dissenting commentary is included in the topic details.
- g. If recommendations are questioned during peer review or post-publication by a qualified individual, or re-evaluation is warranted based on new information detected through Systematic Literature Surveillance, the recommendation is subject to additional internal review.

STEP 7. ADJUST CONCLUSIONS WHEN NEW EVIDENCE IS PUBLISHED

A major advantage of Systematic Literature Surveillance is the ability to get information to the clinician quickly. With internet publishing, new information can be analyzed and provided to clinicians within days rather than years, drastically speeding up the time from research to practice.

By providing clinicians with quick access to the best available evidence for patient care, clinical tools that employ the Systematic Literature Surveillance process have the power to improve the practice of medicine and to ensure the rapid translation of medical knowledge into clinical care.

The Advantages of Systematic Literature Surveillance in Patient Care

The Systematic Literature Surveillance process serves as a conduit for clinicians to remain lifelong learners and to keep up with the rapid pace of medical research. By providing clinicians with quick access to the best available evidence for patient care, clinical tools that employ the Systematic Literature Surveillance process have the power to improve the practice of medicine and to ensure the rapid translation of medical knowledge into clinical care. As time goes on, improvements to the Systematic Literature Surveillance process, as well as to the method of accessing the results of Systematic Literature Surveillance, will continue to make this a more powerful tool for the practicing clinician.

About the Author

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