1 General Issues

1 Introduction

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Case scenario

A 25-year-old woman presented to an emergency department (ED) with an exacerbation of her migraine headaches. Her migraine headaches had previously been well controlled; however, stressful conflicts had recently occurred at work, she had not been able to sleep properly for two nights and she admitted unusually low fluid intake for the previous 2 days. She reported that her headache developed gradually, was associated with nausea and vomiting, and she rated the headache as 9 on a 10-point headache pain scale. She denied fever, syncope or other signs of pathological headaches, and assessed the episode as being "similar to my last migraine headache that brought me to the emergency department 2 years ago".

She improved quickly with intravenous saline and metoclopramide and was ready for discharge home after 90 minutes. Her headache at reassessment was 1 out of 10 and her nausea had resolved. The patient informed you that she was late for an important work meeting that would consume her time for the next 2 days and wondered what she could do to minimize the risk of suffering a recurrence.

Introduction

What is *evidence-based emergency medicine* (EBEM) and why is there such a controversy over the concept and contempt for the phrase? The term evidence-based medicine (EBM) was first coined in the early 1990s by Gordon Guyatt [1] and has now become a stable in the medical lexicon. In addition to EBM's long history, controversy exists regarding its components and value in decision making [2,3]. In most cases, however, it can be described as the combined use of experience, best evidence and patient's preference and values to develop an approach to a clinical problem, often referred to as *evidence-based medical care*.

The migraine headache example may help readers better understand the concept. The patient's question related to prevention of headache and this topic is well covered in the chapter on migraine headaches in this book (See chapter 48). From an evidence perspective, the well-informed clinician knows that there is evidence that a dose of dexamethasone in the emergency department (ED) (best evidence based on a systematic review (SR) of randomized controlled trials (RCTs)) is helpful [4]. Moreover, experience reminds the clinician that patients with moderate to severe migraine headaches also can deteriorate, re-present to the ED, and/or lose valuable time from work and other activities (clinical experience). The clinician is concerned and wishes to protect the patient from any and all of these events (and so does her employer). Unfortunately, the patient protests this decision because corticosteroids cause her to develop acne, retain water and have insomnia. She also has a major weekend function and feels these medications may create havoc with her social life. Despite the clinician's reassurances, she refuses the intravenous corticosteroid treatment (patient preference and values). Readers in clinical practice will be very familiar with this type of scenario.

What is the evidence-based decision in this case? Some traditionalists may suggest that their decision is final and the patient should accept the corticosteroid treatment. The EBM clinician might further use the available evidence to explain the benefits and risks of treatment options, in conjunction with the patient's preference and his/her experience. In the event that agreement cannot be reached between the clinician and the patient, the EBEM approach would propose an alternative "next-best evidence" and similarly reasonable approach. For example, the clinician may recognize that reduction of pain to less than two out of ten reduces headache relapse [5]. Moreover, the addition of education about triggers and very close follow-up may improve outcomes in such patients. It is this combination of evidence, patient preference and clinical experience that coalesces to form the EBEM decision.

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Why EBEM?

The EBM approach may seem intuitive to many emergency practitioners. However, when originally proposed, debate ensued, and in some cases continues [6,7]. This forces the question: why is this being proposed in emergency medicine? In a therapy issue, clinicians must ultimately decide whether the benefits of treatment are worth the costs, inconvenience, and harms associated with the care. This is often a difficult task; however, it is made more difficult by the exponentially increasing volume of literature and the lack of time to search and distill this evidence [8]. Although clinicians of the early 21st century have an urgent need for just-in-time, on-demand clinical information, their time to access such information has likely never been as compressed. Increases in patient volume and complexity, patient care demands, and the lack of access to resources have exacerbated the work frustrations for many clinicians. These concerns often take precedence over seeking the most relevant, up-to-date and comprehensive evidence for patient problems.

Despite the fact that the most common problems posed by patients presenting to emergency rooms are encountered daily around the world, appropriate treatment approaches are often not fully employed and practice variation is impressive. For a variety of reasons, the results from high level evidence such as RCTs are not readily available to busy clinicians and keeping up to date is becoming increasingly difficult. Moreover, a valid, reliable and up-to-date clinical bottom line to guide treatment decisions has been elusive [8].

However, availability of high quality published trials and systematic reviews relevant to an area of practice are not the only components necessary to practicing "best evidence medicine". Clinicians also need rigorously produced, synthesized best evidence information to assist them at the point of care. In emergency care, time is increasingly more precious and the need for this digestible information has never been greater.

Levels of evidence

A wide variety of tools to describe levels of evidence have been developed and employed in clinical medicine to reflect the degree of confidence to which results from research may be accepted as valid. From levels of evidence, strengths of recommendations are generated which are graded according to the strength of the scientific evidence supporting them. These levels of evidence can be criticized for being different with each set of guidelines or report, being overly complex, and being almost universally focused on therapeutic interventions.

Recently, a group of experts in the field of guidelines introduced a grading system as part of an effort to develop a single approach supported by international consensus. The Grades of Recommendation, Assessment, Development and Evaluation (GRADE) Working Group have published their recommendations, which have been adopted by increasing numbers of specialty and health policy organizations [9]. The GRADE system classifies quality of evidence into one of four levels (high, moderate, low and very low) and quality of recommendations in one of two levels (strong and weak).

Once again, an example may be illustrative. In the case scenario described above dealing with therapy, the highest level of evidence (HIGH) is based on RCTs. A single RCT can retain HIGH grading if there are no study limitations, the threats to validity are low, the association is strong and adjustments for all potential confounders have been performed. Although HIGH status is awarded to RCTs, many trials in emergency medicine are not large enough to maintain this evidence status. The evidence would similarly retain its HIGH ranking if meta-analysis of two or more similar trials show consistency of effect and statistically significant relative risk (RR) results (> 2.0 or < 0.5 for reduction) [10]. Fortunately, in this case, the systematic review does support the single clinical trial identified (see Chapter 48).

While considerable debate exists regarding the relative merits of evidence derived from large individual trials versus systematic reviews [11], due to the costs associated with large, multi-centered trials, they remain uncommon across emergency medicine and remain restricted to certain topic areas (e.g., cardiology, rheumatology, stroke, and so forth). While examples of large databases and observational studies do exist in emergency medicine [12], smaller studies are much more common. Consequently, it is likely that systematic reviews will play an increasingly important role in the future decisions made by patients, clinicians, administrators and society in all areas of health care.

MODERATE evidence is based on RCTs that contain flaws that preclude a HIGH evidence rating or observational studies. The RCTs may show either positive trends that are not statistically significant or no trends and are associated with a high risk of false-negative results. The observational studies may be elevated to HIGH evidence (from LOW) in certain cases, such as when a statistically significant relative risk of > 5 (< 0.2) is identified based on direct evidence with no major threats to validity.

Finally, a LOW level of evidence is based on observational studies of any kind (e.g., cohorts, case series, case–control studies or cross-sectional studies). VERY LOW grading can be achieved when evidence is based on observational studies of low quality or the opinion of respected authorities or expert committees as indicated in published consensus conferences or guidelines.

In diagnostic studies, the same rules apply; however, most of the studies in this setting are not RCTs. Given the relatively recent development of the GRADE system, the editors of this text have not required authors to apply this in each chapter; although, given the summary of evidence provided in

each chapter, readers should be able to rate the evidence presented using the general guide. Moreover, future editions of the book will focus on GRADE or similar systems of evidence assessment.

Levels of evidence and systematic reviews

As discussed above, one possible solution to the information dilemma for clinicians is to focus on evidence from systematic reviews (SRs) [13]. SRs address a focused clinical question, utilize comprehensive search strategies to avoid publication and selection biases, assess the quality of the evidence and, if appropriate, employ meta-analytic summary statistics to synthesize the results from research on a particular topic with a defined protocol. They represent an important and rapidly expanding body of literature for the clinician dealing with patients presenting to the emergency setting and they are an integral component of EBM.

Although there has been a recent increase in the production of diagnostic testing SRs, the most common application of SRs is in therapeutic interventions in clinical practice. One important exception is the Rational Clinical Examination (RCE) series published in the *Journal of the American Medical Association* (*JAMA*). This series presents SRs in the field of diagnostic testing (especially clinical examination and laboratory/imaging testing). Finally, the Cochrane Collaboration has developed a Diagnostic Methods Working Group and is planning to introduce diagnostic test systematic reviews to their collection of products in the near future. Unfortunately, the methodology of diagnostic SRs lags behind that of the therapeutic SRs; however, there are strong indications that this is changing.

Despite publications illustrating the importance of methodological quality in conducting and reporting both RCTs [14] and SRs [15], not all SRs are created using the same rigorous methods described above. Like most other research, variable methodological quality has been identified in systematic reviews. High-quality SRs of therapies attempt to identify the literature on a specific therapeutic intervention using a structured, *a priori* and well-defined methodology contained in a protocol. Rigorously conducted SRs are recognizable by their avoidance of publication and selection bias. For example, they include foreign language, both published and unpublished literature, and employ well-described comprehensive search strategies to avoid publication bias. Their trial selection includes studies with similar populations, interventions/controls, outcomes and methodologies and use of more than one "reviewer" to select included studies.

Systematic reviews regarding therapy would most commonly combine evidence from RCTs. In the event that statistical pooling is possible and clinically appropriate, the resultant pooled estimate represents the best "summary estimate" of the treatment effect. A systematic review with summary pooled statistics is referred to as a *meta-analysis*, while one is without summary data is referred to as a *qualitative systematic review*. Both of these options represent valid approaches to reporting SRs and both are now increasingly commonly published in the medical literature.

In the field of emergency medicine, SRs have been evaluated and found to contain serious flaws that potentially introduce bias into their conclusions [16]. This is an alarming picture for the profession, and one that needs to be addressed by members as well as authors and journal editors. Most of this research was completed prior to the establishment of the QUOROM (Quality of Reporting of Meta-analyses) statement; however, recent evidence suggests that this situation has not resulted in dramatic improvements in the quality of published SRs [17]. Consequently, ED physicians must be vigilant in their search for and evaluation of SRs as they pertain to this field.

The Cochrane Collaboration

The Cochrane Collaboration, a multinational, volunteer, collaborative effort on the part of researchers, clinicians from all medical disciplines, and consumers, represents one source of high-quality systematic review information available to most clinicians with very little effort [18]. The Cochrane Library is a compendium of databases and related instructional tools. As such, it is the principal product of the large international volunteer effort in the Cochrane Collaboration.

Within the Collaboration, specific review groups are responsible for developing, completing and updating SRs in specific topic areas. For example, the Cochrane Airway Group (CAG: www.cochrane-airways.ac.uk) is responsible for "airway" topics (e.g., asthma, chronic obstructive pulmonary disease, pulmonary embolism). Reviewers within the Cochrane review groups represent consumers, researchers, physicians, nurses, physiotherapists, educators and others interested in the topic areas. Not all review groups have produced acute care reviews; however, ED topics are particularly well covered by some (e.g., CAG) [19]. Recently the relevance of the Cochrane Collaboration effort to emergency medicine has been enhanced through the advent of the Cochrane Prehospital and Emergency Health Field (CPEHF: www.cochranepehf.org), which is expected to substantially increase the number of reviews with direct relevance to this specialty [20].

Systematic reviews produced by members of the Cochrane Collaboration are the products of *a priori* research protocols, meet rigorous methodological standards, and are peer reviewed for content and methods prior to dissemination. Specifically, this process of review production is designed to reduce bias and ensure validity, using criteria discussed in the *JAMA* User's Guide series [21]. As much as possible, this text book will focus on evidence derived from SRs, and as often as possible, those contained within the Cochrane Library.

The Cochrane Library and emergency medicine

The Cochrane Library is comprised of several databases, three of which deserve some description and discussion here as they relate to this EBEM textbook. The Cochrane Central Register of Controlled Trials (CENTRAL) is an extensive bibliographic database of controlled trials that has been identified through structured searches of electronic databases, and hand-searching by Cochrane review groups. Currently, it contains over 300,000 references (Cochrane Library, 2007, Issue 4) and can function as a primary literature searching approach with therapeutic topics. The Database of Abstracts of Reviews of Effects (DARE) consists of critically appraised structured abstracts of non-Cochrane published reviews that meet standards set by the Centre for Reviews and Dissemination at the University of York, England. Currently, DARE contains over 3500 reviews (Cochrane Library, 2007, Issue 4). The last, and possibly most important, resource is the Cochrane Database of Systematic Reviews (CDSR), a compilation of regularly updated SRs with meta-analytic summary statistics. Currently, the CDSR contains over 1200 protocols and 3500 completed reviews (Cochrane Library, 2007, Issue 4). Contents of the CDSR are contributed by Cochrane review groups, representing various medical topic areas (e.g., airways, stroke, heart, epilepsy, etc.). Within the CDSR, "protocols" describe the objectives of SRs that are in the process of being completed; "completed reviews" include the full text, and usually present summary statistics. Both protocols and reviews are produced using a priori criteria, adhere to rigorous methodological standards and undergo peer review prior to publication. Regular "updates" are required to capture new evidence and address criticisms and/or identified errors.

The quality of systematic reviews contained within the Cochrane Library has been shown to be consistently high for individual topic areas as well as throughout the Cochrane Collaboration [22,23]. Recent evidence evaluated the quality of a random selection of SRs published in 2004 and, long after the production of the QUOROM guidelines, found some intriguing results [24]. First and foremost, the volume of SRs identified suggested a rapid proliferation of SRs in health care. Second, 71% of the reviews involved a therapeutic area, recapitulating our previous comment about SRs being less common in diagnostic areas. Finally, there were large differences identified between Cochrane and non-Cochrane reviews in the quality of reporting several important characteristics; Cochrane reviews were rated as higher quality. Overall, the reviewers reiterated the variable quality of some reviews in the literature and the need to be cautious when using these reviews in health care decisions.

Prehospital and emergency medicine involvement has been limited across the Cochrane Collaboration and in many review groups, consequently topics of interest to emergency physicians have perhaps not been a priority. The development of the CPEHF in 2004 was an important milestone for evidence-based prehospital and emergency medicine [25]. CPHEF was registered as an official entity of the Cochrane Collaboration and now has more than 3000 registered members (F. Archer, personal communication). The focus of CPEHF is prehospital (management up to the delivery in the emergency department), emergency (up to hospitalization) and disaster medicine. One of the functions of the field is to develop and maintain a register of studies relevant to the areas of prehospital and emergency health care. CPEHF has developed a validated search strategy to identify SRs and reports of trials in the Cochrane Library that are based on research that was conducted in the prehospital environment [26].

Evidence-based Emergency Medicine format

We are excited about highlighting the approaches to the diagnosis and treatment of common emergency conditions that will be detailed in this book. The editors of *Evidence-based Emergency Medicine* have attempted to select experts in both emergency medicine (content) as well as evidence-based medicine (methodology) to author this text. Following this introductory section, the remainder of the chapters will focus on individual topic areas.

The chapters in this book have all been organized in a similar fashion using the following format:

1 *Case scenario/vignette*: Each chapter author has been asked to describe a patient scenario upon which the remainder of the chapter will be based. Authors have been instructed to provide a real-world clinical problem.

2 *Questions that arise from the case*: Using the PICO methodology described below, questions will be developed from each clinical case. These clinical scenarios will be used to identify important questions relevant to the diagnosis, therapy, adverse effects, and so forth of conditions commonly encountered in emergency practice. While these questions are not all inclusive, they do represent key questions following discussion among the authors and the section editors.

3 *Literature search*: A brief description of the search strategies employed to identify the relevant research used to answer the clinical question will be provided. In general, the evidence from systematic reviews, especially those available in the Cochrane Library, the *JAMA* RCE series and large health technology assessment (HTA) resources (e.g., Agency for Healthcare Research and Quality (AHRQ: www.ahrq.com), Canadian Agency for Drugs and Technologies in Health (CADTH: www.cadth.ca), National Institute for Health and Clinical Excellence (NICE: www.nice.uk)), will be highlighted.

4 *Summary critical appraisal*: A summary of the available evidence will be provided by the authors, focusing on the key results and their implications. Some authors have elected to produce summary of evidence tables.

5 *Answers/conclusions*: A summary approach to the patient will be presented at the end of each chapter.

Question development

Although we have not rigorously followed the methodology of SRs in this book, there is one aspect of that methodology that we have strictly followed. Each chapter is developed around specific clinical questions. Although most chapters include some background discussion of the topic areas, readers will find that these are much more condensed than they would expect from other emergency medicine textbooks and are limited to materials directly relevant to the specific questions.

Patients presenting with many of the signs and symptoms presented in this book represent typical cases commonly encountered in clinical emergency practice. Many potentially important questions arise from these encounters; all of these questions vary based on the perspective or the person asking the question (e.g., clinician, patient, administrators, primary care providers, public health officers and government policy makers). For example, using the example above, what is the *etiology* of this patient's acute migraine headache? What *diagnostic tests* should be performed (if any) and which can the health care system afford? What *therapy* could be prescribed in the ED to treat the headache? What *additional* therapy can be prescribed in order to reduce the chances of continued headache? What is her *prognosis* over the next 3 weeks with respect to her migraine status? Would instituting a prophylactic therapy improve the *long-term prognosis* for this woman? Finally, would educational interventions *prevent* further exacerbations or reduce their severity?

The success of any search for answers to such clinical questions is spelling them out in a detailed and systematic way [27]. While this skill is important for the policy maker in the office, the patient searching for options, and the researcher performing a systematic review, it is perhaps most important for the busy clinician at the bedside. Some have referred to this process as developing an "answerable question". This is because such an approach, among other things, provides an immediate basis for formulating and executing an effective search strategy for locating relevant and high-quality clinical evidence. In this book we report both general and specific search strategies in connection with the specific questions addressed in each chapter.

Components of a good question

Designing an appropriate clinical question includes consideration of the components of a good question (described below), compartmentalizing the topic area and describing the design of studies to be included. All questions should include focused details on the **p**opulation, **i**ntervention, assessment or exposure (and **c**omparison when relevant), and **o**utcomes associated with the question. This approach is often abbreviated as PICO, but these are only part of the components necessary for developing the question. Each component is examined in further detail below and examples illustrated in Table 1.1.

1 *Population*: A clearly defined population under consideration is the first step in developing a successful question; however, this can be a difficult task at times. The selection should be based on the interests and needs of the clinician and the patient's problem.

2 *Intervention, assessment or exposure*: Well-defined interventions must be articulated prior to searching for answers. For example, corticosteroids may be particularly problematic in searches for migraine headaches. Since corticosteroids can be administered via many routes (e.g., intravenous (IV), oral and intramuscular (IM)) in migraine headache treatment, using varying doses and over different duration, these must all be considered when searching for evidence. Moreover, the use of different agents is common (e.g., dexamethasone, prednisone, methylprednisolone, and so forth) and is clearly an important consideration in question development. Diagnostic assessments are also interventions and when the results are compared to a criterion standard for the disease or condition being sought, performance measures such as sensitivity, specificity and likelihood ratios can be derived. Harmful exposures are not quite the same as "interventions" in that we avoid knowingly recommending them to our patients.

3 *Comparisons*: Most therapeutic interventions are compared to a control treatment. In some cases, the comparison is to a placebo; however, in emergency medicine the comparison is often to standard practice at the time or known effective therapies. For example, in the chapter on migraine headaches, the effectiveness of corticosteroids in preventing recurrent headaches is compared to placebo; however, both groups received standard abortive care in the ED. In the chapter on acute asthma, the effectiveness of inhaled corticosteroids to reduce relapse after discharge is compared to placebo; once again, both groups received standard care (7 days of oral prednisone and short-acting β-agonists) at discharge. It is important for researchers to use the correct dose, route of delivery and timing of treatment in order to determine the true benefit (or harm) of the intervention compared to standard care/placebo in drug trials. This is equally important when the intervention is a non-drug treatment (e.g., education, procedure, technology, etc.), since this will ensure valid comparisons of the intervention and the control.

4 *Outcome*: There are a variety of outcomes reported in any emergency or acute care research study. For example, in acute cardiac studies disposition (e.g., death, admission/discharge, relapse, etc.), clinical outcomes (e.g., recurrent angina, myocardial infarction, pericarditis, etc.), interventions (e.g., angioplasty, coronary artery bypass grafting, etc.), physiological parameters (e.g., vital signs, oxygen saturation, etc.), medication use (e.g., β-blocker use, aspirin use, etc.), adverse effects (e.g., tremor, nausea, tachycardia, etc.), complications (e.g., arrhythmia, pneumonia, etc.), and symptoms (e.g., quality of life, specific symptoms, etc.) may all be reported. In other diseases, some of these events would be rare (e.g., intubation in asthma or discharge in myocardial infarction), and seeking evidence for the influence of interventions on these outcomes would be fruitless. The clinician must select appropriate primary and secondary outcomes prior to beginning their evidence search. The primary outcome should reflect the outcome that is most important to the clinicians, patients, policy makers and/or consumers.

Table 1.1 Example of the PICO methodology for developing clinically appropriate questions in emergency medicine (see text for further details).

Population	Intervention/control	Outcome	Design	Topic
Adults with migraine headache in the ED	Metoclopramide vs systemic DHE	Pain relief and relapses after discharge	RCT	Therapy
Adults with new onset COPD	Exposure to work-related or environmental irritants	Development of COPD	Prospective cohort	Etiology
Adults in the ED with acute swollen leg and chest pain	Use of Well's criteria vs unstructured clinical exam	Diagnosis of DVT/PE	Prospective cohort	Diagnosis
ED adult migraine headache patients discharged home	Corticosteroids vs control	Relapse to additional care	RCT	Therapy/prognosis
Adult contacts of a documented case of meningitis	Ciprofloxacin vs hygiene practices	Prevention of meningitis	RCT	Prevention

COPD, chronic obstructive pulmonary disease; DHE, dihydroergotamine; DVT, deep vein thrombosis; ED, emergency department; RCT, randomized controlled trial; PE, pulmonary embolism.

Often the clinician may also be interested in secondary outcomes, side-effects and patient preference. While patient preference is not often reported in clinical trials and therefore SRs, side-effects and secondary outcomes are commonly encountered. The importance of secondary outcomes is that if their pooled results are concordant with that of the primary outcome, this adds corroborating evidence to the conclusion. In addition, side-effect profiles provide the patients, clinician and others with the opportunity to evaluate the risks associated with the treatment. Unfortunately, the lack of uniform reporting of side-effects often precludes these outcomes from being evaluated with any rigor.

Improving efficiency in question development

Two additional components to be considered in the development of an answerable question for a clinical case are the topic area and the study methodology or design [27].

1 *Topic areas*: While selecting between topic areas may initially appear straightforward, there can be confusion. For example, is chest computerized tomography (CT) testing in pulmonary embolism a diagnostic or a prognostic topic? Clearly, the use of chest CT has been examined as a diagnostic tool compared to clinical signs and symptoms, and a review in this area would encompass a diagnostic domain. When CT testing is used to predict outcome (e.g., death, length of stay, etc.) and complications (e.g., pulmonary hypertension) then the topic would be considered a prognostic question. Since there are other domains of systematic reviews (including therapy, prevention and etiology), by selecting the topic of the clinical question, this further clarifies the approach for the clinician.

2 *Design*: The design of the studies to be selected should also be carefully considered in the initial question formulation. For example, if one is interested in a therapeutic topic, the best level of evidence (HIGH) includes results from large RCTs or SRs [28,29]. The next level of evidence might be small RCTs, which are insufficiently powered. Finally, observational studies (e.g., cohort, case–control, case series) would be considered lower levels of evidence for treatment. It is therefore appropriate and efficient for initial searches for therapy answers to be limited to systematic reviews and randomized controlled trials.

Locating the evidence: literature searching

Clearly, we cannot do justice to literature searching in an introductory chapter on evidence-based emergency medicine. Searching for evidence is a complex and time-consuming task, especially with the rapid growth of journals and publications which has increased the body of evidence available in the peer-reviewed published literature. For example, to ensure that one has identified all relevant possible citations pertaining to a clinical problem, simple searching is often ineffective [30]. Search of MEDLINE, the bibliographic database of the National Library of Medicine, for RCTs using a non-comprehensive search strategy will miss nearly half of the relevant publications, depending on the specialty and topic area [31]. In addition, by not adding other electronic searches (e.g., EMBASE, the European-based electronic database maintained by Elsevier), clinicians run the risk of missing considerable evidence [32]. Hand-searching has been shown to increase the yield of RCT searches; however, this is an unreasonable task for busy clinicians and many researchers [32]. Finally, unpublished and foreign language literature may contain important information relevant to your patient's problem and should not be excluded. Given the volume of literature, the search strategies required and the need for multi-lingual translation, it is hardly surprising that clinicians find it difficult to obtain all of the relevant articles on a particular question in a timely fashion. Several strategies can be used to address this issue. One strategy is to target searches, using designated filters (Table 1.2) [8]. Another, and the choice of this text, is to search for high-quality systematic reviews, especially in therapy, to answer important clinical questions [33]. Finally, seeking the advice of a librarian knowledgeable in the various electronic resources, search terms and search strategies is always worthwhile.

Table 1.2 Common search strategies for identifying evidence from electronic databases using search filters.

Topic	Highest level design	Search terms
Therapy	RCT	Publication type: RCT; controlled clinical trial; clinical trial MeSH headings: RCTs; random allocation; double blind; single blind; placebo(s)
Therapy	SR	Publication type: review; SR; meta-analysis MeSH headings: MEDLINE
Diagnosis	Prospective cohort	Publication type: diagnosis MeSH headings: sensitivity and specificity Text word: sensitivity
Prevention	RCT, SR	See above for RCT and SR
Etiology	Prospective cohort	Text word: risk

MeSH, medical subject heading; RCT, randomized controlled trial; SR, systematic review.

Clinical epidemiology terminology

There is a unique lexicon used in clinical epidemiology in general and in systematic reviews in particular. It may be helpful to readers for the editors to describe several of the important terms here (also see the list of abbreviations in the prelims) since they are used frequently in the forthcoming chapters. Publication bias and selection bias are two important terms. Publication bias refers to the publication of positive results faster, in higher impact journals, and to the exclusion of negative results in the medical literature [34]. Publication bias can be reduced when authors search widely and comprehensively for all published and unpublished literature, irrespective of the publication status, journals or language of publication. Bias can occur in the selection of evidence to cite and can be reduced when multiple authors independently decide which articles to select for evidence synthesis. While this is a problem in many areas of medicine, it seems less of an issue in emergency medicine [34].

The reporting of statistical issues in EBM and especially SRs is particularly important to understand. For dichotomous variables (e.g., admit/discharge, relapse/no relapse, event/no event), individual statistics are usually calculated as odds ratios (OR) or relative risks (RR) with 95% confidence intervals (CIs). Pooling of individual trials is accomplished using sophisticated statistical techniques that employ either a fixed or random effects model. The "weight" of each trial's contribution to the overall pooled result is inversely related to the trial's variance. In practical terms, for dichotomous outcomes, this is largely a function of sample size: the larger the trial, the greater contribution it makes to the pooled estimate.

The results of most efforts to quantitatively pool data are represented as Forrest plots and these figures will be used extensively by authors in this textbook. In such displays, the convention is that the effects favoring the treatment in question are located to the left of the line of unity (1.0), while those favoring the control or comparison arm are located to the right of the line of unity. When the 95% CI of the pooled estimate crosses the line of unity, the result is considered non-significant (Fig. 1.1). In addition, tests of statistical significance are also provided.

For continuous outcomes, weighted mean differences (WMDs) or standardized mean differences (SMDs) and 95% CIs are usually reported. The use of the WMD is common in many systematic reviews and is the difference between the experimental and control group outcomes, when similar units of measure are used [35]. The SMD is used when different units of measure are used for the same outcome. For continuous variables with similar units (e.g., airflow measurements), a WMD or effect size (ES) is calculated. The "weight" of each trial's contribution to the overall pooled result is based on the inverse of the trial's variance. In practical terms, for continuous outcomes, this is largely a function of the standard deviation (SD) and sample size: the lower the SD and the larger the sample size, the greater contribution the study makes to the pooled estimate. For continuous measures with variable units (such as quality of life or other functional scales), the use of an SMD is often used. For example, if quality of life were measured using the same instrument in all studies, a WMD would be performed; however, if the quality of life was measured using multiple methods all producing a "score", an SMD would be calculated. For both the SMD and WMD, the convention is the opposite of that for dichotomous variables, that is, effects favoring the treatment in question are located to the right of the line of unity (0) while those favoring the control or comparison arm are plotted to the left. Once again, when the 95% CI crosses the line of no effect, the result is considered non-significant.

Number needed to treat (NNT) is another method of expressing a measure of effect [36]. In the reviews contained in the Cochrane Library, the absolute risk reduction (ARR) is represented by the risk reduction statistic, and the inverse of this (and its 95% CI) provides the NNT estimation. Another convenient method to calculate the NNT is to use on-line calculators (www.nntonline.net). Finally, less exact methods are available to estimate the NNT; however, caution is advised, since these approaches often result in gross approximations of NNT.

Heterogeneity among pooled estimates is usually tested and reported [37]. There are a number of ways of describing

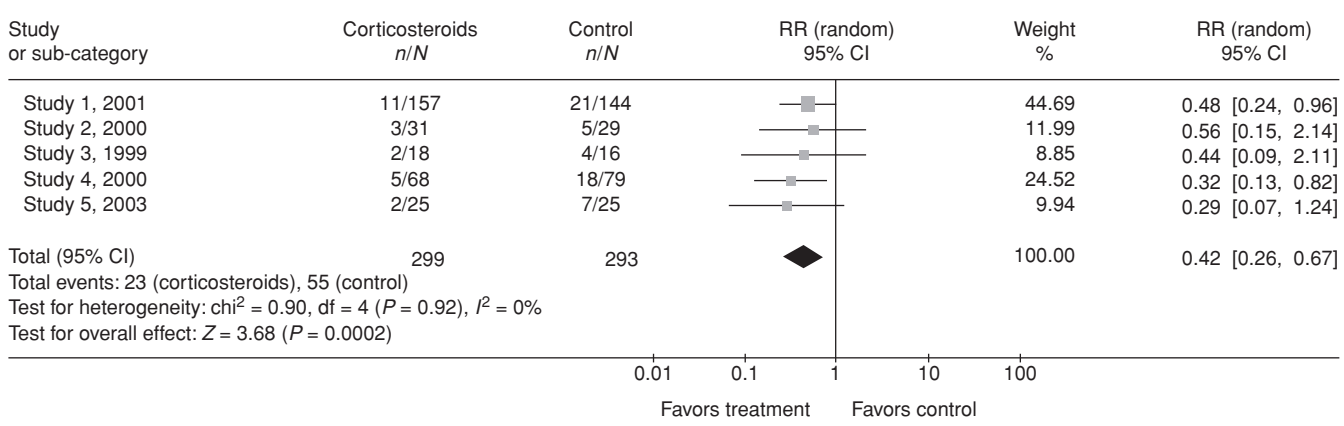

Figure 1.1 Typical systematic review summary figure (referred to as a Forrest plot) used in therapy trials. Note: that in this Forrest plot, five trials have been conducted that compared corticosteroids to placebo to prevent a relapse event. Each study is represented by the point estimate for the outcome in question and by confidence intervals on either side of that value. The vertical line corresponds to a relative risk (RR) of 1.0; studies where the confidence interval crosses the 1.0 line (studies 2, 3 and 5) demonstrate no statistically significant difference between the groups (i.e., those receiving any corticosteroids versus those receiving placebo). Values to the left and ***not*** crossing the vertical line (studies 1 and 4) indicate a clear benefit of corticosteroids. Values to the right and ***not*** crossing the vertical line (Study 1 and 4 in this example), indicate that patients receiving placebo had better outcomes than those receiving corticosteroids. The large horizontal black diamond at the bottom of the figure corresponds to the pooled results of the individual studies. The "weight'' column represents the percentage contribution of each study to the pooled result. The individual and pooled RR and 95% CIs are displayed to the right of the diagram. Finally, the test for heterogeneity of the pooled result and the overall effect are depicted in the left lower corner as both I^2 and chi-squared statistics (see text for further details).

heterogeneity statistically; the Cochrane reviews often report the *I*-squared (I^2) statistic [38]. Pooled statistics assessed for heterogeneity using the I^2 statistic are provided with a percentage measurement of heterogeneity; heterogeneity can broadly be classified as limited ($I^2 < 30\%$), moderate ($30\% < I^2 < 75\%$) or severe ($I^2 > 75\%$). Sensitivity and subgroup analyses are often performed to identify sources of heterogeneity, when indicated. Caution has been advised when interpreting subgroup analyses and practical approaches to them have been published [39].

Collecting and interpreting the evidence for clinical practice

Evidence-based medicine relies on the synthesis and reporting of evidence using a format that may be unfamiliar to clinicians (see lexicon above). With multiple publications on a specific topic often identified, some evidence can be summarized statistically as pooled likelihood ratio (LR) for diagnostic test questions or

Table 1.3 Selected evidence-based emergency medicine (EBEM) websites.

Organization	Website address
Cochrane Collaboration	http://www.cochrane.org
Cochrane Prehospital and Emergency Health Field (CPEHF)	http://www.cochranepehf.org
Bandolier (various EBM topics)	http://www.jr2.ox.ac.uk/bandolier/
Annals of Emergency Medicine EBEM Section	http://www.annemergmed.com
BestBets	http://www.bestbets.org
ACP Journal / *EBM Journal*	http://ebm.bmjjournals.com/
Agency for Health Care Policy and Research (AHRQ)	http://www.ahrq.gov
Centre for Evidence-Based Medicine (Oxford, UK)	http://www.cebm.net
Canadian Agency for Drugs and Technologies in Health (CADTH)	http://www.cadth.ca
National Institute for Health and Clinical EXcellence (NICE)	http://www.nice.org.uk
Centre for Reviews and Dissemination (CRD)	http://www.york.ac.uk/inst/crd/
VirtualRx (NNT calculations)	http://www.nntonline.com/ebm/visualrx/nnt.asp

This list is neither comprehensive nor complete; it represents some of the EBEM resources of use to the authors.

pooled outcome measures (e.g., OR, RR, NNT) in therapy questions. These efforts are made possible when the population, intervention/exposure, control, outcome measure and the designs of the identified studies demonstrate similarities. At other times, these PICO features preclude pooling of evidence and the best possible summary of evidence is descriptive or qualitative. Wherever possible, these approaches will be applied in this text in an effort to distill the evidence for the practicing emergency clinician. There are many text resources as well as internet-based resources available to the reader that can provide additional information, calculations and interpretations of these pooled effect measures (Table 1.3).

Conclusions

Much progress has been made in emergency medicine over the past quarter-century in the areas of diagnosis, therapy, prevention and prognosis. The synthesis of this evidence has been undertaken by many researchers and there is now increasingly valid and reliable evidence for the management of many common conditions presenting to the emergency department. This book attempts to summarize this evidence using a system that values best evidence using relevant examples from clinical practice. We recognize it is not yet comprehensive in all clinical areas; however, as the first evidence-based emergency text, we hope that it is both illustrative and iterative. We anticipate both refinements and substantial expansions of this pilot text in the future. Our goal is to improve the translation of knowledge from the evidence to the bedside in emergency medicine and we hope you will find this approach helpful in improving the clinical care provided at the bedside.

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Conflicts of interest

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