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EVIDENCE BASED RESEARCH SERIES

# Evidence-Based Research Series-Paper 1: What Evidence-Based Research is and why is it important?

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## Abstract

**Objectives:** There is considerable actual and potential waste in research. Evidence-based research ensures worthwhile and valuable research. The aim of this series, which this article introduces, is to describe the evidence-based research approach.

**Study Design and Setting:** In this first article of a three-article series, we introduce the evidence-based research approach. Evidence-based research is the use of prior research in a systematic and transparent way to inform a new study so that it is answering questions that matter in a valid, efficient, and accessible manner.

**Results:** We describe evidence-based research and provide an overview of the approach of systematically and transparently using previous research before starting a new study to justify and design the new study (article #2 in series) and—on study completion—place its results in the context with what is already known (article #3 in series).

**Conclusion:** This series introduces evidence-based research as an approach to minimize unnecessary and irrelevant clinical health research that is unscientific, wasteful, and unethical. 

*Keywords::* Evidence-based research; Systematic review; Evidence synthesis; Research ethics; Medical ethics; Clinical health research; Clinical trials

## 1. Introduction

In this, the first of three articles, we aim to define and describe evidence-based research. We introduce here, and in the subsequent articles provide more details for, the use of an evidence-based research approach before embarking on new research to justify and design the new study (article #2 in series) and, after the completion of the study, to place its results of the new study in the context of earlier similar studies (article #3 in series). Evidence-based research is the use of prior research in a systematic and transparent way to inform a new study so that it is answering questions that matter in a valid, efficient, and accessible manner [1]. Previously we introduced evidence-based research focusing on its possible implications for different stakeholders, including researchers, funders, editors, and patients [2]. Our objective in this series is to describe how a clinical researcher can adopt an evidence-based research approach—and why it is important to do so.

## 2. Need for evidence-based research

Unnecessary clinical research is unethical as it puts patients at avoidable risk, limits the funding available for

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The authors have no conflicts of interest to report. The authors of this report are responsible for its content.

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**What is new?**

**Key findings**

- We introduce an approach to research called "evidence-based research" to systematically use existing evidence to make decisions about new studies.

**What this adds to what is known?**

- Over the last 2 decades, several metaresearch studies have shown the need to improve research practice to reduce waste.
- The evidence-based research approach aims to ensure that studies of value are conducted by planning and designing new studies and placing new results in the context of the existing evidence.

**What is the implication and what should change now?**

- To ensure valid and valuable studies, researchers should adopt an evidence-based research approach for planning and reporting studies.

important and relevant research, and may diminish society's trust in research. Lack of systematic consideration of prior research assessing the same clinical question has meant that thousands of patients over many years have been recruited to clinical trials well after the intervention was proven to be effective or not effective [3−10].

We know from metaresearch studies that researchers do not commonly consider existing evidence. In cases where systematic reviews of similar studies were available, they were not considered when planning the new study [9,11]. We also know that authors of new studies tend to cite a small unrepresentative selective set of earlier similar studies [12−16]. When authors of clinical research do refer to earlier studies, publications that concur with the authors' opinion, supportive and statistically significant studies, are more often cited than those that are critical or statistically nonsignificant [16−23]. Selection of references is often based on preferences and strategic considerations [24,25].

We also know that systematic reviews are rarely used to inform the design of a new study so that researchers are implementing lessons learned from prior studies [11,12,26]. Furthermore, the results of new studies are rarely placed in the context of the existing evidence through the use of a systematic synthesis of prior studies in the discussion section of the new study [26−31].

Redundant studies could be avoided if clinical researchers considered prior similar studies in a systematic and transparent way when preparing a new study. More relevant questions and more informative study designs could be developed, and more useful interpretation of new results could be achieved if they were based on knowledge of the results from earlier studies. We have called this approach evidence-based research [1].

Traditionally, researchers use their scientific environment and context, personal interests and ambitions, and the epidemiological and basic science knowledge base (underpinning research) as the basis for formulating a new research question. The evidence-based research approach suggests that, in addition to these factors, a systematic and transparent approach should be followed to explicitly use all earlier studies and to consider end user perspectives (See Figure 1). Thus, the evidence-based research approach acknowledges the importance of researchers' own context and "a plausible explanation for how the interventions might work, if this is not obvious" (underpinning research) [32] when a new study is planned, but emphasizes that a systematic synthesis of earlier similar studies and a similar synthesis of end users' perspectives must be added to avoid irrelevant and redundant studies.

This is an ethical question. Benjamin Freedman wrote in 1987: "A … distinct understanding of the requirement of scientific merit focuses upon 'value' rather than (mere) 'validity.' A study may be well-designed relative to its hypothesis, and therefore be scientifically valid, but nonetheless be of no value, generally because the hypothesis itself is trivial or otherwise uninteresting." [33]. Emanuel et al., in discussing the ethics of clinical research, elaborated on the need for clinical research to be both valid and of value [34]. They stated that a nonvaluable study is characterized by (a) nongeneralizable results, (b) a trivial hypothesis (trifling), (c) a substantial overlap with existing knowledge, (d) results that hardly ever could be disseminated, and (e) interventions that could hardly ever be implemented in practice [34]. Although validity considers the quality of the design and execution of the study, value reflects the relevance of the study for society in general and for end users in particular. More specifically, a new study should be worthwhile.

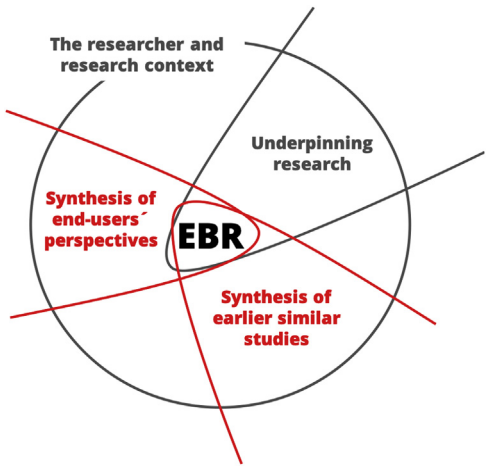


**Fig. 1.** The elements of an evidence-based research approach.

Consequently, a new study should be justified both on the question of validity and the question of value.

In recent years, other authors have specified approaches to review all current knowledge to inform new studies. Table 1 presents examples of some of these studies.

We acknowledge that researchers previously have worked on individual parts of the evidence-based research approach, but our intention is to present a more comprehensive evidence-based research approach. The evidence-based research approach is both a new concept and as old as the scientific method itself. In addition, during the last 3 decades, many authors have written about the need to be evidence-based when planning new studies. As an example, the late Professor Douglas Altman wrote in 1994: "We need less research, better research, and research done for the right reasons." [39]. Sir Iain Chalmers, commenting about a metaresearch study, stated "New research should not be designed or implemented without first assessing systematically what is known from existing research. … The failure to conduct that assessment represents a lack of scientific self-discipline that results in an inexcusable waste of public resources." [40]. Our aim with this series is therefore not to simply reiterate the need to be evidence-based performing research, but to give some specific guidance on how to do that. Article 2 in this series discusses how to justify and design a new study explicitly using the existing evidence, whereas article 3 outlines how to place the new results in the context of earlier similar studies.

The series focuses on clinical research. It is unknown whether other scientific disciplines or basic science within health (animal studies and bench research) have the same challenges as clinical research. However, looking at the nature and character of the problem (e.g., Thornley's study that includes researchers from social, physical, biological, and life sciences [41] or examples in animal research [42]), it is reasonable to expect the same lack of systematic approach when considering earlier research in other domains. The traditions and habits in science seem to fundamentally be the same, but the way different disciplines work will vary, and thus methods, procedures, and technologies probably need to be adjusted or developed within the context of the different disciplines. Nonetheless, the methods, procedures, and technologies of the evidence-based research approach being developed within clinical health research could be adopted by other disciplines.

## 3. The evidence-based research approach

Figure 2 presents the three key phases of research and illustrates the use of an evidence-based research approach during the planning phase before the actual study (for justifying the question and designing new study, article #2) and after its completion and when reporting of the study results (for placing the new results in the context of earlier studies, article #3). The first phase deals with the challenge of whether a research question is justifiable? Ethic committees, funding agencies, and other review processes before the start of a new study currently focuses on the internal validity of the study to determine whether the study should be conducted. This is indisputably a key element in deciding whether a study should proceed but whether the study is worthwhile seems just as important.

In the evidence-based research approach, a systematic review is identified or prepared and subsequently used to justify the research question as well as to design the most informative study. As the systematic review explicitly describes a number of variables from earlier studies, it is possible to identify, for example, the most relevant subgroup of patients, intervention, or comparison for the new study. However, although the use of a systematic review is a necessary prerequisite, it is of course not sufficient for the justification and design of a new study; knowledge of the end users' perspectives is also important.

After the completion and during the reporting of the study, the results of the new study should be interpreted and reported within the context of earlier similar studies. As a systematic review has provided the foundation for justifying the study, it can—updated as required—also be used as the foundation for discussion of the new findings.

This synthesis will lead to one of two outcomes: the first one will conclusively answer whether the results can be used for clinical decision-making. If this is not the case, the other option is that more research is needed, with the

**Table 1.** Examples of studies suggesting use of systematic reviews to inform new studies

| Suggested use of systematic reviews to inform new studies | Studies |
|---|---|
| Flowcharts of how to use systematic reviews to justify and design new studies. | Sutton 2009, Thompson 2012, Li 2012 [35–37]. |
| Frameworks of how to use systematic reviews to justify and design new studies. | Robinson 2011, Clayton 2017. |
| How to calculate sample size for future primary studies based on systematic reviews of earlier similar studies. | Goudie 2010, Nikolakopoulou 2014, Rosenthal 2017 [12]. |
| An example of an analysis to decide when there are enough studies within a given area. | Henderson 1995. |
| A comprehensive framework for all phases in clinical research including the use of systematic reviews to justify the new study | von Niederhausern 2018 [38] |

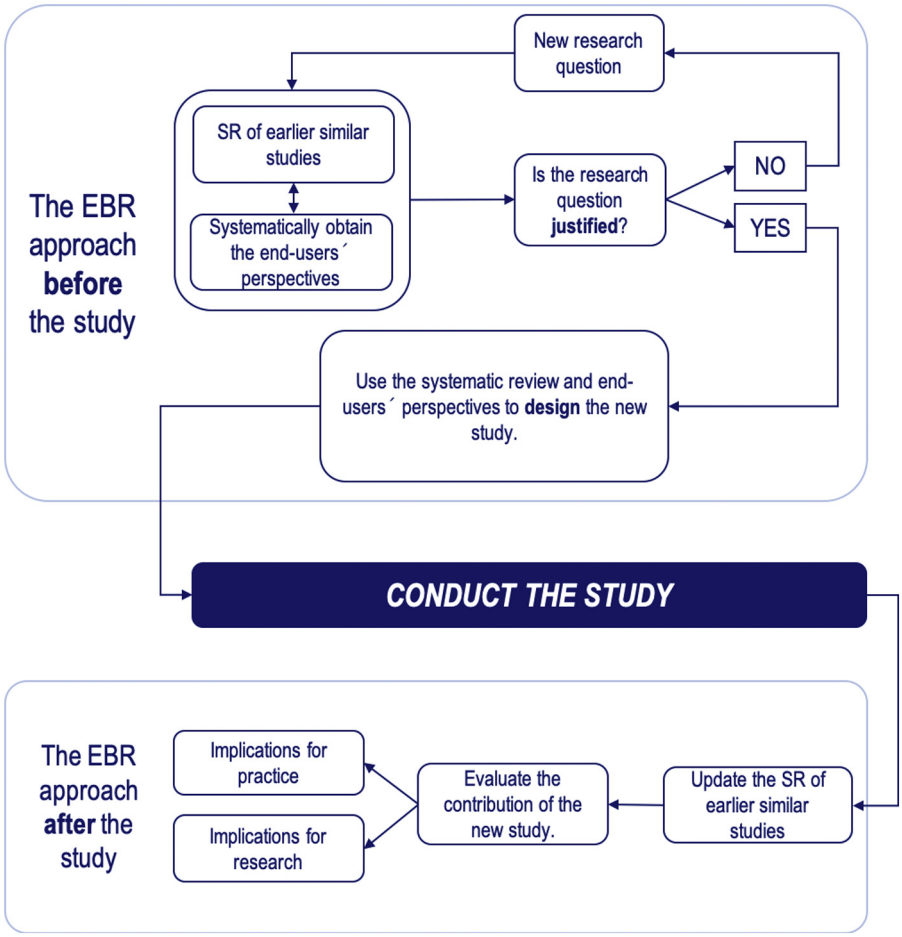


**Fig. 2.** The evidence-based research approach and outline.

systematic review specifying the continuing evidence gap to be specified in detail. Thus, evidence-based medicine (EBM) and evidence-based research are complementary: if the systematic review shows ambiguous results, there is a need for further research; if the results are conclusive, the clinician (or other decision makers) can make use of these results for clinical decisions. The benefit of this complementary approach is twofold: with an unambiguous conclusion, the clinician can use the results in practice and researchers will simultaneously avoid subsequent redundant clinical research. With an ambiguous conclusion, we have demonstrated further research is needed and are simultaneously avoiding the premature implementation of therapies into practice that may lead to unnecessary future 'medical reversal' [43].

## 4. Implementation of an evidence-based research approach in clinical research

The evidence-based research approach demands new knowledge and skills of the clinical researcher. It also demands a new perspective from a number of stakeholders including end users (in health, typically the patients), ethic committees, funding agencies, and editors and reviewers of scientific journals [2]. Still, it is a fulfillment of a scientific ideal that seems as old as science itself. When Gilbert wrote in 1600 that he had read all that was published about magnets, he was probably correct because the amount of information written and published at that time was manageable (here quoted from [44]). In the centuries to follow, the number of scientific publications increased enormously causing Lord Rayleigh to say in 1884: "If, as is sometimes supposed, science consisted in nothing but the laborious accumulation of facts, it would soon come to a standstill, crushed, as it were, under its own weight" (here quoted from [45]). In the following hundred years or so, the situation got considerably worse. The number of scientific publications skyrocketed, and there was no way any scientist could ever get a full picture of all that had been published. Then came the digital revolution, and everything changed. Since the beginning of the 1990s, through the emergence of relevant searchable databases, it has become an achievable goal to identify almost all studies relevant for to a specific clinical question. It is no coincidence that the EBM movement, the launch of Cochrane and the Campbell

Collaboration, and the development of systematic review methodology happened simultaneously with fundamental changes in information technology. For 500 years, it has been an ideal that ‘‘discovery and explanation go hand in hand, in which not only are new facts presented, but their relation to old ones is pointed out’’ (Lord Rayleigh, 1884). Now this ideal is within reach.

Unfortunately, metaresearch shows that researchers do not always use the available technologies to fulfill this fundamental pillar of science. We have a golden opportunity to take advantage of the digital tools at hand and to implement knowledge and skills so that we can be evidence-based when planning new research and when placing new results in context.

Methods and procedures for implementing the evidence-based research approach by different stakeholders need to be developed and tested, including those for the efficient production, updating, and dissemination of systematic reviews (e.g., through digital tools and automation). New metaresearch is required to continuously evaluate and improve research practices. To promote the concept of evidence-based research and to support a more efficient production, updating, and dissemination of systematic reviews, an international network (The Evidence-Based Research Network (ebrnetwork.org)) was established in 2014.

## 5. Limitations of implementing the evidence-based research approach

Several factors need to be in place before a researcher can become evidence-based when planning and reporting a new study. First, evidence synthesis needs to be accepted as an important scientific endeavor in itself. A recent study showed that less than half of all European universities accepted a systematic review as part of a PhD thesis [46]. Second, all stakeholders and researchers need to acknowledge the importance and hence the implications of using the evidence-based research approach in the planning, approval, support, and publication of research. Furthermore, the methods, processes, and technology related to the production of systematic reviews need to continuously be extended and improved, for example, through the automation of tasks related to the production of systematic reviews [47], or the continuous updating of systematic reviews via so called ‘‘living systematic reviews’’ [48]. Finally, ever since the invention of modern science, it has predominantly focused on new discoveries [44], rather than on bringing together knowledge in a way that systematically and transparently acknowledges its many contributors. As Light and Pillemer put it in 1984: ‘Novelty in and of itself is shallow without links to the past. … For science to be cumulative, an intermediate step between past and future research is necessary: synthesis of existing evidence’ [49].

To implement the evidence-based research approach, the concept should hence not only be promoted, but also supported and expected by key stakeholders in clinical research such as policy makers, patients, clinicians, research ethics committees, funding agencies, and scientific journals. Although the basic scientific approach is part of the DNA of science, the systematic use of earlier studies is not. In relation to habits developed over hundreds of years, 15 to 20 years are a very short timeframe to bring about a cultural change. The results by Robinson and Goodman showing that authors only refer to 21% of earlier studies are very disappointing [13], but maybe we should not be so surprised. Researchers have never been taught, so have never learned to systematically consider earlier research before and after conducting a study. They know that they have to cite earlier research, but it is accepted practice to preferentially choose the newest, the biggest, or the best studies, or those that support their hypothesis or results. Several metaresearch studies have clearly showed that authors of scientific articles are biased when referring to earlier studies. For example, studies have demonstrated that significant and positive results are much more frequently cited than studies with nonsignificant and negative results [35]. All these require a fundamental culture change that will not be easy; hence, we need to remove as many obstacles as possible to enable and further the adoption of the evidence-based research approach.

Finally, the ability to implement the evidence-based research approach will be limited by locally varying factors such as access to electronic databases and full-text articles, supporting software, knowledge and skills, financial support, and the time available. This may be especially challenging for low- and middle-income countries. Ironically, these countries stand to benefit the most from the evidence-based research approach: where research funding is scarce and research capacity is restricted, the opportunity cost and impact on patient care from research waste may be exacerbated.

## 6. Final remarks

In the last few years, several initiatives have been made in promoting and supporting an evidence-based research approach within science. In December 2014, The Lancet introduced a new initiative requiring authors of new studies to provide answers to three questions at submission: what was the evidence before the study? what is the added value of this study?, and what are the implications of all available evidence? [36]. Today, many other journals are asking for the same information when discussing the importance of the new study. Recently a number of national funding agencies (e.g., NIHR in the UK, PCORI in the USA, and ZonMW from the Netherlands) formulated 10 guiding principles for funders to ensure value in research (See https://sites.google.com/view/evir-funders-forum/home and [37]), including one

stating that ‘‘Research should only be funded if set in the context of one or more existing systematic reviews of what is already known or an otherwise robust demonstration of a research gap’’ (principle #2) and another stating that ‘‘New evidence should be placed in the context of existing knowledge to inform appropriate interpretation and use of findings. When appropriate and when it will add value to evidence users, systematic reviews should be updated following primary research.’’ (principle #9). In 2018, the European Union approved a COST Action to establish an international European-based network of now all COST member countries (39 European countries), aiming to raise awareness of the need to use systematic reviews when planning new studies and when placing new results in context (see https://evbres.eu/ and https://www.cost.eu/actions/CA17117/#tabs|Name:overview).

The objective of this series is to help clinical researchers to consider and use the evidence-based research approach. The loss of life, health, and money through redundant and unnecessary studies demands urgent action.

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