

White paper for European Commission "The need for an Evidence-Based Research approach in health science"

From the COST Action "EVBRES" (CA 17117, evbres.eu)

Introduction

"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. In applied fields like health care, failure to prepare scientifically defensible reviews of relevant animal and human data results not only in wasted resources but also in unnecessary suffering and premature death" Iain Chalmersⁱ.

However, research on research (meta-research) clearly shows that at best less than 50% of clinical health researchers assessed what is known from existing researchⁱⁱ. As this can lead to redundant research at least 33 million EUROS alone from the Norwegian Research Council alone is lost to unnecessary clinical health research for 2019ⁱⁱⁱ. Combined with the amount used for health research at the Norwegian hospitals the waste of research amounts to 123 million EUROS alone in Norway^{iv}.

Further, more than 2,000 redundant clinical trials on statins among patients with coronary artery disease were identified from mainland China. Such trials have been harming patients who have experienced more than 3,000 unnecessary major adverse cardiac events, including nearly 600 deaths^v.

It is hypothesised that "including the perspectives of end users of the research, which include patients, physicians, and other health care stakeholders, will enhance the relevance of research to actual health decisions these end users face." Frank 2014^{vi}.

However, meta-research clearly shows that only 0.006% of new clinical studies engage the patients in their research^{vii}.

One way to diminish redundant and unnecessary research would be if funding agencies demanded that the applicants used systematic reviews to justify and design their new study. However, an evaluation of whether the most influential funders in UK, USA, Canada, Australia, Germany, France, The Netherlands, Norway and Denmark ask for a systematic review to justify the new study, only one out of eleven were doing that^{viii}.

The approach to deal with these unethical flaws in clinical health research is called "Evidence-Based Research"^{ix}.

Evidence-Based Research

A necessary requirement for evidence-based healthcare is the existence of relevant and essential research. However, health researchers do not use a systematic approach when justifying new studies, thus many redundant studies are conducted. In addition, there is a discrepancy between the research needed by end users and the actual research funded,

conducted and published. To address this challenge, an approach called "Evidence-Based Research" has been developed and promoted in the last 6 years, the last 2 years through the COST Action "EVBRES" (CA 17117, evbres.eu). This approach will make better use of and help to ensure excellent science and will allow researchers and health care workers to disseminate and exploit researcher findings.

To embark on research without systematically reviewing what is already known, particularly when the research involves people or animals, is unethical, unscientific, and wasteful. Thus, EVBRES defines "Evidence-Based Research" (EBR) as *the use of prior research in a systematic and transparent way to inform a new study so that the research is answering questions that matter in a valid, efficient and accessible manner.*

A systematic and transparent methodology should be used when acquiring end users' perspectives, and when synthesising the existing evidence for a specific research question. Thus, the EBR approach provides a research infrastructure for excellent science. Without this approach too many redundant studies are performed and published – wasting time, resources and money, and may – due to too many patients receiving unnecessary placebo or suboptimal treatment – result in harm to health and life.

The evidence showing the need to introduce an EBR approach in health research

A scoping review (under preparation) identified 83 research-on-research (meta-research) studies indicating that a systematic and transparent consideration of existing evidence is rarely used (1) when citing earlier similar studies; (2) to justify new studies; (3) to design new studies or (4) when interpreting and presenting new findings.

Why are researchers not evidence-based?

The same scoping review highlighted a range of possible biases related to how researchers reference earlier studies. Around half showed the presence of citation bias, and nearly a quarter found additional biases, for example papers from high-impact journals being cited more often than those in low-impact journals, and articles by high-prestige authors being referenced more frequently.

Lord Rayleigh observed in 1884 that for science to be worthwhile it needs to be in the context of earlier research, but that scientists often failed to do this^x. Not systematically using citations to justify and design of a new study following a scientific approach may have been excusable as too difficult and time-consuming before the digital revolution, but not in 2020 when the potential of digitisation and new technologies can be harnessed to make the process efficient and effective.

Science is cumulative

One of the key characteristics of science is the cumulative way in which knowledge develops. For science to be cumulative, synthesis of existing evidence is necessary: This is often executed as a systematic review^{xi}. To be systematic and transparent the authors of a systematic review must include all studies fulfilling the inclusion criteria, not only those that suit the authors or bolster their agenda. Thus, EVBRES promotes that when justifying their new study, health researchers should search for and critically appraise a systematic review of studies similar to the new study they are planning; and, where possible, systematic reviews

of qualitative studies or surveys on the end user perspective to put citizens' needs and concerns at the centre of research. This process is not necessarily easy and readily accessible but requires development and tests as a "process innovation".

EVBRES promotes strategically prioritisation and maximizes use of research funds. Digitization has allowed world-wide access to studies and allows reviews to be done more efficiently. EVBRES will enable and support the next generation of health science, clinicians, technology, researchers and innovations.

Conclusion

A necessary and important pre-requisite for evidence-based practice in health is the presence of relevant and important research, i.e. research that is filling a knowledge gap and fulfilling a documented end user need. Unfortunately, research on research indicates that new studies are not prepared based on such criteria but rather on researchers' preferences and strategic considerations. This leads to redundant studies and research waste.

The concept of EBR is suggested as a solution, however the current knowledge base for evaluating the underlying issue is sparse. Even less is known about the barriers/facilitators to using an EBR approach, and once identified these will need to be addressed. Finally, the overall impact of implementing an EBR approach in health research will need to be evaluated, yet there is great potential to improve the impact of investments in research and innovation.

We envision EBR as an integral part of the evidence-based ecosystem, working together to ensure access to innovative, sustainable and high-quality health care.

Call to action

Therefore, the COST Action "EVBRES" strongly recommend that the European Commission:

- make the EBR approach a part of funding criteria
- further the implementation of EBR by creating a call to fund EBR relevant projects

For further information including suggested research topics for an Evidence-Based Research call, contact

Professor Hans Lund

Chair of EVBRES

hans.lund@hvl.no

ⁱ Fergusson D, Glass KC, Hutton B, Shapiro S. Randomized controlled trials of aprotinin in cardiac surgery: could clinical equipoise have stopped the bleeding? *Clinical trials*. 2005;2(3):218-29; discussion 29-32.

ⁱⁱ Glasziou/Chalmers 2009 indicated 85% total waste. This was based upon an assumption that 50%, two systematic reviews (SR EBR Justify and SR EBR Design) indicates that only 42% uses a systematic review(SR) to justify the new study and only 44% uses a SR to design the new study.

ⁱⁱⁱ The website https://www.helseomsorg21monitor.no/figur/14?_C3%85rstall=%5B%222019%22%5D provides information of how much the Norwegian Research Council (NFR) support health related research. The total amounts to 132,4 million EUROS for 2019. Assuming that 50% is not consulting previous research systematically and transparently there will be a risk for redundant and unnecessary research being performed. Assuming that half of the researchers not consulting earlier research perform redundant research (= 25%) leads to an annual waste of 33 million EUROS.

^{iv} A report for 2017 (<https://nifu.brage.unit.no/nifu-xmlui/handle/11250/2566830>) showed that the Norwegian Health system used 360 million EUROS in 2017 upon research employment and equipment's. 25% (See Footnote 2) of these amounts to 90 million EUROS. Together with the 33 million from the Norwegian Council the total waste is 123 million EUROS on one year.

^v Jia Y. et al., Redundant Clinical Trials Are Hurting Patients: An Example of Randomized Clinical Trials Conducted in mainland China Evaluating Statins among Patients with Coronary Artery Disease. (Under revision)

^{vi} Frank L, Basch E, Selby JV, Patient-Centered Outcomes Research I. The PCORI perspective on patient-centered outcomes research. JAMA. 2014;312(15):1513-4.

^{vii} Fergusson D, Monfaredi Z, Pussegoda K, Garritty C, Lyddiatt A, Shea B, et al. The prevalence of patient engagement in published trials: a systematic review. Research Involvement and Engagement. 2018;4(1):17.

^{viii} Nasser M, Clarke M, Chalmers I, Brurberg KG, Nykvist H, Lund H, et al. What are funders doing to minimise waste in research? Lancet. 2017;389(10073):1006-7.

^{ix} Lund H, Brunnhuber K, Juhl C, Robinson K, Leenaars M, Dorch BF, et al. Towards evidence based research. BMJ. 2016;355:i5440.

Lund H, Juhl CB, Nørgaard B, Draborg E, Henriksen M, Andreassen J, et al. Using an Evidence-Based Research approach before a new study is conducted to ensure value. Journal of Clinical Epidemiology. 2020.

Robinson KA, Brunnhuber K, Ciliska D, Juhl CB, Christensen R, Lund H. What Evidence-Based Research is and why is it important? Journal of Clinical Epidemiology. 2020.

Lund H, Juhl CB, Nørgaard B, Draborg E, Henriksen M, Andreassen J, et al. Using an Evidence-Based Research approach to place your results into context after the study is performed to ensure usefulness of the conclusion. Journal of Clinical Epidemiology. 2020.

^x Chalmers I, Hedges LV, Cooper H. A brief history of research synthesis. Eval Health Prof. 2002;25(1):12-37.

^{xi} Light RJ, Pillemer DB. Summing up. The science of reviewing research. Boston: Harvard University Press; 1984.