A new network to promote evidence-based research

To embark on research without reviewing systematically evidence of what is already known, particularly when the research involves people or animals, is unethical, unscientific, and wasteful.[1,2] More than two decades have passed since Antman and colleagues[3] showed that research on some treatments for myocardial infarction had gone on for as long as a decade after benefit or harm had been established in earlier research. Failure to analyse epidemiological research cumulatively has also had devastating effects. Systematic review of preventable risk factors for sudden infant death syndrome from 1970 onwards would have led to earlier recognition of the risks of the prone sleeping position and might have prevented more than 10 000 infant deaths in the UK and at least 50 000 in Europe, the USA, and Australasia.[4]

The serious consequences of failure to base plans for new research on systematic reviews of existing evidence is not limited to clinical and epidemiological research. After Horn and coworkers[5] did not detect any beneficial effect of calcium antagonists on acute ischemic stroke in a systematic review of 7521 participants in 28 clinical trials, they reviewed 20 relevant animal studies. They found that none of those studies provided convincing evidence to justify the decision to extend research to people.

In addition to the avoidable harm done to people and animals, failure to review existing evidence systematically before undertaking additional preclinical, clinical, and epidemiological research has resulted in avoidable waste of research resources. New studies have been designed without taking adequate account of the lessons from earlier research, including the need to study larger sample sizes to address important uncertainties.[1,2,6,7]

What should research funders, research regulators, researchers, academic institutions, and journals do to reduce this sometimes lethal research waste? Some research funders have been clear. The National Institute for Health Research in England, for example, advises research applicants for support of new primary research as follows:

> Where a systematic review already exists that summarises the available evidence this should be referenced, as well as including reference to any relevant literature published subsequent to that systematic review. Where no such systematic review exists it is expected that the applicants will undertake an appropriate review of the currently available and relevant evidence (using as appropriate a predetermined and described methodology that systematically identifies, critically appraises and then synthesises the available evidence) and then present a summary of the findings of this in their proposal. All applicants must also include reference to relevant on-going studies, eg, from trial registries.[8]

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Among research regulators, the guidance for researchers issued by the Health Research Authority in the UK now states "Any project should build on a review of current knowledge. Replication to check the validity of previous research is justified, but unnecessary duplication is unethical."[9]

Research on research has exposed a general failure to refer to existing evidence when reporting additional primary research.[7] Other research has shown that this unsatisfactory situation exists even in reports published in prestigious general medical journals.[2,10] Some research funders and researchers are dealing with the problem;[11] and some journals, including *The Lancet*,[12] have introduced editorial policies that require researchers to use systematic reviews to put reports of new research in context. However, many funders, research regulators, and academic institutions still do not seem to take the problem seriously.

Why should patients and the public trust the research community if it fails to make efficient use of the results of research, most of which they have funded? Just a few weeks before his death, the Italian research funder, researcher, and cancer patient Alessandro Liberati called for a new governance strategy for research, "starting from an analysis of existing and ongoing research, produced independently of vested interests".[13]

5 years ago Karen Robinson used the term "evidence-based research" to encapsulate what is required.[14] She pointed out that although use of research synthesis to make evidence-informed decisions is now expected in health care, evidence-based research offers a way to reduce research waste and ensure that new trials are designed to maximise the information gained from them. On Dec 1–3, 2014, at the Evidence-Based Research meeting in Bergen, Norway, three Scandinavian researchers[15] and participants from around the world will inaugurate an international Evidence-Based Research (EBR) Network. This network will press funders, regulators, researchers, academic institutions, and journals to implement the

For the **EBR Network** see http://www.ebrnetwork.org/

changes that are needed to promote evidence-based research. One of the objectives of the EBR Network is that all doctoral students, supervisors, and senior researchers should learn the methodology of systematic reviews and use these research syntheses to anchor more effectively questions for additional primary research. We wish the new EBR Network well and urge the research community to support it.

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We declare no competing interests. We will both participate in the Bergen Evidence-Based Research meeting to inaugurate the Evidence-Based Research Network.

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Alteplase in acute ischaemic stroke: the need for speed

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Doctors treating patients who have had an acute ischaemic stroke must feel the need for speed more feverishly than a racing driver. Stroke does not hurt. There is none of the pain that might be registered on the face of a patient with acute myocardial infarction or the visceral sight of blood in the case of trauma to evoke a sense of immediacy. Yet stroke is exactly like acute myocardial infarction and acute trauma in the need for very fast treatment.

In *The Lancet*, Jonathan Emberson and colleagues present a pre-planned analysis of pooled individual data for 6756 patients from all the major trials of thrombolysis for treatment of stroke.[1] Overall, thrombolysis with alteplase unequivocally resulted in more patients with an excellent neurological outcome at 3–6 months compared with control. This overall outcome included an increase in the number of early fatal intracerebral haemorrhages, but the result is definitive. Thrombolysis is an effective treatment, especially when given fast.

Time is the major modifier of the effect of treatment: faster treatment results in a much greater treatment effect.[1] In Emberson and colleagues' analysis, treatment within 3 h resulted in a good outcome for about 33% of patients who took alteplase compared with 23% who took control (odds ratio [OR] 1·75, 95% CI 1·35–2·27); delay of more than 3·0 h but less than 4·5 h resulted in good outcome for 35% versus 30% (OR 1·26, 95% CI 1·05–1·51); and delay of more than 4·5 h resulted in good outcome for 33% versus 31% (OR 1·15, 95% CI 0·95–1·40). Age and stroke severity did not modify the effect of treatment; both young and old patients, and those who had both mild and severe strokes, benefitted from thrombolysis.

Audits[2,3] show that patients with ischaemic stroke are offered thrombolysis too rarely or, if they are offered it, too slowly. Quick treatment requires efficient processes and a team approach. Pre-hospital systems to identify patients and bring them to the appropriate hospitals, emergency department swarming, rapid simple