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Don't just do it, do it right: evidence for better health in low and middle income countries

Evidence for better health outcomes involves a two-step process: getting the right sort of evidence and getting this evidence used [1].

Getting the right evidence

The need for the right sort of evidence is best exemplified by the widespread use of hormone replacement therapy by post-menopausal women, previously recommended by professional organisations and physicians worldwide to reduce cardiovascular risks, that was based largely on evidence from observational studies [2]. A recent Cochrane systematic review pooled the results of 19 randomised controlled trials (RCTs) of hormonal therapy (oestrogen alone or combined with progestin) versus placebo, involving 41,904 peri-menopausal and post-menopausal women with a minimum follow up of one year, and found an increased risk of venous thrombo-embolism, coronary events, strokes, gallbladder disease, breast cancer (with combined therapy) and dementia (in healthy women over 65 years) compared to placebo [3]. The reviewers concluded that the routine, long-term use of combined or oestrogen-only therapy was not recommended due to substantially increased health risks over benefits.

This sobering example of how wrong we can be in our health-policies, guidelines and clinical practice, unless we have the right sort of evidence is, unfortunately, not an isolated one. Numerous examples exist where systematic reviews of well-conducted RCTs have challenged established beliefs, helped optimise care and resource utilisation, prevented harm, and saved lives [1, 4]. In some of these examples, the initial use of better ways to evaluate the reliability and adequacy of evidence might have saved numerous lives and prevented harm.

Evidence that is convincing

The least biased evidence comes from systematic reviews of primary studies with designs appropriate for particular healthcare questions. For questions related to the efficacy and safety of interventions, RCTs that are designed, conducted, interpreted and reported in ways that encourage confidence that empirically confirmed methods were used to reduce bias, confounding and the play of chance in the primary studies [5], as well as in the systematic reviews of these trials [6], are most likely to yield results that can be trusted [7]. For questions related to aetiology, prognosis, and the long-term effects of interventions, systematic reviews of a variety of observational study designs that adhere to internationally accepted reporting

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standards provide the least biased evidence [7, 8]. These reporting standards are readily available [9], but their elements need to be incorporated into study designs and protocols if the validity and transparency of the final reports are to improve. Attempts to ensure this, at least for interventional trials, are underway [10].

Evidence for low and middle income countries

Sufficiently reliable evidence for the efficacy and safety of all the interventions used in healthcare is not available. Even when available, whether such evidence is always relevant to the healthcare needs of low and middle income countries is also a question. There is simply not enough interventional research conducted in low and middle income countries that is of relevance to their healthcare needs, in contrast to the increasing number of out-sourced trials that are being conducted in these countries. Published research from many low and middle income countries are often deficient in standards of reporting, raising doubts about the reliability of their findings [11, 12]. More primary research relevant to local health is needed, with methods that would yield valid results and are prospectively registered in publicly available trials registries to ensure transparency and accountability [13]. Also needed is more secondary research, in the form of systematic reviews based on these primary studies, in order that gaps in the knowledge of what works best in these settings can be filled.

Getting the evidence used

Access to reliable evidence

The best single source of reliable evidence for health-decisions is The Cochrane Library (www.thecochranelibrary.com). This is an online collection of six evidence-based databases that contain information regarding nearly all published systematic reviews and controlled clinical trials on the effects of interventions used in healthcare in the world. Systematic reviews use pre-determined, explicit and reproducible methods to systematically and comprehensively identify from multiple sources all the relevant studies on a particular topic, then appraise them reliably for risk of bias, extract data and, if appropriate, statistically aggregate them using a technique called meta-analysis. Issue 4 of the 2009 *Cochrane Database of Systematic Reviews* (CDSR) [produced by 52 review groups of The Cochrane Collaboration (www.cochrane.org)] contains 5933 systematic reviews or protocols of systematic reviews in progress. Cochrane systematic reviews are continuously evolving their methods and are considered to be of better quality, more up-to-date, and less biased in their methods and interpretation than non-Cochrane systematic reviews, and are free of conflicted sources of funding [14, 15]. They evaluate pharmacological and non-pharmacological interventions and, increasingly, more complex interventions pertinent to public health, primary care and health systems.

The full contents of this resource are now available to over half the world's population living in high, middle and low income countries either by individual, institutional or national subscriptions, or through international initiatives such as the World Health Organization's Access to Research Initiative (HINARI; http://www.who.int/hinari/en/) [16]. People in low and middle income countries without the above-mentioned modes of full access have access only to the abstracts and plain language summaries of systematic reviews. This is unfortunate, because it is precisely these people, with competing priorities and limited resources, who need the best evidence for safety and efficacy of health interventions.

Investing in evidence

In 2007, a far-sighted initiative of the Indian Council of Medical Research to purchase a national subscription to the Cochrane Library led to a dramatic and sustained increase in the frequency of searches and full text downloads of systematic reviews over the subsequent three years by people in India [16]. This example of responsible health-leadership, of investing in access to reliable evidence to improve health outcomes, could be used by health professionals and consumer groups in countries in the region without access to lobby for national or wider access to this resource.

From evidence to policy and practice

Evidence does not necessarily translate automatically to clinical practice guidelines or health policy since it needs to be used within the context of local needs, resources, preferences and priorities. Evidence leads to changes in health policy if it is considered reliable, relevant to local needs, obtained locally or in similar conditions, actively disseminated or presented and interpreted appropriately to policy makers, and involves minimal programmatic changes or financial re-allocations. Such circumstances may, for example, have facilitated the change in health policy in the national malaria control guidelines in India and Sri Lanka with regard to dosing regimens with primaquine for preventing relapses of *Plasmodium vivax* malaria [17].

Health-policy makers do not easily understand evidence provided by health researchers unless it is summarized and presented in the context of their programmatic needs. Reliable evidence may not always be available and policy makers are often prompted to use whatever evidence that is available because of the need to act [18]. Implementers of health policies or guidelines may then not follow these guidelines, unless they are convinced about their reliability, utility and practicality. Initiatives aimed to help health policy makers and their health advisors to understand and use evidence appropriately would improve health-outcomes.

The Grading of Recommendations: Assessment, Development, and Evaluation (GRADE) approach to developing guidelines (http://www. gradeworkinggroup.org) separates the quality of evidence from the strength of recommendations. GRADE utilises a pragmatic, explicit and sequential approach to evaluate the overall quality of evidence for each important outcome in systematic reviews comparing health interventions in the form of summary profiles. These profiles are then discussed by a multidisciplinary panel of relevant stakeholders that incorporate judgments about the underlying values and preferences between management options and outcomes, the balance between risks and benefits, as well as between health-benefits and resource costs, before grading the strength of recommendations and formulating guidelines [19]. The Evidence Informed Policy Network [EVIPNet] is an initiative of the WHO (http://www.evipnet.org) that focuses on promoting the systematic use of research evidence in policy making in low and middle income countries. National teams of policy makers, researchers and citizens are facilitated to develop policy briefs offering options that are based on reliable or best available evidence (increasingly using the GRADE approach), and that are locally applicable. This initiative also aims to help develop capacity within countries to undertake relevant research to provide local evidence, while improving health policies and strengthening health systems [20].

If health-policy makers and researchers work together to understand the others' perspectives, and to develop the evidence base and health policies, then not only would they be doing the right thing, but they would also be doing it right.

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