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Scaling up oral rehydration salts and zinc for the treatment of diarrhoea

Is cheap and effective and could accelerate reductions in child mortality

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In the years after the launch of the millennium development goals, the health economist Jeffrey Sachs emphasised investment in malaria control as the "lowest hanging fruit" in the battle to reduce child mortality.[1] Such investment is paying off: cases of malaria and deaths from the disease, which mostly occur in young children, have fallen by more than 50% in nine African countries since 2000 through scaling up of malaria control tools.[2] Yet despite this progress in controlling malaria and in scaling up other interventions such as vaccines, most countries are still not on track to achieve millennium development goal 4—that of reducing child mortality by two thirds from 1990 to 2015. With only four years until the deadline, we must now pursue other "low hanging fruit" that can rapidly reduce child mortality in developing countries.

Investment in the treatment of diarrhoea with oral rehydration salts (ORS) plus zinc is one of the best opportunities to achieve such rapid impact.[3] Acute diarrhoea is the second biggest cause of death in children worldwide, causing 1.2 million deaths each year.[4] Rotavirus vaccines, clean water, sanitation, and other preventive measures are important in reducing this burden. However, vaccines are only partially effective and will not prevent many deaths,[5] and other preventive interventions are relatively costly or difficult to scale up quickly.[6 7] Treatment with ORS and zinc could rapidly and cost efficiently avert most of the deaths not prevented by vaccines.[6]

A systematic review estimated that universal coverage with ORS would reduce diarrhoea related deaths by 93%.[8] A second systematic review estimated that in zinc deficient populations, zinc treatment reduces diarrhoea related deaths by 23%.[9] Yet only about 30% of children with diarrhoea in high burden countries receive ORS,[10] and fewer than 1% receive ORS plus zinc.[6] The use of ORS has stagnated globally since 1995; this could partly be because of its lack of impact on the symptoms of diarrhoea and the decline in funding for diarrhoea control programmes.[10]

Scaling up the provision of zinc and ORS could rapidly reduce child mortality for four reasons. Firstly, although it has been almost eight years since the World Health Organization recommended combination treatment with zinc and ORS,[3] few countries have implemented basic interventions to increase the currently low use of adjunctive zinc. Such interventions would include marketing zinc to caregivers and distributing it in large volumes through both public and private facilities.[4] Even limited additional investment in such interventions could have a large effect.

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Secondly, children with diarrhoea can be reached and given appropriate treatment easily. Most children currently obtain some form of treatment for diarrhoea, but most of them receive inappropriate treatments such as antibiotics and antidiarrhoeal agents.[11] Merely switching the treatments children receive, which is less challenging than trying to change caregivers' treatment seeking behaviour, could therefore drive substantial increases in ORS and zinc coverage.

Thirdly, and in contrast to treatments for malaria or pneumonia, effective treatment of diarrhoea does not need to be carefully targeted to selected children in whom a definitive diagnosis is made. A strategy of "flooding the market" with ORS and zinc—distributing them through all outlets where caregivers seek treatment—could be pursued safely,[12] with no threat of drug resistance, for example.

Lastly, a full course of zinc and ORS treatment costs less than $0.50 (£0.3; €0.38), and the marketing, training, and distribution necessary to drive product uptake could also be implemented at comparatively modest cost. Moreover, public funding for procurement of zinc and ORS in many countries would be further moderated by the fact that most treatment for diarrhoea is delivered through the private sector and paid for out of pocket.

Recent programmes in Bangladesh, Benin, India, and Nepal (summarised at www.zinctaskforce.org/programmatic-experiences) achieved rapid increases in zinc or ORS coverage over a short period, with relatively limited funds, by implementing targeted interventions that created demand for—and widespread supply of—the products. Although these countries still face obstacles to achieving high coverage with both treatments, such as entrenched preferences for antibiotics, these are small compared with the challenges that have been successfully overcome in recent years to scale up treatment for malaria and HIV.

What will it take to scale up the delivery of ORS and zinc for the treatment of diarrhoea worldwide? An essential first step is to focus attention on the problem. The United Nations will shortly be launching the Commission on Commodities for Women's and Children's Health to mobilise the health community to identify new ways to increase access to essential health products such as zinc and ORS. Furthermore, for the first time, the 10 countries with the highest burden of diarrhoea have developed ambitious plans to scale up coverage of effective treatments of diarrhoea and pneumonia.

Dedicated resources and practical operational support are now needed to translate those countries' plans into success. ORS and zinc treatment for diarrhoea should appeal to any donor seeking a high return on investment and the ability to have a rapid effect on child mortality. Contributions from early donors could be leveraged with other private and public contributions to realise a dramatic reduction in child deaths from diarrhoea and a further leap towards achieving the millennium development goals.

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BMJ blogs: Richard Smith: A proposal that could be implemented today and save 5000 lives

Physical activity for cancer survivors

Beneficial in the short term, but longer term outcomes are lacking

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In 2008, more than 12 million people worldwide were diagnosed with cancer (http://globocan.iarc.fr/). Because of improvements in early diagnosis and the introduction of more aggressive treatments over the past 20 years, cancer survivors are now living longer.[1] However, treatment often leads to a range of undesirable and debilitating adverse effects.

In the linked meta-analysis, Fong and colleagues assess the effects of physical activity after treatment for cancer on 48 separate health related outcomes.[2] The potential for exercise interventions to benefit survivors of cancer is a burgeoning area of research, and systematic reviews and meta-analyses have reported that exercise can reduce fatigue and improve functional outcomes and health related quality of life.[3-5] These reports have also called for larger trials that have a greater focus on study quality and adverse events and longer follow-up.

Fong and colleagues' meta-analysis reviewed 34 randomised trials (of which 22 were dedicated breast cancer studies) that assessed the effects of aerobic exercise, and in some studies also resistance training, after cancer treatment over a median duration of 13 weeks (range 3-60 weeks). Their meta-analysis aimed to surpass the methodological quality of previous reviews by assessing heterogeneity and publication bias, and they included nine new studies not included in the most recent update.[5] The results show significant low to moderate benefits of physical activity interventions on body mass index, body weight, fatigue, depression, peak oxygen consumption, peak power output, the six minute walk test, upper body strength, and health related function. Significant improvements were also reported for lower limb strength and right hand grip strength, but with significant heterogeneity between studies. Consideration of publication bias did not alter their conclusions.

The authors recommended that more research was needed in cancer types other than breast cancer. Although this may be true, the meta-analysis omitted three randomised controlled trials in men with prostate cancer that seem to meet the inclusion criteria.[6-8] This might have been because the search strategy was missing key nomenclature from exercise science ("aerobic" and "resistance" as forms of exercise training). In this respect, the search strategy differed from that of a previous systematic review.[3]

Despite the evidence of improved functional and quality of life outcomes, the key question remains: does habitual exercise reduce cancer specific mortality? Evidence from observational studies implies that increased exercise results in improved survival.[9-11] However, there are caveats: conclusions from these observational studies are limited by assumptions about causality and cannot rule out bias as a result of occult recurrence—physically active patients might reduce or stop their physical activity as a result of occult recurrence and subsequently be wrongly classified as currently sedentary at the time of death. None of the randomised trials in Fong and colleagues' review assessed mortality or cancer recurrence, but insulin-like growth factor was reduced by 12.0 ng/mL (95% confidence interval 23.3 to 0.5) in four studies of patients with breast cancer. The insulin-like growth factor axis might be a useful pathway to target in the treatment of breast cancer, but evidence of benefit is far from conclusive.[12] In the absence of reliable surrogates, data from randomised controlled trials with cancer specific recurrence and mortality outcomes would provide a more robust scientific basis for advocating habitual exercise to reduce the risk of dying from cancer.

Regular exercise benefits cancer survivors

So where do we go from here? There is clear evidence supporting the short term positive benefits of regular exercise in cancer survivors. However, evidence on longer term interventions is needed to assess possible adverse events and compliance rates. It is also unclear whether physical activity should be self directed or provided as part of a therapeutic intervention—is it sufficient to tell people with cancer to exercise more or should exercise be considered a deliverable treatment?

To know whether regular exercise improves cancer survival, more information is needed in several areas. Firstly, a dose-response curve for different cancers and patient groups—which identifies the frequency, duration, and intensity of exercise that confers benefit would be useful. Secondly, a better understanding of the cognitive determinants of behaviour change, how to support long term healthy lifestyle behaviours, and some appreciation of how the inability to comply with exercise recommendations might affect wellbeing is needed. Thirdly, it would be useful to know how exercise interventions fit into the debate on the availability and allocation of healthcare resources in an economic climate of shrinking healthcare budgets. These questions can be answered only through adequately powered long term randomised controlled trials, with cancer specific mortality or recurrence and cost effectiveness as primary outcomes. UK research infrastructure (such as the ProtecT network in prostate cancer) and expertise in both oncology and exercise science are excellent, so high quality studies are deliverable. National funding bodies need to provide financial support for well designed trials in a range of cancer populations.

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RESEARCH, p 17
ANALYSIS, p 22

The size of the benefit shown . . . and the low cost of enoxaparin provide sufficient evidence that enoxaparin is an attractive alternative to unfractionated heparin and should be considered for treatment of patients undergoing primary PCI in particular


SPL

Enoxaparin for anticoagulation in patients undergoing PCI

An effective and safe alternative to unfractionated heparin

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Recent decades have seen a dramatic reduction in short term and long term mortality after acute coronary syndromes, partly owing to the development of effective drug treatments and interventional strategies.[1] Outcomes after percutaneous coronary intervention (PCI) have improved remarkably because of rapid technical developments and systematic evaluation of periprocedural antithrombotic agents. However, experts agree that anticoagulation is also a crucial component of the management of acute coronary syndromes. The anticoagulants currently available for PCI include unfractionated heparin, bivalirudin, and enoxaparin.[2] The linked meta-analysis by Silvain and colleagues adds value by synthesising a large body of literature on the relative effectiveness and safety of the anticoagulant enoxaparin in PCI.[3]

In the 23 studies covered by the meta-analysis, most of the more than 30 000 patients had an acute coronary syndrome, and in all studies enoxaparin was compared with unfractionated heparin during PCI. Unfractionated heparin has long been considered a cornerstone of angiography and PCI, and it is widely used despite its pharmacological limitations, which include unpredictable effect and no evidence of a clear dose-effect relation. In fact, the use of unfractionated heparin in PCI still lacks strong scientific support, and no randomised trial has evaluated its efficacy.

Enoxaparin has a more predictable dose-effect relation than unfractionated heparin, and several trials have shown that it is at least as effective as unfractionated heparin in patients with acute coronary syndromes and a reduced risk of bleeding. However, few trials have specifically evaluated enoxaparin versus unfractionated heparin for patients undergoing PCI, and none has been powered to look at mortality.

Other newer anticoagulants have also been evaluated in randomised trials. In the OASIS-6 trial, fondaparinux was shown to have similar efficacy to enoxaparin, with a lower bleeding risk and a significantly reduced risk of death in patients with acute coronary syndromes.[4] However, in the context of primary PCI, fondaparinux was found to be potentially harmful, and the consensus is that it should not be used in patients undergoing primary PCI. Fondaparinux achieves a lower level of anticoagulation and, because it does not inhibit contact activation, a standard dose of unfractionated heparin is also needed during PCI in patients with acute coronary syndromes to reduce the risk of thrombotic complications and catheter thrombosis.

Bivalirudin has emerged as a predictable and effective anticoagulant with a short half life, and it is recommended over combined unfractionated heparin and a glucoprotein IIb/IIIa inhibitor for use in primary PCI.[2] The HORIZONS-AMI trial showed its superiority over the combination of unfractionated heparin and a glucoprotein IIb/IIIa blocker in patients undergoing primary PCI. Patients allocated to bivalirudin had a greatly reduced risk of bleeding and reduced all cause mortality and death from cardiovascular disease at 30 days,[5] which was maintained up to three years. However, a large proportion of patients received unfractionated heparin before randomisation, and about 10% received bailout glucoprotein IIb/IIIa blockers, which makes it difficult to evaluate the true effect of bivalirudin.

Silvain and colleagues found that death was reduced by 34% in patients who received enoxaparin compared with those who received unfractionated heparin, which was statistically significant. They also found that it reduced the risk of complications of myocardial infarction by 25% and that of risk of major bleeding events by 28% compared with unfractionated heparin. The results were consistent across subgroups, types of cohorts, and types of studies.

Are these results clinically meaningful? The overall benefit of enoxaparin over unfractionated heparin was driven by a reduction in death that may have been underpinned by lower rates of myocardial infarction and a reduced incidence of bleeding in the enoxaparin groups. The findings are in line with the those of two recent trials—the PLATO trial, which compared ticagrelor and clopidogrel in the treatment of acute coronary syndromes,[6] and the HORIZONS study, which compared bivalirudin and unfractionated heparin plus a glucoprotein IIb/IIIa blocker in primary PCI.[5 7] These suggested that, with a favourable balance between safety and efficacy, mortality can be significantly reduced. In the current study, the effect was greatest in patients with ST elevation myocardial infarction, who have a high short term risk of ischaemic complications and high risk of bleeding. These findings, if true, would motivate a strong recommendation for the use of enoxaparin over unfractionated heparin for PCI, independent of indication for the intervention.

The study has major limitations, however, as the authors acknowledge. The meta-analysis was based on reported outcome data from published and unpublished studies, rather than on aggregated data on individual patients. Observational non-randomised studies were included in addition to randomised trials, and the risk ratio was lowest in lower quality studies. Many of the randomised trials were designed to evaluate the efficacy of enoxaparin in broader patient cohorts not necessarily undergoing PCI so only subgroups of some of the trials were included in analyses. Furthermore, all cause mortality and death from cardiovascular disease were combined as a single end point and definitions of bleeding varied.

The ultimate question is whether this study provides stronger evidence for the use of enoxaparin rather than unfractionated heparin in patients undergoing PCI than the best of the included trials had already provided. Is the evidence now sufficient to warrant a change in guidelines for PCI? No large individual randomised trial has shown a significant reduction in mortality or important clinical end points for enoxaparin. However, the size of the benefit shown in the current large meta-analysis, the consistency of results in different subgroups, the agreement with findings from other large trials of new anticoagulants, and the low cost of enoxaparin provide sufficient evidence that enoxaparin is an attractive alternative to unfractionated heparin and should be considered for treatment of patients undergoing PCI in general, and primary PCI in particular.

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RESEARCH, p 16

In the UK, the Treasury's agenda for growth has set a demanding target for NHS trusts to recruit the first patient into a clinical trial within 70 days of "receiving a valid protocol"

A risk adapted approach to the governance of clinical trials

The research community needs to support a new initiative to reduce the regulatory burden

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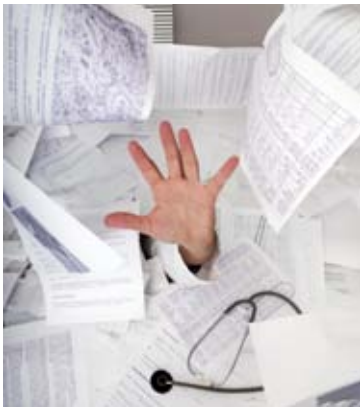
Over the past three to five years, there has been a barrage of criticism and dissent about the complex and bureaucratic systems that govern clinical research in the United Kingdom. This has culminated in sweeping recommendations, made in a report by the UK's Academy of Medical Sciences,[1] which have been endorsed by government.[2] However, many of these recommendations (such as revision of the European Union Clinical Trials Directive and establishment of a health research regulatory agency) will take time and require new legislation, so initiatives to tackle these problems now are timely and welcome.

One such initiative is the implementation, since April 2011, by the Medicines and Healthcare Products Regulatory Agency (MHRA) of a risk adapted approach to the regulation of clinical trials of investigational medicinal products.[3] This approach defines three types of trial according to the risks associated with the product—none (A), some (B), and markedly higher (C) than for standard medical care. A type A trial would typically investigate products used according to their licensed indications in the EU. A type B trial might be of a product, licensed in the EU, which is being assessed for a new indication, or perhaps at a different dosage. A type C trial would be of a product not yet licensed that continues to require full regulatory and safety monitoring. In a helpful supplementary clause, a trial may also be classified as type A if the drug is not licensed for the indication, but off-label use is well established in clinical practice, as is often the case in paediatrics and oncology.



Regulation has just got less overwhelming

The new approach to approval means that type A trials need only be notified to the MHRA and may proceed after 14 days from receipt of notification if the MHRA has not raised objections. For type A and some type B trials, the requirements to provide information, packaging, and labelling of the product can be based on what is already used in clinical practice, with minimal or no trial specific modifications. For type A trials, adverse event monitoring, a particularly onerous and costly requirement of the EU Clinical Trials Directive, will be modified in the light of the available safety data about the product. Similar adjustments apply to the requirements for record keeping, product storage, documentation, and inspection; the closer the trial protocol is to established clinical practice, the less should be the extra burden of trial specific procedures. By following established clinical practice, this approach specifically tries to redress the balance by moving away from perverse disincentives to research, encapsulated in the apocryphal comment, "I need permission to give a drug to half of my patients, but not to give it to them all."[4]

What has been the impact of this initiative? Trials sponsored by the drug industry are usually for licensing purposes and so are mainly type C, with some type B. However there are lots of questions about the effectiveness of drugs used in routine clinical practice that are dealt with by public funding bodies, and it has been estimated that more than 80% of investigational medicinal product trials funded under the UK's Health Technology Assessment and Efficacy, Mechanisms and Evaluation programmes are type A (T Walley, personal communication, 2011).

So has this initiative been greeted with widespread enthusiasm by the UK clinical research community, with a consequent flurry of notifications of type A and B trials to the MHRA? Unfortunately, it seems that this project is either not known about or has been treated with some suspicion by users, who may not quite believe that it is true. In the first three months of operation, more than half of the trials eligible for submission as notifications were submitted for full clinical trial authorisation (MHRA, personal communication, 2011). The National Institute for Health Research undertook a small survey of research teams, clinical trial units, and NHS trust research and development offices to gather comments and opinion about this new guidance.[5] It found that, although these approaches were generally welcomed, there was a clear reluctance to relax the highly developed processes associated with applications for clinical trial authorisation, which were well embedded in NHS research and development offices. This may relate to concerns about how this guidance might be implemented. There is uneasiness about a "no response" being interpreted as definitive approval, particularly from an agency associated with an adversarial approach to regulation.

These winds of change are blowing across other continents—the US Food and Drug Administration and the European Medicines Agency have stated that they wish to develop a regulatory approach that recognises the need to calibrate requirements to clinical trial risk.[6 7] In the UK, the Treasury's agenda for growth has set a demanding target for NHS trusts to recruit the first patient into a clinical trial within 70 days of "receiving a valid protocol."[2] The Academy of Medical Sciences' report says much about the need for "proportionality" and "symmetry" in the approach to regulation and decries the "prevailing risk averse culture" in some NHS trusts. Now that we have an important new initiative to remove an unnecessary regulatory barrier, the clinical research community needs to get behind this and support its implementation so that the UK can begin to step up to its government's ambition to "be a leader in proportionate regulation."[2]

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SEVENTH INTERNATIONAL CONGRESS ON
PEER REVIEW AND
BIOMEDICAL PUBLICATION
September 8-10, 2013, Chicago, Illinois

Peer Review and Biomedical Publication: call for research

Seventh International Congress, September 2013

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The primary aims of biomedical peer review are to select and improve research and other academic work for funding and publication by identifying and reducing bias and increasing the validity, quality, credibility, and worth of scientific reports. This remains a difficult balance.[1] Widespread advances in technology and communications have improved the speed, efficiency, and reach of scientific publication and have transformed the ways scientists, authors, reviewers, editors, clinicians, and the public interact with information and with each other. But these same advances also threaten the very nature of peer review and scientific publication. The need to critically evaluate the purpose, foundations, developments, and future prospects of this entire enterprise—from research proposal through and beyond publication—has never been stronger.

Since the first announcement in 1986, we have held six peer review congresses at four yearly intervals, with the aim of placing peer review and scientific publication under the same evaluation that science undergoes. The success of these congresses is clear from the stimulus they have given to new research into the processes whereby scientific work is funded, presented and disseminated, peer reviewed, edited, published, enhanced, accessed, and used by others to change practice, influence funding and policy decisions, inspire discourse and debate, and stimulate new research.[2-9] This progress has been measured in the increase in the number of abstracts submitted to each congress (from 50 for the first to more than 200 for each of the last two) and in Medline citations to peer review research (from 109 in 1994 to 382 in 2010).

We now announce the Seventh International Congress on Peer Review and Biomedical Publication to be held in Chicago, Illinois, 8-10 September 2013. This congress, organised by *JAMA* and the *BMJ*, will feature three days of presentations of original research. As with the previous congresses, the aims of the 2013 congress are to improve the quality and credibility of peer review and selection processes used by journals and funders; to help advance the quality, efficiency, effectiveness, and equity of biomedical publication; and to increase the dissemination of scientific information throughout the world. As before, we urge scientists, editors, publishers, funders, readers, and all who are interested in the processes by which science is funded and published to get going on their research.

In addition to the topics traditionally dealt with during the peer review congresses, such as the effects of peer review and editorial processes on the quality of scientific reporting,[10] abstracts summarising original high quality research on any aspect of scientific peer review, publication, and information exchange are welcome. The box provides examples of suggested topics. We also are eager to see new research on the technological advances and innovations that continue to influence all aspects of biomedical publication and the dissemination of scientific information. The increasing sophistication of research into these issues means that preference will be given to well developed studies with generalisable results (such as multijournal, prospective, multiyear trials and controlled studies). Retrospective studies, systematic reviews, bibliometric and other data analyses, surveys, and other types of studies will also be considered. Abstracts that report new research and findings will be given priority.

The deadline for submission of abstracts is 1 March 2013. Additional announcements and instructions for preparing and submitting abstracts will be available soon on the Peer Review Congress website (www.jama-peer.org).

Topics of interest for the Seventh International Congress on Peer Review and Biomedical Publication

Editorial and peer review decision making and responsibilities
- Mechanisms of peer review and editorial decision making used by journals and funders
- Evaluations of the quality, validity, and practicality of peer review and editorial decision making
- Quality assurance for reviewers and editors
- Editorial policies and responsibilities
- Editorial freedom and integrity
- Peer review of grant proposals

Research and publication ethics
- Ethical concerns for researchers, authors, reviewers, editors, publishers, and funders
- Authorship, contributorship, and responsibility for published material
- Conflicts of interest
- Research and publication misconduct
- Confidentiality
- Effects of funding and sponsorship on research and publication
- Influence of external stakeholders: funders, journal owners, advertisers and sponsors, policy makers, legal representatives, and the news media

Evaluations of and mechanisms for improving the quality of reporting
- Effectiveness of guidelines and standards designed to improve the quality of scientific publication
- Evaluations of the quality of print and online information
- Quality and reliability of data presentation and scientific images
- Quality and use of online supplemental content
- Quality and effectiveness of new forms of scientific articles

Models for peer review and scientific publication
- Online publication
- Open access
- Open peer review
- Data sharing and access
- Prepublication posting and release of information
- Postpublication review, communications, and influence
- Changes in readership and usage of peer reviewed published content
- Presentation, enhancement, and quality of scientific information in multimedia and new media
- Quality, use, and effects of publication metrics and usage statistics
- Quality and influence of sponsored supplements and related media, grey literature, and other forms of publication
- Quality and effectiveness of content tagging, mark-up, and structures
- The future of scientific publication

Dissemination of scientific and scholarly information
- Methods for improving the quality, efficiency, and equitable distribution of biomedical information
- New technologies that affect the quality, integrity, and dissemination of and access to biomedical information
- The impact of social networking and new media on science critique and dissemination

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At the heart of bridging the gap between knowing what interventions can improve health and delivering appropriate healthcare to patients is the delivery of efficacious interventions in ways that allow their implementation

Safe and effective healthcare in low and middle income countries

Research is needed into creating workable systems that can deliver and sustain interventions

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	World	Africa	Americas	Eastern Mediterranean	Europe	South east Asia	Western Pacific
Under 5 mortality per 1000 live births	65	142	18	78	14	63	21
Measles immunisation % coverage	81	73	93	83	94	75	93
Maternal mortality per 100 000 live births	400	900	99	420	27	450	82
Skilled birth attendant % of births	66	47	92	59	96	49	92
Contraceptive use % of women aged 15-49	62	24	71	43	68	58	83
HIV prevalence % of adults aged 15-45	0.8	4.9	0.5	0.2	0.5	0.3	0.1
Malaria mortality per 100 000 population	17	104	0.5	7.5	–	2.1	0.3
Tuberculosis treatment success rate %	86	79	82	88	67	88	92
Water % using improved sources	87	61	96	83	98	86	90
Sanitation % using improved facilities	60	34	87	61	94	40	62

On track | Insufficient progress | Off track

Health millennium development goal scorecard for World Health Organization regions. Adapted, with permission, from the WHO report[2]

Many resource constrained countries are unlikely to attain their millennium development goal targets by 2015,[1] despite major global efforts and much progress (figure).[2 3] For example, only 23 countries are currently estimated to be on track to achieve the target of a 75% reduction in maternal mortality.[4] In addition, the rate of new HIV infections continues to outpace the number of HIV positive patients who start treatment—for every five people newly infected with HIV only two begin treatment each year, and about 5.5 million people needing treatment for HIV in low and middle income countries still do not receive it.[5 6]

At the heart of bridging the gap between knowing what interventions can improve health and delivering appropriate healthcare to patients is the delivery of efficacious interventions in ways that allow their implementation. A statement from the African Academies of Science meeting in Accra, Ghana, in December 2009 pointed out that the lives of four million women, newborns, and children in sub-Saharan Africa could be saved each year if well established, currently available, affordable healthcare interventions could be implemented across the region.[7]

If we want to see a different kind of outcome, we have to change the system. Stakeholders need to be willing to change the status quo. A key question is, how can we change the conversation about improving health systems from just "where will we get more resources?" to include "what ideas can we harness to improve the system?" It is possible to improve the delivery of effective interventions in resource constrained settings. A recent study of 27 collaborative improvement projects that covered a range of global health priorities in 12 low and middle income countries found that 88% were able to achieve 80% compliance with evidence based standards and maintain it for more than a year of observation.[8]

What is needed is research into creating systems capabilities that will allow healthcare providers to continually adapt interventions so that they work for more patients in more contexts. Successful implementation of interventions depends on the recognition of the different epidemiological and contextual conditions that exist, and the interactions between them.[9]

The greater the scope and scale of improvement in healthcare systems, the greater the need for effective leadership to drive this change. The Salzburg Global Seminar, "Improving health care in low and middle income economies: what are the next steps and how do we get there?", to be held in Salzburg, Austria, from 22 to 27 April 2012 (www.salzburgglobal.org) will bring together 60 global health leaders from more than 20 countries to consider, among other things, how to sustain successful improvement efforts and strengthen health systems globally.

The capacity of low and middle income countries to change their healthcare systems in order to deliver better outcomes can be enhanced only by the involvement of high level government figures and health systems providers within the country. Change must involve care providers throughout the system, from highest level policy makers to practitioners at the sharp end of care delivery—in homes, where much of healthcare takes place—through primary healthcare centres, regional hospitals, and tertiary centres. Only by ensuring that simple, evidence based, high impact interventions reach all patients every time that they are needed can the millennium development goals be achieved, so that countries can avoid continuing to fall behind in health status.

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