An evaluation of oxygen systems for treatment of childhood pneumonia

[1†], [1†], [1], [2], [1], [2], [1], [1*]

Abstract

could save lives of up to 122,000 children from pneumonia annually. Following 12 CHNRI criteria, the experts expressed very high levels of optimism (over 80%) for answerability, low development cost and low product cost; high levels of optimism (60-80%) for low implementation cost, likelihood of efficacy, deliverability, acceptance to end users and health workers; and moderate levels of optimism (40-60%) for impact on equity, affordability and sustainability. The median estimate of potential effectiveness of oxygen systems to reduce the overall childhood pneumonia mortality was 20% (interquartile range: 10-35%, min. 0%, max. 50%). However, problems with oxygen systems in terms of affordability,

To provide a systematic approach to priority setting in international health, The Child Health and Nutrition Research Initiative (CHNRI) has developed a common framework to score interventions that aim to reduce disease burden [11-15] and implemented this methodology for research prioritization in a wide range of contexts [16-20]. This paper aims to use this framework in order to assess oxygen systems as a method for reducing paediatric mortality from pneumonia and to enable the comparison of oxygen systems to other relevant interventions (see also other publications in this series).

Me h ds

For this project, a two stage CHNRI framework was used to assess the utility of oxygen systems. The first stage involved a thorough literature review of predefined criteria for scoring interventions against childhood pneumonia, laid out by CHNRI [11-15]. Criteria were chosen to best reflect the key elements of any intervention that should be taken into account for priority setting and included: (i) answerability, (ii) cost of development, (iii) cost of product, (iv) cost of implementation, (v) efficacy and effectiveness, (vi) deliverability, (vii) affordability, (viii) sustainability, (ix) maximum potential for disease burden reduction, (x) acceptability to health workers, (xi9 acceptability to end users, and (xii) effect on equity. An illustration of the format of this approach is outlined in Figure 1.

The second stage of the framework involved an expert opinion analysis, which made use of the opinions of 20 experts in relevant fields and included five basic scientists, five public health researchers, five international policy makers and five pharmaceutical representatives. Of these representatives, those involved in policy and pharmaceuticals participated on the condition of anonymity, because of highly sensitive nature of their involvement in similar exercises.

CHNRI exercise – stage I: Identification and selection of studies

A literature search was performed for articles relating to oxygen therapy for paediatric hospital care in the developing world between 1950 and 2009. Using relevant keywords, we searched the databases of Pubmed, Pubmed Central, The Cochrane Library and those of developing countries including: LILACS - the Latin American and Caribbean Health Sciences Literature database, and IndMed - the Indian biomedical database. Titles and abstracts were reviewed for relevance. The references of relevant articles were screened to identify further useful articles.

A total of 315 articles were retrieved from PubMed, 862 from Pubmed Central, 22 from the Cochrane Library, 3 from IndMed and none from LILACS. After review of the titles of all articles and the references of those deemed useful, 96 full texts were located for inclusion in the study. Guidelines for oxygen use in developing countries were also located from the WHO website, and articles were taken from the International Union Against Tuberculosis and Lung Diseases. Details of the search and inclusion and exclusion criteria can be found in the Supplementary Table S1 in Additional File 1.

For sections covering Answerability and Efficacy, a separate search was conducted using relevant keywords, up to 2009

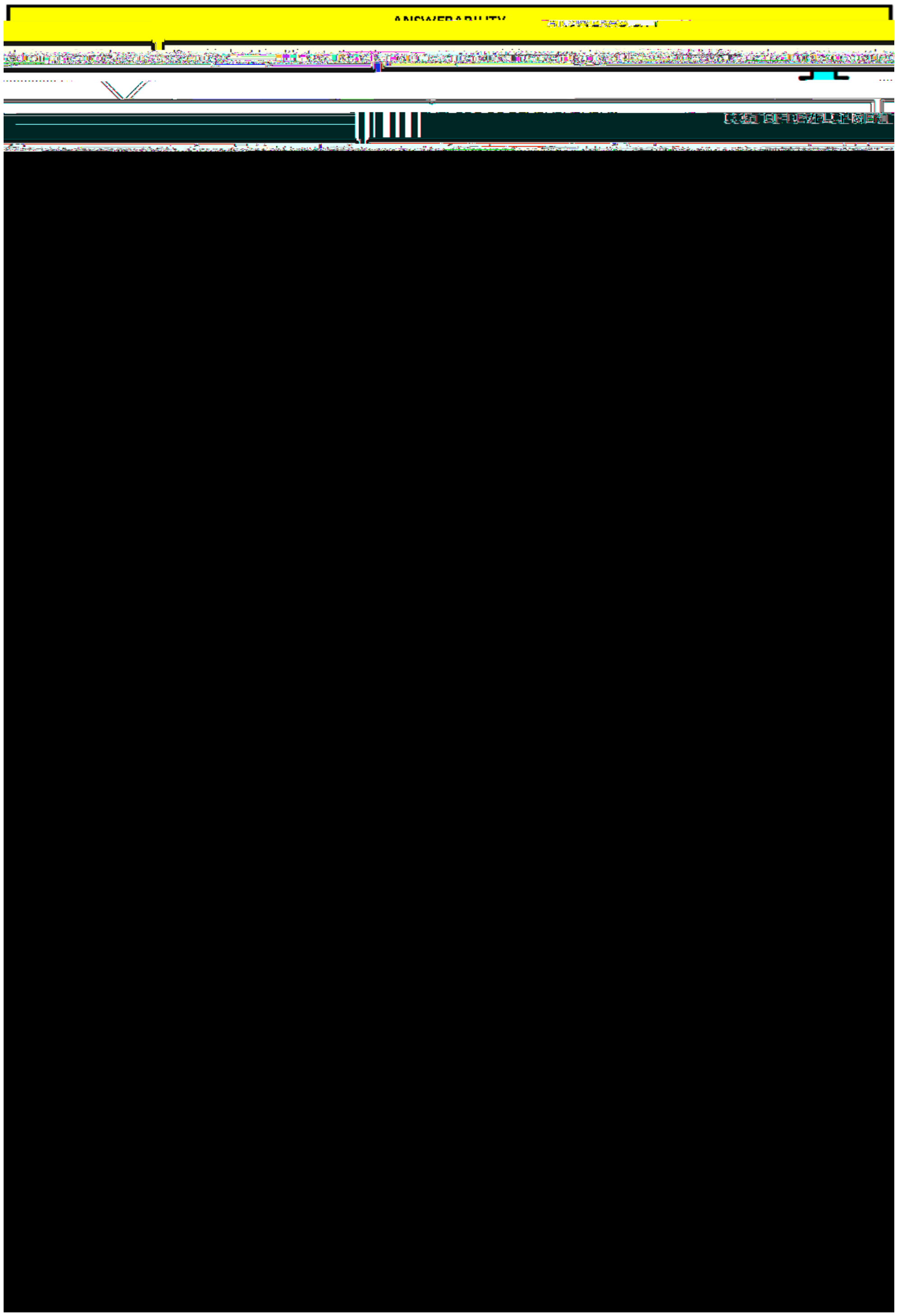

Fig e 1

had previous experience of working in developing country settings.

The experts met during September 2009 to conduct the 2nd stage of CHNRI expert opinion exercise. All invited experts discussed the evidence provided in CHNRI stage I, and then answered questions from CHNRI framework Supplementary Table S2 in Additional File 1. Their answers could have been "Yes" (1 point), "No" (0 points), "Neither Yes nor No" (0.5 points) or "Don't know" (blank). Their "collective optimism

transport in the lung almost immediately rendered oxygen as the standard treatment of "anoxemia" [22,23]. Due to the early and enthusiastic uptake of this treatment, empirical evidence for its benefit is virtually non existent. Any fully randomised controlled trial to establish the efficacy of oxygen therapy would require the withholding of oxygen from a control group, but once the theoretical basis for oxygen was understood, withholding oxygen in this way immediately became unethical.

Efficacy - The impact of the oxygen systems under ideal conditions

No controlled trial has ever measured the therapeutic impact of oxygen in humans directly, but it is possible to estimate the effect in other ways. For example, mortality rates from studies prior to the introduction of oxygen therapy can be compared with those afterwards [21]. Due to the variability in severity between pneumonia outbreaks, one must have an adequate indicator of disease severity to be enable a meaningful comparison.

In some early studies, arterial oxygen saturations were recorded without the administration of oxygen therapy [24]. The outcomes of these patients can be compared with those from a similar time period in which oxygen saturations were taken and oxygen therapy provided [21]. When adjusted for illness severity, this comparison shows a mortality rate of 39% amongst those treated with oxygen and 74% in those without [21]. Although this suggests a significant impact, the patient numbers in those studies were far too small to provide statistical significance - in the study of Stadie (1919) there were only 34 patients in non-oxygen group [24]. Furthermore, these studies all took place in the pre-antibiotic era (hence the very high case fatality ratios) and so are of questionable relevance to the situation today [25-28].

Studies on guinea pigs infected with streptococci support the benefit of oxygen therapy: for animals kept in air mortality was 94%, while it was 49% for animals kept in 50% oxygen [21]. This empirical evidence is insufficient to make estimates of efficacy for oxygen therapy, but the current clinical consensus strongly, and subsequent studies support the efficacy of oxygen therapy. There is a strong theoretical and experiential basis, founded on decades of beneficial experiences of oxygen therapy in clinical practice, such that it is now a universally accepted standard of care in the management of hypoxaemia. The incorporation into most treatment algorithms of severe pneumonia in the world throughout the last century further establishes the benefit of oxygen therapy [6,23,29,30]. Therefore, it can be safely assumed that oxygen is an important part of treatment in severe pneumonia.

Efficacy and effectiveness - The impact of oxygen systems in the population

The effectiveness of an oxygen system depends upon three stages in its delivery: the correct identification of patients requiring treatment; an effective method of administration; and adequate monitoring and eventual

The mortality rates of more than 11,000 children were compared from five hospitals before (2001-2004) and after (2005-2007) the implementation of such a system.

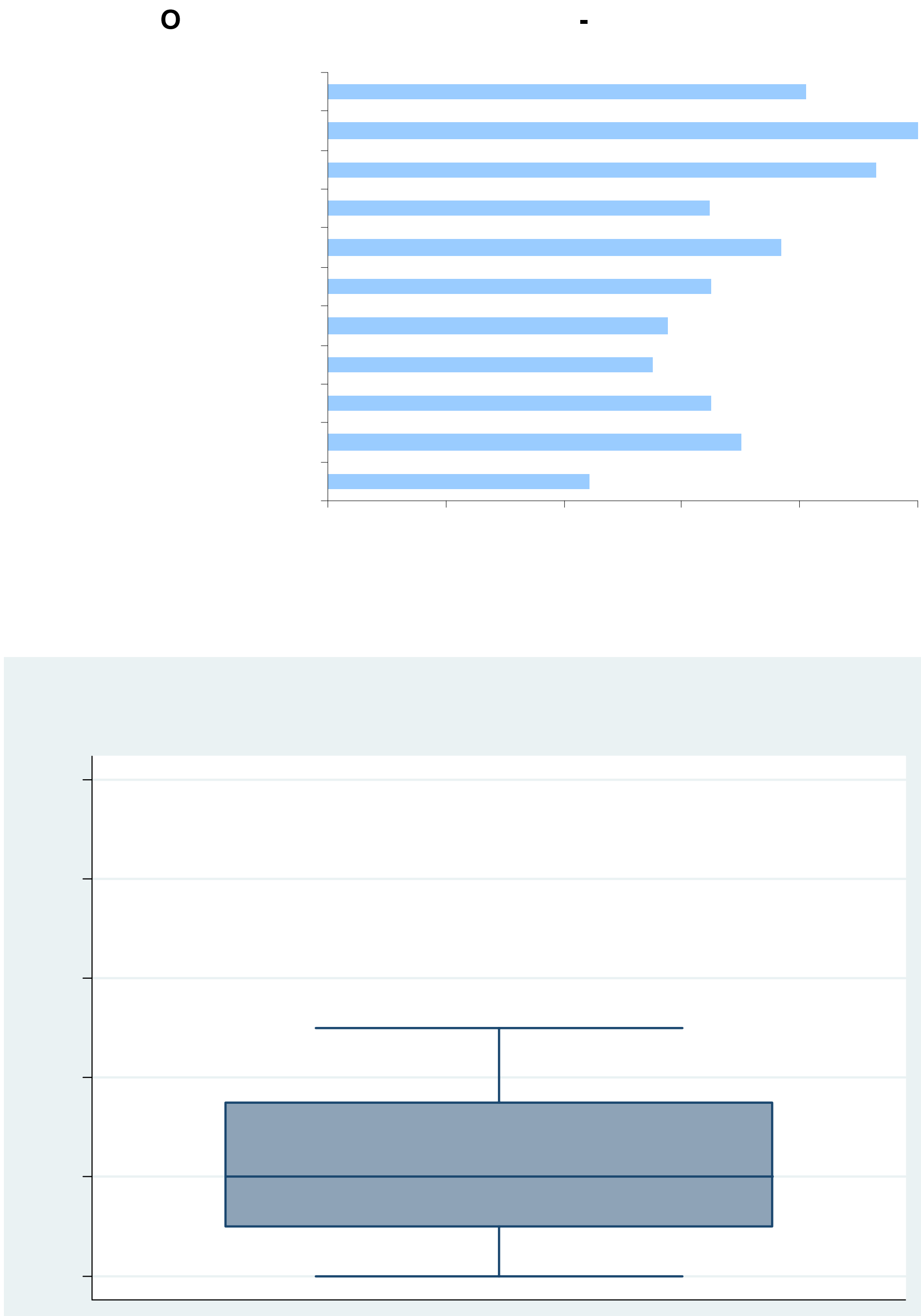

Fig e 3 – . ( ) .2 % (1 , %), . %, . %.

Papua New Guinea with some success [10,48,52]. Those machines that fulfil both international standards (under the International Organisation for Standardisation) have been found most effective and durable when put to hard use [48].

There are several concentrator models on the market that are mostly appropriate for developing countries; however official WHO/UNICEF specifications have not yet been published [53,54].

For the reasons of cost and accessibility, many researchers have advised the use of concentrators [21,48,52]. However, although electricity is reaching ever more remote regions of the world, it can be unreliable [21,48,52]. A study in Malawi showed that cuts of greater than 3 hours were frequent in hospitals [48]. Howie (2009) developed an options assessment tool to determine the most appropriate form of oxygen supply

Medical personnel should be well versed in the indications, monitoring and discontinuation of oxygen therapy systems in all regions, it could be expected to save between 68,000 and 122,000 lives. Because only one study was used to drive this global estimate, it should only be used as a rough guide and generalisation should be performed with caution before further evidence is gathered.

During our expert opinion analysis, the median maximum disease burden reduction of oxygen systems against childhood pneumonia was estimated at 20%, interquartile range of 10-35% (Figure 3).

Acceptability and equity

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