Profile of Published Cochrane Systematic Reviews in Child Health From Low- and Middle-Income Countries

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Objective: Setting priorities in health research is a challenge at the global and national levels. Use of evidence-based approach is uncommon and needs to be promoted in low-and middle-income countries (LMIC). We describe profile of Cochrane systematic reviews focussing on participation from LMIC. Methods: We searched six Cochrane review groups producing reviews relevant to child health in low- and middle-income countries for published Cochrane systematic reviews from 1 March, 2009 till 18 March, 2015 in the Cochrane Library. Results: A total of 669 Cochrane systematic reviews from six review groups were found. Low proportion of lead authors from low- and middle-income countries was found in 4 out of 6 review groups. About 50% of the reviews showed inconclusive evidence. 101/669 (15%) empty reviews were found needing more primary studies. Conclusions: The proportion of Cochrane authors from low- and middle-income countries is low. Capacity-building in systematic reviews and good quality primary research in these countries is warranted.

Keywords: Diarrhea, Evidence-based medicine, Health policy, Meta-analysis.

Priority-setting in health research is a challenge at the global, national and local levels. Most low- and middle-income countries (LMIC) do not have a systematic priority setting mechanism in place; occasionally, there are disease-driven or funder-driven approaches for prioritization, but these tend to be reactionary approaches. Strategic priority-setting is essential to promote and provide direction to research and innovation in a resource-constrained environment. There is no agreed best practice for priority-setting, though the US National Institute of Health (NIH), the World Health Organization (WHO) and the Child Health and Nutrition Research Initiative (CHNRI) have proposed a methodology [1-3]. Priority-setting using an evidence-based approach is uncommon and needs to be promoted in LMIC settings as it provides information and tools to help with priority setting [4].

Systematic reviews based on a number of primary studies, are placed at the top of the evidence pyramid [5], and are considered important for policy decision-making [6,7]. The knowledge emerging from systematic reviews assist health planners to set priorities for health research, implement proven interventions, and use limited resources judiciously. However, the information about systematic reviews addressing problems of LMIC is scant. We analyzed child relevant Cochrane systematic reviews [8] to find the publication of LMIC knowledge gaps and to prepare a list of primary research questions, for potential uptake in research agenda in LMIC.

Methods

We identified top six Cochrane Review Groups reported to have the maximum number of child-relevant systematic reviews in the Cochrane Library [6]. We used a working definition of child-relevant systematic reviews as one that intended to use children (0-18 yrs) as their populations, exclusively, or along with an adult population of both genders. An information specialist searched the databases of six Cochrane Review Groups (ranked in order of their contribution towards child-related SRs): (Acute Respiratory Infections [ARI]; Infectious Diseases; Neonatal; Cystic Fibrosis and Genetic Disorders; Airways; Developmental, Psychosocial and Learning Problems) from 1st March, 2009 till 18th March, 2015 in the Cochrane Library. We screened all systematic reviews from a LMIC perspective, noted their use of GRADE to assess the quality of evidence, and collected information on the conclusiveness of the review to find research leads for the future. We used the search strategy developed by Bow, et al. [6].
The records identified from the search were screened by two authors for inclusion. Any discrepancies were sorted out by discussion among authors to reach a final decision. An electronic data extraction form was developed in Microsoft Excel, pilot tested and refined for this purpose. The title, author information, objectives, methods, main results and authors’ conclusions sections of the included Cochrane reviews from the six Cochrane review groups were abstracted. We used the affiliations provided in the authors’ section of the review to judge whether the corresponding author belonged to a LMIC or not. Information on the country where the trials were conducted was extracted from the ‘Characteristics of included studies’ tables. To categorize the country of corresponding authors we referred to the human development index classification as high, medium or low as defined by the United Nations [9] and income level (high, upper-middle, lower-middle, or low income according to the World bank [10]). We used standard definitions to classify interventions as pharmacological, behavioral, physical environment-related, psychosocial, or other. Type of study design: RCTs or quasi-RCTs; number of trials in the reviews; types of intervention; total number and type of participants: children and/or adults; disease/condition being addressed, use of meta-analysis and evaluation of evidence as per GRADE was extracted from the ‘Data collection and analysis section’ of the reviews. Information about gap in knowledge was inferred from the ‘Overall completeness and applicability of evidence’ and ‘Quality of the evidence’ sections. If the reviews reported ‘inconclusive evidence’, we looked for any reasons cited.

Evidence as per Grading Recommendation Assessment Development Evaluation [11] was classified as low, moderate, or high. If GRADE was not used in a review, we examined and categorized the reviews as those that assessed allocation concealment, risk of bias, and used the Jadad scale [12].

We explored each variable separately in the data set using univariate method to summarize the range of values and also the central tendency, wherever possible. Analyses were carried out within the six Cochrane review groups individually and also overall.

**RESULTS**

We identified 669 Cochrane systematic reviews addressing research questions of importance to LMICs; most (176, 26.3%) from the Airways group (Table I).

Corresponding authors were from LMICs in 122 (18.2%) reviews, and 22.3% of included trials had been conducted in these countries.

**TABLE I**

<table>
<thead>
<tr>
<th>CRG name</th>
<th>Number of Corresponding authors from LMIC (n=122)</th>
<th>Number of systematic reviews included in reviews (n=669)</th>
<th>Trials included in reviews (n=296)</th>
<th>LMIC (n=149)</th>
<th>Trials included in reviews (n=122)</th>
<th>LMIC (n=560)</th>
<th>RCTs (n=344)</th>
<th>Inconclusive evidence due to small sample size (n=204)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airways</td>
<td>176</td>
<td>176</td>
<td>129</td>
<td>9</td>
<td>86</td>
<td></td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>Neonatal</td>
<td>155</td>
<td>129</td>
<td>129</td>
<td>15</td>
<td>129</td>
<td></td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>ARI</td>
<td>97</td>
<td>97</td>
<td>91</td>
<td>7</td>
<td>97</td>
<td></td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>Cystic Developmental disease</td>
<td>100</td>
<td>100</td>
<td>71</td>
<td>25</td>
<td>100</td>
<td></td>
<td>44</td>
<td>44</td>
</tr>
<tr>
<td>Infectious disease</td>
<td>63</td>
<td>78</td>
<td>60</td>
<td>15</td>
<td>78</td>
<td></td>
<td>48</td>
<td>48</td>
</tr>
</tbody>
</table>

Number of Cochrane Reviews after deleting empty (without any trials) reviews: ARI, acute respiratory infections; CRG, Cochrane Review Group; LMIC, low- and middle-income countries; RCT, randomized controlled trial.
As expected, Neonatal group reviews ($n=155$) had 100% neonatal participants, whereas the combined proportion of pediatric participants in the remaining five groups was 32.5% (167 out of 514). Use of meta-analysis in systematic reviews was quite common (61.3%); although, use of GRADE for assessing the quality of evidence was low (31.4%) and not uniform across groups (Table 1). The proportion of reviews that reported evidence to be conclusive also varied widely across groups (data not shown), and overall 396 (59.2%) reviews reported the evidence as insufficient.

Systematic reviews from all the six review groups cited not having sufficient number of randomized controlled trials (51.4%) and small sample size (30.5%) in included studies as the reasons for insufficient evidence. The median number of RCTs included in the reviews was 12, 9, 8, 8, 5 and 4 in Infectious diseases, Airways, Acute respiratory infections, Developmental, Neonatal and Cystic fibrosis groups, respectively. About 15% ($101$ out of 669) of systematic reviews across the six review groups were ‘empty reviews’ (29% in the Cystic fibrosis and Genetic diseases group; <1% in the ARI group) (Web Appendix 1).

**DISCUSSION**

Our study showed that the proportion of Cochrane authors from LMICs is low as compared to the high-income countries; very few RCTs conducted in LMICs were included in Cochrane reviews. Use of meta-analysis was observed to be high; but the use of GRADE by different groups was variable. Our study is limited to the top six Cochrane review groups, which produce approximately 50% of reviews including children as participants [6].

Our finding of low proportion of Cochrane authors from LMICs is in agreement with other publications reporting more than half of systematic reviews being produced in high-income countries. Other authors have reported that most primary studies are conducted in the US, UK, Canada with limited application to LMICs [13,14]. The reasons for inconclusive evidence reported by authors were: lack of sufficient number of trials included in the reviews and small sample sizes in the studies included, similar to report by Willhelm, et al. [15], who listed the common reasons for inconclusive reviews as small number of patients, insufficient data, insufficient methodological quality, and heterogeneity of studies. Reasons for lack of studies from LMICs in Cochrane reviews could be: lack of well conducted trials in LMICs/ or poor quality of trials leading to their exclusion from the review process [16]; absence of electronic databases prior to 1980s; non-publication of negative trials; stringent regulatory mechanisms; and lack of funding. Our study findings suggest that capacity-building in methodology of systematic reviews in India and other LMIC needs to be increased in order to bridge the existing gap. Systematic reviews with conclusive evidence should be used to prevent research waste (of repeated trials with same objectives). At the same time, systematic reviews with inconclusive evidence should prompt more research to reach conclusive answers. Our study showed that reaching conclusive evidence is difficult to achieve even while synthesizing evidence in systematic reviews.

**WHAT THIS STUDY ADDS**

- There is limited involvement of authors from LMICs in generating evidence from systematic reviews.
- A list of titles registered with Cochrane that were empty reviews (101) at the time of the study is presented for researchers to take up these topics as primary research.

**REFERENCES**


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Cochrane Airways Group


Cochrane Cystic Fibrosis and Genetic Disorders Group


Cochrane Neonatal Group


Cochrane Developmental, Psychosocial and Learning Problems Group


Cochrane Infectious Diseases Group


Cochrane ARI Group