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Providing oxygen to children in hospitals: a realist review

Hamish Graham,a Shidan Tosif,a Amy Gray,a Shamim Qazi,b Harry Campbell,c David Peel,d Barbara McPakee & Trevor Dukea

Objective To identify and describe interventions to improve oxygen therapy in hospitals in low-resource settings, and to determine the factors that contribute to success and failure in different contexts.

Methods Using realist review methods, we scanned the literature and contacted experts in the field to identify possible mechanistic theories of how interventions to improve oxygen therapy systems might work. Then we systematically searched online databases for evaluations of improved oxygen systems in hospitals in low- or middle-income countries. We extracted data on the effectiveness, processes and underlying theory of selected projects, and used these data to test the candidate theories and identify the features of successful projects.

Findings We included 20 improved oxygen therapy projects (45 papers) from 15 countries. These used various approaches to improving oxygen therapy, and reported clinical, quality of care and technical outcomes. Four effectiveness studies demonstrated positive clinical outcomes for childhood pneumonia, with large variation between programmes and hospitals. We identified factors that help or hinder success, and proposed a practical framework depicting the key requirements for hospitals to effectively provide oxygen therapy to children. To improve clinical outcomes, oxygen improvement programmes must achieve good access to oxygen and good use of oxygen, which should be facilitated by a broad quality improvement capacity, by a strong managerial and policy support and multidisciplinary teamwork.

Conclusion Our findings can inform practitioners and policy-makers about how to improve oxygen therapy in low-resource settings, and may be relevant for other interventions involving the introduction of health technologies.

Abstracts in عربي, 中文, Français, Русский и Espanol at the end of each article.

Introduction

Oxygen is an essential medical therapy that has been saving lives for over 100 years.1 Oxygen therapy is used not only for pneumonia and other primary lung diseases but also many other conditions that result in hypoxaemia, such as sepsis, severe malaria, status epilepticus, trauma, obstetric and neonatal conditions (respiratory distress, apnoea, asphyxia, sepsis), surgical care and anaesthesia. A systematic review estimated that, globally, hypoxaemia affects about 13% of children admitted to hospital with pneumonia, about 20% of sick neonates and 10–15% of children admitted with conditions such as malaria, meningitis or convulsions.2 Given that hypoxaemia is a major risk factor for death,2,4 oxygen therapy is important for improving child health outcomes.

Effective oxygen therapy requires prompt and accurate detection of hypoxaemia and appropriate administration of oxygen, combined with good clinical evaluation and management of the underlying condition.3 Improvements in the technology and affordability of pulse oximetry — the standard method for detecting hypoxaemia — are enhancing its accessibility for hospitals in low-resource settings.1 Oxygen may be supplied by oxygen cylinders, oxygen concentrators or larger oxygen plants, each of which have unique advantages and disadvantages, particularly when used in hot, humid or dusty environments.1,5 The World Health Organization (WHO) has produced guidelines on the clinical use of oxygen4–6 and oxygen equipment.7

Despite these advances, the availability of pulse oximetry and oxygen supplies remains limited in regions of the world where they are most needed.10 Furthermore, workforce limitations and health-system failures limit the ability to maintain, sustain or effectively use oxygen even when it is available.1 A solution to this must be multifaceted, and is likely to be context-specific.

We aimed to identify and describe interventions to improve oxygen therapy in hospitals in low-resource settings, and to determine the factors that contribute to the success or failure of interventions in different contexts.

Methods

We used a realist review approach11 to study not only whether oxygen therapy interventions work, but also how and why complex programmes work in particular contexts and settings. Realist review is a theory-driven systematic review method that involves identifying key mechanistic theories about how projects might work, searching the evidence about project implementation and impact (including variability between contexts), and then testing the evidence with respect to the theories.11–14 Our review was prospectively registered on the PROSPERO register of systematic reviews (CRD42015032405).

Identification of theories

We made a preliminary scan of the literature to identify potential theories to explain how improved oxygen therapy systems could impact on clinical outcomes. This resulted in a list of candidate theories, each describing a mechanism through which the intervention influences particular outcomes in particular contexts. We consulted key experts and stake-
holders, including interviewing the authors of five large-scale oxygen therapy projects. Interviews were recorded and transcribed for accuracy, but were not formally analysed and were used only to assist in identifying emerging themes.

**Search strategy**

We made a systematic search of online databases (MEDLINE®, Embase®, CI-NAHIL, AIM, LILACS, the Index Medicus for the Eastern Mediterranean Region, the Index Medicus for South-East Asia Region, the Western Pacific Region Index Medicus, CAB Global Health, Health Systems Evidence, PubMed® (for e-publications) and Google Scholar (first 500 citations)) on 10 August 2016. We searched variations of keywords “child,” “oxygen concentrator,” “oxygen cylinder,” “oxygen therapy,” “oxygen delivery,” “oxygen administration” and “developing country” (MEDLINE® search; Box 1). We also searched websites (e.g. WHO and the International Union Against Tuberculosis and Lung Disease), contacted oxygen therapy experts and reviewed the reference lists of included studies to identify additional published and unpublished studies.

We included any evaluation of an improved oxygen therapy system involving a hospital in a low- or middle-income country (World Bank definitions at the time of the study). An improved oxygen therapy system included introduction of an improved oxygen source (oxygen concentrator, cylinder or plant) with or without: other equipment (e.g. pulse oximeters, oxygen delivery devices); education (e.g. training materials or visits); health-system or quality improvement activities (e.g. financing, supply chain, supervision). Two investigators independently reviewed the titles, abstract and full-text of the studies for inclusion, with the adjudication of a third reviewer where consensus could not be reached.

We assessed the quality of each study on two criteria: relevance (i.e. addresses the candidate theories about how improving oxygen systems lead to improved clinical outcomes); and rigour (i.e. provides credible data to reach a conclusion). Most studies contributed to the testing of a particular theory more than others. We only reported results where there were credible data.

To assess the quality of studies reporting clinical outcomes we used the Effective Public Health Practice Project quality assessment tool for quantitative studies.15,16

**Data extraction and synthesis**

We used a data collection form adapted from the Cochrane Effective Practice and Organisation of Care (EPOC) group17 and process evaluation18 tools. For each project we extracted data on the theory (implicit or explicit); context (e.g. facility characteristics, oxygen capacity and needs); interventions (using Cochrane EPOC categories); processes (e.g. quality, fidelity to the intended beneficiaries); and outcomes (clinical, quality of care, cost, equipment function).

The data were recorded in a series of tables, enabling possible mechanistic theories to be explored within individual projects and between projects. After repeatedly exploring the partially developed theories, we aggregated them into major theoretical themes. We then analysed the available data to support, negate or refine the theories, thereby identifying key factors affecting the success of projects.

**Results**

Of 2433 records screened, 72 full-text articles were assessed for eligibility (Fig. 1). We included 45 papers describing 20 projects involving an intervention(s) to improve oxygen therapy systems, from 15 countries. Data from two of the projects have not been published yet (Gray et al., Centre for International Child Health (CICH), Parkville, Australia, unpublished data, 26 January 2017 and Morpeth M et al., CICH, Parkville, Australia, unpublished data, 26 January 2017) and will hereafter be referred to as Gray et al. and Morpeth et al. Most projects (15) used non-comparative evaluation methods, one project used a contemporaneous control and four used a historical control.

The earliest projects (in the 1980s) introduced oxygen concentrators primarily for anaesthetic purposes, and evaluated their technical function and cost implications (Table 1). Since the late 1980s, seven large-scale paediatric oxygen projects have been evaluated, involving complex interventions targeting technicians, clinicians and often administrators and policy-makers (Table 2). Recently, four projects have explored the utility of improved power supplies for oxygen concentrators, including solar power systems (Table 1 and Table 2). Four large-scale effectiveness studies demonstrated reduced inhospital mortality from pneumonia and other hypoxaemic conditions among children aged <5 years follow-
<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Context</th>
<th>Intervention(s)</th>
<th>Data source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1982</td>
<td>Democratic Republic of the Congo</td>
<td>Setting: single, remote mission hospital. Challenges: limited oxygen cylinder supply (logistic and cost barriers); Assets: reliable hydroelectric power supply. Aims: to achieve more reliable and affordable oxygen supply for anaesthetic use.</td>
<td>Equipment: one oxygen concentrator (Mountain Medical). Clinical training: not described.</td>
<td>A brief report provided limited data on equipment function and its various clinical uses.</td>
</tr>
<tr>
<td>1986</td>
<td>Barbados</td>
<td>Setting: single referral hospital. Challenges: limited oxygen cylinder supply (logistic and cost barriers); low technician capacity; no routine maintenance. Aims: to achieve more reliable and affordable oxygen supply for general use.</td>
<td>Equipment: one large oxygen concentrator (Rimer-Alco, 13 L/min) connected to a compressor and fed into a piped oxygen supply system. Clinical training: not described.</td>
<td>A historical review of anaesthesia services provided data on equipment function, cost and oxygen demand.</td>
</tr>
<tr>
<td>1986</td>
<td>Ghana</td>
<td>Setting: single referral hospital (Korle Bu hospital). Challenges: frequently interrupted oxygen cylinder supply (logistic and cost barriers). Aims: to achieve more reliable oxygen supply for general use.</td>
<td>Equipment: one large oxygen concentrator (Linde) with oxygen reservoir, fed into a piped oxygen supply system. Maintenance: provided by local agents of manufacturer. Clinical training: not described.</td>
<td>A retrospective evaluation reported on equipment function and oxygen access.</td>
</tr>
<tr>
<td>1993</td>
<td>Nepal</td>
<td>Setting: 1 government referral hospital and 1 private hospital in Kathmandu. Challenges: limited oxygen cylinder supply (logistic and cost barriers); high costs to patients, resulting in prioritization and limited use of oxygen. Assets: skilled staff. Aims: to achieve more reliable and affordable oxygen supply for neonatal use.</td>
<td>Equipment: two oxygen concentrators (DeVilbiss). Clinical training: not described.</td>
<td>A retrospective evaluation reported on equipment function and use and on clinical outcomes.</td>
</tr>
<tr>
<td>1993</td>
<td>Nigeria</td>
<td>Setting: single neonatal ward in referral hospital. Challenges: limited oxygen cylinder supply (logistic and cost barriers); high costs to patients, resulting in prioritization and limited use of oxygen. Assets: skilled staff. Aims: to achieve more reliable and affordable oxygen supply for neonatal use.</td>
<td>Equipment: one oxygen concentrator (Puritan-Bennett); car battery for back-up power. Maintenance: informal, supervised by project lead. Clinical training: informal (details unspecified), including use of pulse oximetry and delivery devices to give oxygen to preterm neonates. Financial: small-scale oxygen insurance scheme set up to distribute cost burden, with small contribution from all patients.</td>
<td>A retrospective evaluation reported on concentrator use, function and cost.</td>
</tr>
<tr>
<td>1998</td>
<td>Gambia</td>
<td>Setting: single rural mission hospital. Challenges: severe limitations in electricity (available for only a few hours at night using generator); limited oxygen cylinder supply (logistic and cost barriers). Assets: prior experience with solar power; established equipment maintenance system. Aims: to provide reliable power to enable uninterrupted use of oxygen concentrator.</td>
<td>Equipment: one oxygen concentrator (unspecified); hybrid solar power supply (24 × 90 W PV panels; 6 × 150 Ah 12 V batteries). Maintenance: 1-day maintenance training for staff (details unspecified), plus detailed maintenance schedule. Clinical training: not described. Supervision: visits by project team every 3-6 months.</td>
<td>A retrospective evaluation reported on equipment function and cost implications.</td>
</tr>
</tbody>
</table>

(continues . . )
an intervention to improve oxygen therapy (Table 3). Due to heterogeneity in reported outcomes and insufficient comparable data, a meta-analysis was not possible.

Overall, projects used a variety of strategies to improve oxygen therapy. We identified five themes (Box 2), each containing multiple mechanisms that explain how interventions to improve oxygen therapy work (or not) in different contexts. We tested these theories using data from all included projects and identified key factors reducing or enhancing the efficacy of oxygen therapy projects (Box 3).

### Oxygen access

Increasing the availability of oxygen therapy to patients was an implicit aim in virtually all the intervention projects we studied, but few studies evaluated it. Hospitals in most projects had some access to oxygen cylinders (Gray et al.),21,22,24–26,35 or concentrators before the intervention, but supply was limited by depletion of cylinders (which are costly and difficult to refill) and broken equipment. The only baseline data on oxygen availability to patients were from Papua New Guinea, where oxygen was available for 326 (87%) of 375 children who had hypoxaemia on admission.36

Two large-scale projects reported increased access to oxygen cylinders or concentrators compared with the baseline.16,48,50 Most projects reported increased oxygen use (more patients given oxygen or greater volume of oxygen provided to patients; Morpeth et al.)19,24,25,28,34–37,48,49,53 while some reported fewer referrals for hypoxaemia (Gray et al.),26,34 and decreased dependence on oxygen cylinders (Gray et al.),21,22,24–27,34–36,49 Data from Papua New Guinea suggested that hospitals with poorer access to oxygen (and pulse...
Table 2. Large-scale interventions to improve oxygen therapy systems in low-resource settings, identified by a systematic literature search

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Context</th>
<th>Intervention(s)</th>
<th>Data source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1986</td>
<td>Malawi</td>
<td>Setting: all government hospitals nationally. Challenges: limited oxygen cylinder supply (logistic, cost and supplier barriers); variation in anaesthetic equipment; minimally trained anaesthetic technicians; weak maintenance systems; lack of spare parts and tools. Aims: to achieve uniform oxygen-anaesthetic practice nationally.</td>
<td>Equipment: 104 oxygen concentrators (DeVilbiss) and 44 specially-designed anaesthetic machines (S&amp;W). Maintenance: three maintenance centres; spare parts; tools. Two technicians were trained in Denmark for 3 months; six were trained locally by project team. Supervision: 6 monthly field visits by technicians from project centre, with retraining. Clinical training: not described. Partners: Malawi government and DANIDA.</td>
<td>Two retrospective technical studies reported equipment use and function, and cost data.13,14</td>
</tr>
<tr>
<td>1994</td>
<td>Egypt</td>
<td>Setting: 13 district hospitals in upper Egypt. Challenges: limited oxygen cylinder supply (logistic and cost barriers). Aims: to improve oxygen access and thereby reduce childhood pneumonia deaths.</td>
<td>Equipment: 22 oxygen concentrators (DeVilbiss; Healthdyne; Puritan-Bennett). Maintenance: multidisciplinary team approach. Basic equipment training was given to a nominated doctor in each facility, who supervised use and care of equipment and completed a logbook. Training was by the project team, including an anaesthetist. Different, detailed training was given to engineers at project centre who visited every 3–4 months (re-training after 1 year). Clinical training: not described. Supervision: central coordination team conducted regular field visits. Partners: Egypt health ministry’s Child Survival Project with WHO and USAID.</td>
<td>A prospective evaluation reported on concentrator use and function at 12 months, and on general user feedback.35</td>
</tr>
<tr>
<td>2000</td>
<td>Malawi</td>
<td>Setting: 25 district and regional government hospitals. Challenges: low baseline clinical knowledge and skills of staff; poor access to oxygen; lack of guidelines; poor clinical documentation. Assets: initial sites were chosen if they had a functioning programme for management of acute respiratory infection or integrated management of childhood illness, and commitment from the district health office. Aims: to improve pneumonia case management and thereby reduce childhood pneumonia deaths. This was based on the theory that improved clinician capacity (skill and knowledge), together with a system that enables clinicians to follow guidelines (medications, equipment, support), would lead to improved quality of care (as per guidelines) and thus better clinical outcomes.</td>
<td>Strategy: based on the International Union Against Tuberculosis and Lung Disease (The Union) health-service delivery model, including political commitment; standardized diagnosis and treatment; clinical training; improved medication access; and recording and reporting child pneumonia outcomes. Improved oxygen systems were added to the initial plan, starting in 2002. Guidelines: an inpatient recording form for every child with pneumonia was introduced as both a clinical algorithm and a data collection form. Equipment: 26 oxygen concentrators (DeVilbiss), with flow-splitters in paediatric wards and 2–3 years’ supply of spare parts. Clinical training: comprehensive pneumonia-care training, including oxygen-related training, for nurses and medical officers (5-day course). Training was by project team at central location. Coverage was high (about 25% of health workforce), but follow-up in-service training failed. Maintenance: trained technicians from health ministry. Intention was to provide 3-monthly maintenance visits, but few visits were conducted, activities were not documented, and spare parts were lost.37 Partners: Malawi health ministry, The Union, the Bill &amp; Melinda Gates Foundation and the Government of Scotland.</td>
<td>A nonrandomized field trial38 reported clinical outcomes. Long-term clinical and quality of care data were obtained from retrospective audits39,40 and qualitative studies,41–44 and provided by various reports19,35 and a thesis.36 An external evaluation37 and a cross-sectional assessment of concentrators39 provided equipment data.</td>
</tr>
</tbody>
</table>

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Improving oxygen therapy for children

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Context</th>
<th>Intervention(s)</th>
<th>Data source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>Gambia</td>
<td>Setting: four hospitals and health centres. Challenges: limited oxygen access. Assets: well-trained biomedical engineers. Aims: to achieve more reliable and affordable oxygen supply for paediatric use.</td>
<td>Equipment: 27 oxygen concentrators (Airsep) introduced over 7 years, with uninterruptable power supply. Pulse oximetry was introduced later. Maintenance: computer-based record system, 3-monthly visits by trained biomedical engineers; preventive maintenance protocol for users. The maintenance structure was effective, with maintenance visits occurring 3–4 times annually (even to the most distant facilities) and accurate logbook completion for 8 years of follow-up. Clinical training: not described. Partners: the Medical Research Council of the Gambia.</td>
<td>An audit(^{69}) and implementation report(^{10}) provided data on equipment use and function, cost and user feedback. Data on context came from needs analyses.(^{52,71})</td>
</tr>
<tr>
<td>2005</td>
<td>Papua New Guinea</td>
<td>Setting: five district and provincial hospitals in the highlands and coastal areas of Papua New Guinea. Challenges: limited oxygen access. Pneumonia was the leading cause of child mortality in the country, and the burden of disease was particularly high in the remote, high-altitude, highland villages. Assets: adequate power supply; motivated senior staff. Aims: to improve quality of pneumonia care and thereby reduce childhood pneumonia deaths. This was based on principles of quality improvement and participatory development with minimal external support.</td>
<td>Equipment: 15 oxygen concentrators (Airsep) in paediatric wards, with flow-splitters and pulse oximeters (and careful procurement of equipment, tools and adequate spare parts). Pulse oximetry (with user-training) was introduced 1 year before intervention, to build skills and awareness about hypoxaemia and oxygen therapy, and to obtain accurate baseline data. Clinical training: for nurses and medical officers, on-site by local paediatricians, focusing on pneumonia and the use of oxygen. Guidelines: clinical guidelines and maintenance protocols. Supervision: multidisciplinary team provided oversight at national level, with regular support visits to participating hospitals; participatory data collection, analysis and action involving hospitals and health ministry. Other: emphasis on patient-centred care; attention to the work environment (e.g. high-dependency areas for grouping the sickest children together). Partners: the Medical Research Council of the Gambia, the National Department of Health and WHO.</td>
<td>A before-and-after effectiveness study(^{61}) reported clinical outcomes and cost-effectiveness. Project evaluations(^{30,31}), and hypoxaemia studies;(^{32}) also provided baseline epidemiological and contextual data. Two modelling papers reported cost data.(^{32,58})</td>
</tr>
<tr>
<td>2011</td>
<td>Lao People's Democratic Republic</td>
<td>Setting: 10 district hospitals across five provinces. Challenges: hospitals operated on a user-pay system, and cost of oxygen was seen as the major barrier to patient access. Assets: adequate power supply; support from hospital leadership (10 control hospitals were from the same province). Aims: to provide a more cost-effective oxygen solution to hospitals, enabling hospitals to reduce the cost burden on patients; to enable clinicians to provide oxygen to all children and neonates who need it, and to achieve better clinical outcomes.</td>
<td>Equipment: 3–6 oxygen concentrators (Airsep) per hospital with pulse oximeters and a Sureflow flowmeter assembly (Airsep), enabling individual titration of oxygen from a single concentrator to up to five patients simultaneously; nasal prongs; and an oxygen analyser to test the concentrator oxygen purity. Maintenance: training for central and provincial engineers and a technician from each hospital was provided by biomedical engineer at a central location. Clinical training: 2-day practice-based training at each hospital by project team, including a paediatrician. Training material was translated into Lao. Financial: through a collaborative process, all hospitals decided to make oxygen from concentrators freely available to all patients. Supervision: supervision visits by coordinators (at 3, 12 and 24 months). Partners: Lao People's Democratic Republic health ministry, WHO and Japanese government.</td>
<td>A controlled before-and-after study reported on clinical outcomes; quality of care; and implementation data (Gray AZ et al., CICH, unpublished data, 26 January 2017; Morpeth M et al., CICH, unpublished data, 26 January 2017). Project reports provided additional contextual and implementation data.(^{50–41})</td>
</tr>
</tbody>
</table>


Notes: Large-scale projects involved complex interventions targeting technicians, clinicians and often administrators and policy-makers. Equipment manufacturers: Airsep, Buffalo, United States of America (USA) (subsidiary of Chart Inc.); DeVilbiss Healthcare, Mannheim, Germany (subsidiary of Medical Depot Inc.); Healthdyne, Marietta, USA; Longfei, Yueqing, China; Nellcor Puritan Bennett, Boulder, USA (subsidiary of Medtronic plc.); Simonsen & Weel, Albertslund, Denmark.

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oximetry) at baseline achieved greater reductions in pneumonia case-fatality rates post-intervention than hospitals with reasonable access at baseline.31,56

We identified three major determinants of oxygen availability: (i) equipment; (ii) maintenance; and (iii) affordability.

**Equipment**

Although the provision of quality, user-friendly equipment is necessary for an improved oxygen therapy system, it is not easy to achieve. Baseline data from several projects documented poor quality and broken equipment that had often been donated by international donors but did not suit the needs of its users or the environmental conditions29,46–50,53,59 Studies consistently reported the importance of procuring oxygen concentrators that were proven to work in hot and humid conditions. This was based on observations of maintenance problems and premature equipment failure when projects provided untested concentrators or used a variety of concentrator types (Gray et al.).3,24,35,37,46 Some projects used flow-splitters to share oxygen between multiple patients (users would change the size of outlet nozzles to control flow rates), but these were frequently malfunctioning (e.g. missing plugs, blocked tubing) or used incorrectly, resulting in no gas flow to patients.29,48 This led to the development of flowmeter assemblies, allowing individual titration of gas to multiple patients without changing plugs or connections (Gray et al.).3,24

Pulse oximeters were not used in most of the oxygen projects before 2005. Where pulse oximeters were used, they were valued as both a diagnostic aid (determining which children require oxygen therapy) and therapeutic aid (giving staff and patients confidence in oxygen therapy; Gray et al.).3,49,52,56 Limited data suggested that the introduction of pulse oximetry can improve oxygen use and reduce pneumonia case fatality rates, even with suboptimal oxygen access.54

Oxygen delivery devices varied between projects. Nasal prongs were easiest for health-care workers, and some projects reported confusion when multiple options were provided to inexperienced users.24,35,37,46 Some projects used flow-splitters to share oxygen between multiple patients (users would change the size of outlet nozzles to control flow rates), but these were frequently malfunctioning (e.g. missing plugs, blocked tubing) or used incorrectly, resulting in no gas flow to patients.29,48 This led to the development of flowmeter assemblies, allowing individual titration of gas to multiple patients without changing plugs or connections (Gray et al.).3,24

Power supplies were a major factor limiting the use of oxygen concentrators.49,51,53,57 Uninterruptable power supply systems are useful if power outages are infrequent (e.g. less than daily) and brief (e.g. less than 20 minutes), but not if power failures are frequent or prolonged.54 Solar power with battery storage is feasible, but requires experienced technicians and quality products.26,30,31

**Maintenance**

For users and technicians to provide reliable equipment maintenance and repair they need the capacity (knowledge and skills); opportunity (transport and access to spare parts); and motivation (role recognition and anticipated benefit). The Gambia provided a positive case study involving: well-trained biomedical engineers; a schedule for preventive maintenance; spare parts; electronic work orders (facilitating access to engineers); and a maintenance protocol for users.49,50 They reported excellent long-term equipment function: 21/27 (78%) of oxygen concentrators working at 8-year follow-up; and minimal equipment down-time (5.2% of total cumulative hours in service).39 They identified problems

<table>
<thead>
<tr>
<th>Country, year</th>
<th>Total sample size No.</th>
<th>Before intervention</th>
<th>After intervention</th>
<th>Absolute risk reduction, %</th>
<th>Unadjusted RR or OR (95% CI)</th>
<th>EPHPP study quality rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lao People’s Democratic Republic, 2011</td>
<td></td>
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<tr>
<td>Pneumonia deaths</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Control group</td>
<td>1355</td>
<td>712</td>
<td>12 (1.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention group</td>
<td>1412</td>
<td>711</td>
<td>19 (2.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malawi, 2000</td>
<td></td>
<td></td>
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<tr>
<td>Pneumonia deaths</td>
<td>47228</td>
<td>389</td>
<td>73 (18.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papua New Guinea, 2005</td>
<td></td>
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<td></td>
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<tr>
<td>Pneumonia deaths</td>
<td>11291</td>
<td>7161</td>
<td>356 (5.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other deaths</td>
<td>21044</td>
<td>13354</td>
<td>778 (5.8)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sierra Leone, 2013</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>All-cause deaths</td>
<td>1822</td>
<td>920</td>
<td>34 (3.7)</td>
<td></td>
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</tr>
</tbody>
</table>

CI: confidence interval; EPHPP: Effective Public Health Practice Project; NA: not available; OR: odds ratio; RR: relative risk.

a Morpeth M et al., CICH, unpublished data, 26 January 2017.

b Relative risk.

c Data from year 2000. Malawi case-fatality rate in 2000 was derived from only 3 months of data; the rate for all of 2001 was 13.3%.

d Data from year 2005.

e Odds ratio. Malawi investigators used stepped-wedge methodology. The chronological data did not represent actual before-and-after intervention phases; the odds ratio was derived using unadjusted statistical methods.

Notes: Studies were restricted to children aged < 5 years admitted to the paediatric ward. All studies used a before-and-after intervention study design.
Box 1. MEDLINE® search for publications on interventions to improve oxygen therapy systems in low-resource settings

Search run on 10 August 2016

1. (newborn* or neonat* or infan* or preschooler* or pre-schooler* or toddler* or child* or adolescen* or pediatric* or paediatric*).af.

2. (sd or ec or is or mt or th).fs.

3. developing countries/

4. (austere or (low adj2 resource*) or (limited adj2 resource*) or transitioning econom* or emerging countr* or developing countr* or ("low income" or "middle income" or "low to middle income") and countr*) or "third world" or (underdeveloped adj countr*) or (under adj developed adj countr*) or (LMIC).mp.

5. exp africa/

6. americas/ or exp caribbean region/ or exp central america/ or latin america/ or mexico/ or exp south america/

7. europe/ or exp europe, eastern/ or exp transcaucasia/

8. antarctic regions/ or exp atlantic islands/ or exp indian ocean islands/ or exp pacific islands/

9. New Guinea/

10. asia/ or exp asia, central/ or asia, southeastern/ or borneo/ or cambodia/ or east timor/ or indonesiia/ or laos/ or malaysia/ or mekong valley/ or myanmar/ or philippines/ or thailand/ or vietnam/ or asia, western/ or bangladesh/ or bhutan/ or india/ or middle east/ or afghanistan/ or iran/ or iraq/ or joseph/ or lebanon/ or oman/ or saudi arabia/ or syria/ or turkey/ or yemen/ or nepal/ or pakistan/ or iri lanka/ or far east/ or china/ or tibet/ or exp korea/ or mongolia/

11. (Afghanistan or Albania or Algeria or Angola or Antigua or Arigua or Armenia or Austria or Azerbaijan or Bangladesh or Barbados or Barbuda or Belarus or Belize or Benin or Bhutan or Bolivia or Bosnia or Botswana or Brazil or Bulgaria or "Burkina Faso" or Burma or Burundi or Cambodia or Cameroon or "Cape Verde" or Cabo Verde" or "Central African Republic" or Chad or Chile or China or Colomba or Comoros or Congo or (Cook adj Island*) or "Costa Rica" or "Cote D'ivoire" or Croatia or Cuba or "Czech Republic" or Czechoslovakia or Djibouti or Dominica or Dominican or "East Timor" or Ecuador or Egypt or "El Salvador" or "Equatorial Guinea" or Eritrea or Estonia or Ethiopia or Fiji or Futuna or Gabon or Gambia or Georgia or Ghana or Grenada or Guatemala or Guinea or "Guinea Bissau" or Guyana or Haiti or Herzegov/ or Honduras or Hungary or India or Indonesia or Iran or Iraq or "Ivory Coast" or Jamaica or Jordan or Kazakhstan or Kenya or Kiribati or Korea or Kosovo or "Kyrgyz Republic" or Kyrgyzstan or Laos or (Lao adj People* adj Democratic adj Republic) or "Lao PDR" or Latvia or Lebanon or Lesotho or Liberia or Libya or Lithuania or Macedonia or Madagascar or Malawi or Malaysia or Maldives or Mali or (Marshall adj Island*) or Mauritania or Mauritius or Mexico or Micronesia or Moldova or Mongolia or Montserrat or Montenegro or Morocco or Mozambique or Myanmar or Namibia or Nauru or Nepal or "New Guinea" or Nicaragua or Niue or Niger or Nigeria or Oman or Pakistan or Palau or Panama or "Papua New Guinea" or Paraguay or Peru or Philippines or Poland or Yemen or Romania or Russia or Rwanda or "Saint Kitts Nevis" or "St Kitts Nevis" or "Saint Vincent Grenadines" or Samoa or "St Vincent Grenadines" or "Saint Lucia" or "St Lucia" or "Saint Helena" or "Saint Helena" or "Sao Tome Principe" or "Sao Tome and Principe" or "Saudi Arabia" or Senegal or Serbia or Seychelles or "Sierra Leone" or Slovak or "South Africa" or Solomon Island* or Somalia or "Sri Lanka" or Sudan or Suriname or Swaziland or Syria or Tajikistan or Tanzania or Thailand or Tibet or "Timmer Leste" or Togo or Tokelau or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Tuvalu or Uganda or Ukrainian or Uruguay or Uzbekistan or Vanuatu or Vietnam or "Wallis Futuna" or "West Bank" or Yemen or Zambia or Zimbabwe or Zaire).mp.

12. (africa or americas or caribbean or "central america" or "latin america" or "south america" or "eastern europe" or Transcaucasia or antarctic or (atlantic adj island*) or (indian adj ocean adj island*) or (pacific adj island*) or polynesia or "central asia" or (southeast* adj) or (south adj east* adj) or borneo or mokong or "western asia" or "middle east" or "far east").mp.

13. 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12

14. (oxygen adj2 (concentrator* or cylinder* or therap* or delivery or administ*)).tw,kw,hw.

15. 2 and 13 and 14

early (e.g. 37/53 (70%) repair needs identified and fixed during preventive maintenance visits) and showed that, while one third of concentrators needed repair each year, most repairs were cheap and simple (annual spare parts cost around 15 United States dollars per concentrator and required 50 person-hours).68 Other projects with reasonable maintenance systems also reported good equipment function up to 3 years post-implementation (Gray et al.).23,34,35,52,33 Projects where maintenance systems failed reported high equipment down-time and early equipment malfunction.21,29,36

Many projects reported deficiencies in maintenance activities (e.g. site visits, spare parts, record-keeping and care by users), resulting in missed opportunities for early repair (Gray et al.).35,37,46,49,53,60 Projects that integrated maintenance activities into existing (usually government) biomedical maintenance systems achieved success proportional to the quality of the existing system and its capacity to incorporate additional needs (Gray et al.).34,35,46,53,60

Affordability

Oxygen must be affordable for patients and hospitals. In user-pay hospitals oxygen was reported to be expensive for patients, contributing to delayed presentation, early discharge, and high patient debt burden (Gray et al.).24,60 In the Lao People’s Democratic Republic, oxygen from concentrators was provided free of charge, thus reducing the cost of oxygen to patients and decreasing early discharge rates for unwell patients (Gray et al., Morpeth et al.).48 In Nigeria, a neonatal unit used an oxygen insurance scheme to distribute the cost burden among all admitted patients and allow sustainable cost recovery.24 Many projects reported that concentrator-based oxygen systems were relatively more cost-efficient than cylinder-based systems.19,21,24,25,27,28,34,49,52,57,58,61 Demonstrated cost-efficiency can support the sustainability and future expansion of oxygen therapy.25,24,26,49 but this may be limited if the decision-making body does not identify both financial and clinical benefits (Gray et al.).34,57,58
Oxygen use
All the large-scale oxygen projects, and many single-site projects, aimed to improve how health-care workers used oxygen. However, while the overall use of oxygen increased, it was usually lower than expected based on admission and case-mix data, suggesting underuse of oxygen (Gray et al.).\(^{25,27,35,37}\) The highest mean concentrator use (around 15–18 hours/day) was reported by two hospitals with high caseloads and close supervision by project doctors;\(^{25,27,35,37}\) other projects reported a mean use of less than 6 hours per day (Morpeth et al.).\(^{35,37,48,49}\)

Post-implementation data from the Lao People’s Democratic Republic, Malawi and Papua New Guinea showed persisting deficiencies in practice (< 50% of children with pneumonia received pulse oximetry; 22–80% of hypoxaemic children received oxygen) with great variation between hospitals (Morpeth et al.).\(^{40}\) Hospitals with good pulse oximetry and oxygen practices achieved better clinical outcomes, with greater improvement if they started from a low baseline (Morpeth et al.).\(^{40}\)

Appropriate oxygen use was influenced by: (i) knowledge and skills; (ii) motivation; and (iii) work environment.\(^{42}\)

Knowledge and skills
Low knowledge and skills among health workers was almost universally reported, and many health workers had misconceptions and fears about oxygen therapy that affected their motivation (e.g. fear of the concentrator technology or belief that oxygen therapy caused death). Many projects provided initial training, and these generally showed improved knowledge and skills (Gray et al.).\(^{38,45,52,53,61}\) High training coverage rates and in-service re-training were regarded as important in hospitals that faced chronic staff shortages and high staff turnover.\(^{45,53}\) However, the proportion of staff trained correlated poorly with practice change or clinical outcomes, suggesting that training the right people in the right way may be more important than training more people.\(^{38,52,61}\)

Motivation
The greatest reported motivator for staff was witnessing the benefits of oxygen first-hand (Gray et al.).\(^{35,27,28,35,37,48}\) Challenges to motivation included: confusion about equipment and guidelines; associating oxygen therapy with death; technical difficulties; and competing workplace priorities (Gray et al.).\(^{46,53}\) This was best addressed by practical on-site training addressing specific challenges and needs (Gray et al.);\(^{35}\) and regular on-site supervision (Gray et al.).\(^{46,48,49}\)

Work environment
The physical and social environment could enable or inhibit good practice in oxygen therapy. For example, creation of high-dependency spaces within wards prioritized care for sick patients; endorsing protocols created new practice norms; wall-charts reminded users about oxygen use; logbooks facilitated regular equipment maintenance; flowmeter assemblies enabled oxygen delivery to multiple patients; pulse oximetry enabled identification of hypoxaemic children, helped involve families in care and overcome fears about oxygen; and oxygen analysers gave users confidence that the concentrator worked (Gray et al.).\(^{38,45,46,48,49}\)

Box 2. Theoretical themes identified to explain how interventions to improve oxygen therapy systems in low-resource settings might work

| Theme 1 (oxygen access) recognizes that lack of oxygen in health-care facilities is a major barrier to care, and proposes that making oxygen therapy available will enable more children to be treated and with better outcomes. These projects typically emphasized the importance of quality oxygen equipment and effective maintenance programmes and some also addressed financial barriers to access. |
| Theme 2 (oxygen use) recognizes that health-care workers may not use oxygen effectively, and proposes that building the capacity and motivation of health workers will enable children to be treated appropriately and have better outcomes. These projects typically emphasized training and supervision of clinical staff, including retraining and follow-up to ensure sustainability. |
| Theme 3 (broad care practices) recognizes that broader issues of quality of care impact on clinical outcomes, and proposes that strengthening these processes will enable higher quality of care and better outcomes. These projects emphasized broader quality of care issues, such as supply of essential medications, clinical review and feedback and record-keeping. |
| Theme 4 (supportive management) recognizes that managerial and political support is essential, and proposes that engagement with managers and policy-makers will support successful implementation and sustainability. These projects emphasized the engagement and responsibility of stakeholders at district, regional and national level in planning, implementation and evaluation. |
| Theme 5 (hospital team) recognizes that hospital-level responsibility and action influences success, and proposes that enhancing the motivation of the hospital team will drive improvements in the use of oxygen and the care of equipment. This theme has not been overtly reported in previous oxygen therapy projects, but was frequently cited in interviews as a strong predictor of success by those involved. |

Broadly care practices
The projects in the Lao People’s Democratic Republic, Malawi and Papua New Guinea embedded improved oxygen systems within broader measures to improve quality of care. All reported changes that extended beyond oxygen-related care, such as improved staffing; reaching neglected populations; strengthening supply chains; and addressing other care deficits (Gray et al.).\(^{46,53}\) While it was not possible to separate the effects of these quality of care interventions from the effects of the oxygen-related interventions, hospitals that improved the broader aspects of care typically reported the biggest improvements in outcomes (Gray et al.).\(^{46,52,53,56}\)

Supportive management
All the large-scale oxygen therapy projects required some degree of regional and national government support. In Egypt, the Lao People’s Democratic Republic and Papua New Guinea effective relationships with government biomedical departments and the support of a multidisciplinary national oxygen team strongly facilitated equipment
Box 3. **Contextual and programmatic factors that influenced the efficacy of interventions to improve oxygen therapy systems in low-resource settings, positively (+) or negatively (−)**

**Contextual factors**

Strong evidence across multiple studies:

- (+) Target hospital has unmet need for oxygen (e.g. high prevalence of pneumonia or hypoxaemia);
- (+) Target hospital has limited access to oxygen (though not necessarily no access);
- (+) Hospital managers recognize the need for improved oxygen systems;
- (+) Functional maintenance system in place, with ability to meet additional needs of oxygen equipment (particularly regular preventive maintenance);
- (+) Ward environment and culture facilitates good oxygen therapy practices (e.g. adequate space, patient-centred care, good interdisciplinary relationships);
- (+) Hospital power supply is adequate;
- (−) High turnover of skilled clinicians (without transfer of knowledge);
- (−) Weak existing maintenance system is unable to meet additional needs of oxygen equipment.

Limited evidence from one or few studies:

- (+) Target hospital starts from low baseline of clinical care (i.e. has more possibility to show improvement);
- (+) Hospital staff members have some experience using oxygen;
- (−) Oxygen is expensive to patients.

**Programmatic factors**

Strong evidence across multiple studies:

- (+) Clinician in ward leadership role supervises and supports oxygen use;
- (+) Uniform procurement of oxygen equipment that is high quality and appropriate for the environmental conditions;
- (+) Skilled technicians, and spare parts and tools, are available for installation and maintenance of equipment;
- (+) Ongoing cost of oxygen to hospital is adequately financed;
- (+) Hospital is the recipient of financial benefits (from improved oxygen system) and has control over future spending on oxygen therapy;
- (+) Clinical use of oxygen and pulse oximetry is monitored and deficiencies are addressed;
- (+) Problems related to unreliable power supply are resolved;
- (−) Lack of skilled technicians and tools and spare parts;
- (−) Weak support of maintenance team by responsible body.a

Limited evidence from one or few studies:

- (+) Hospital leaders are involved in needs assessment, planning, implementation and review;
- (+) Quality, user-friendly equipment is available to detect hypoxaemia (pulse oximetry);
- (+) Oxygen analyser available to assess oxygen concentrator function;
- (+) Quality, user-friendly equipment delivery devices are available (including safe mechanism for titrating oxygen flow to individual patients);
- (+) Well organized hospital multidisciplinary team is responsible for oxygen therapy activities;
- (+) Hospitals are supported to measure outcomes of therapy and respond (i.e. quality improvement);
- (+) Broader aspects of quality of care are improved (e.g. medical supplies, record-keeping);
- (+) Costs of oxygen therapy to patients are minimized;
- (+) Country’s health ministry (or similar) provides ongoing support for activities related to oxygen therapy;
- (−) Training of clinicians is not done on-site;
- (−) Maintenance capacity is not made available locally.

Possible factors that might be tested in future studies:

- (+) Capacity of health workers to pass on knowledge and skills is developed.

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a Responsible body could be the hospital management, or state or federal government department, or a nongovernmental organization.

Notes: The factors were identified from a systematic literature search and analysis of 45 studies from 20 projects in 15 countries, involving intervention(s) to improve oxygen therapy systems (Table 1 and Table 2). All projects involved the introduction of oxygen therapy equipment. Many projects also included additional interventions targeting technicians, clinicians, administrators and policy-makers. Contextual refers to factors in the environment in which the project was introduced that influence the success of the project, such as characteristics of participating health facilities and existing capacity for oxygen therapy. Programmatic refers to factors about the intervention or programme itself that influence success, such as what was done and how it was implemented.
**Hospital team**

Investigators from many projects observed that ownership and acceptance of the project by hospital staff was a key determinant of success, enhancing responsive problem-solving; equipment care and maintenance; clinical use of oxygen; continuity of knowledge and skills; and general quality of care (Gray et al.). Limited data suggests that hospital-level ownership was greater when staff were convinced of the potential benefits of improved oxygen systems, and were actively involved in oxygen improvement activities as a multidisciplinary team.

Achieving hospital-level ownership may be more challenging for large-scale programmes that are initiated externally. A common approach was to find a responsible person at each hospital who would be the primary contact and local project leader. When it worked, this strategy created a local champion who had ready access to technical expertise and local staff, and ideally shared responsibility with a multidisciplinary team (Gray et al.). This failed if the responsible person left their employment or lacked the power to effect change (Gray et al.).

While external agencies often brought funding and technical expertise to oxygen projects, studies reported that agencies could also be disruptive influences on hospital and health systems (Gray et al.). Success depended on effective local participation (in planning, implementation and evaluation); clear communication between stakeholders (including priorities, roles and responsibilities); and ongoing support of local implementers (Gray et al.).

**Discussion**

The safe and effective provision of oxygen is a challenge for doctors, hospital administrators and government officials globally. Typically, some oxygen therapy equipment is available, but without the maintenance capacity to keep it functioning or the clinical expertise to use it effectively (Gray et al.). While WHO guidelines offer advice on the technical specifications and the clinical application of oxygen, there has been little guidance on how to bring about changes in practice. In shifting the focus from what works to what happens, realist review methods hold great promise for improving our understanding of how to bridge the implementation gap. This is relevant for oxygen, and many other similarly simple, life-saving therapies that countries are struggling to scale up.

We identified a multilayered array of mechanisms that need to work together to achieve results. In broad terms, hospitals need good access to oxygen and effective use of oxygen, which should be facilitated by a broad quality improvement capacity, a strong managerial and policy support and multidisciplinary teamwork (Fig. 2). Within each domain, additional mechanisms are at play. It is the interaction of these processes, together with various contextual factors that determines the outcomes.

This framework is work in progress and it needs further testing. While there is substantial evidence to support some aspects of this framework, there is little evidence to support other aspects. Important future questions include: (i) the role of various policy-makers and managers in supporting the effective use of oxygen; (ii) the function of a multidisciplinary hospital oxygen team; (iii) the influence of broader care practices and potential role of quality improvement teams; (iv) the role of alternative energy sources in ensuring adequate power; and (v) how to integrate pulse oximetry and good oxygen practices more effectively into routine care. Those who are implementing an oxygen therapy system should not only evaluate the effectiveness of their programme, but test the mechanisms through which their programme works.

Our review had some limitations. First, realist reviews cannot explore all potential theories or all contextual influences. We decided to include a wide range of interventions, but prioritized the exploration of theories that were most generalizable and applicable to low-resource hospitals providing general care for children. Our search criteria were therefore

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**Fig. 2. Improving outcomes with effective oxygen therapy: a framework depicting the key requirements of an effective oxygen system**

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**O2**: oxygen.
In conclusion, our framework offers a practical, evidence-based approach to improving oxygen therapy in low-resource settings and may be relevant for other programmes involving the introduction of health technologies. It will assist practitioners and policy-makers to evaluate their current system(s), and create solutions that are appropriate for their context. It will assist implementers to understand and optimize their activities, providing both the flexibility and structure to adapt to different settings and respond to evolving needs.

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Systematic reviews
Improving oxygen therapy for children
Hamish Graham et al.
Proporcionar oxígeno a niños en hospitales: una revisión realista

Objetivo
Identificar y describir las intervenciones para mejorar la oxigenoterapia en hospitales de entornos con pocos recursos y determinar los factores que contribuyen al éxito y al fracaso en diferentes contextos.

Métodos
Utilizando métodos de revisión realistas, se analizaron los documentos y se contactó con expertos en el campo para identificar posibles teorías mecanicistas sobre cómo pueden funcionar las intervenciones a la hora de mejorar los sistemas de la oxigenoterapia. Posteriormente, y de forma sistemática, se realizaron búsquedas en bases de datos en línea con el objetivo de encontrar evaluaciones de sistemas con oxígeno mejorados en hospitales de países con ingresos bajos o medios. Se extrajo información sobre la eficacia, los procesos y la teoría subyacente de los proyectos seleccionados y se utilizó dicha información para probar las posibles teorías e identificar las características de los proyectos que tuvieron éxito.

Resultados
Se incluyeron 20 proyectos de oxigenoterapia mejorados (45 documentos) de 15 países. Estos proyectos utilizaban distintos enfoques para mejorar la oxigenoterapia e informaban de resultados en materia clínica, técnica y de calidad de los servicios. Cuatro estudios de eficacia demostraron resultados clínicos positivos para la neumonía infantil, con una gran diferencia entre programas y hospitales. Se identificaron factores que contribuyen u obstaculizan el éxito, y se propuso un marco práctico que representaba los requisitos fundamentales para que los hospitales proporcionen una oxigenoterapia de forma eficaz a los hospitales proporcionen una oxigenoterapia de forma eficaz.
los niños. Para mejorar los resultados clínicos, los programas de mejora del oxígeno deben lograr un buen acceso al oxígeno y un buen uso del mismo, lo que debería verse facilitado por una amplia capacidad de mejora de la calidad, un apoyo de gestión y político sólido y trabajo en equipo multidisciplinar.

**Conclusión** Los resultados pueden informar a los médicos y responsables políticos sobre cómo mejorar la oxigenoterapia en entornos con pocos recursos, y pueden ser relevantes para otras intervenciones que impliquen la introducción de tecnologías sanitarias.


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