INPLASY PROTOCOL

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Review Stage at time of this submission: Formal screening of search results against eligibility criteria.

Conflicts of interest: There are no conflicts of interest.

Cost-Effectiveness of Neonatal Surgery for Congenital Anomalies in Low- and Middle-Income Countries: A Systematic Review Protocol

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Review question / Objective: Aim: To conduct a systematic review that identifies and analyzes cost-effectiveness of neonatal surgical interventions for congenital anomalies in LMICs. **Objectives: 1.** To systematically identify studies on cost-effectiveness of neonatal surgery for congenital anomalies in LMICs; **2.** Evaluate the cost-effectiveness of neonatal surgery for congenital anomalies in LMICs; **3.** To provide an evidence-based summary of cost-effectiveness of neonatal surgery for congenital anomalies in LMICs to direct future interventions and investments in neonatal surgery; **4.** Critically appraise the quality of the studies included in the systematic review.

Condition being studied: Congenital anomalies or conditions in which patients are born with a developmental defect of anomaly in a low and middle income country.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 May 2020 and was last updated on 23 May 2020 (registration number INPLASY202050085).

INTRODUCTION

Review question / Objective: Aim: To conduct a systematic review that identifies and analyzes cost-effectiveness of neonatal surgical interventions for congenital anomalies in LMICs. **Objectives:**

1. To systematically identify studies on cost-effectiveness of neonatal surgery for congenital anomalies in LMICs; 2. Evaluate the cost-effectiveness of neonatal surgery for congenital anomalies in LMICs; 3. To provide an evidence-based summary of cost-effectiveness of neonatal surgery for

congenital anomalies in LMICs to direct future interventions and investments in neonatal surgery; 4. Critically appraise the quality of the studies included in the systematic review.

Rationale: Congenital anomalies constitute a global health burden, estimated at over 591,000 deaths in total worldwide each year. Of these, more than 90% occur in LMICs. Surgical interventions in LMICs have been found to be cost-effective but have been not specifically studied in neonatal surgery. Given that congenital anomalies have a substantial lifelong impact on children, it would be anticipated that treating them would reduce the burden of disease.

Condition being studied: Congenital anomalies or conditions in which patients are born with a developmental defect of anomaly in a low and middle income country.

METHODS

Search strategy: A systematic literature review will be conducted in the PubMed, MEDLINE, and Embase, and Cochrane Library databases for relevant articles on cost-effectiveness of neonatal surgery for congenital anomalies in LMICs. The following search strings will be used: 1. Congenital anomalies; 2. LMICs; 3. Cost-effectiveness of surgical interventions.

Participant or population: Neonates with congenital anomalies undergoing surgical intervention in low and middle income countries.

Intervention: Any surgical or operative interventions. Procedures performed antenatally or after the first 28 days of life will be excluded.

Comparator: When available, cost and outcomes data will be compared between procedures completed in high income countries.

Study designs to be included: Published, peer-reviewed journal articles will be

included. Studies with a lack of explicit methodology and results will be excluded. Case reports, ed.

Eligibility criteria: Conditions: Abdominal Wall Defect, Aganglionosis, Anal Atresia, Anorectal Malformation, Anorectal Stenosis, Apple Peel Syndrome, Biliary Atresia, Birth Defects, Bladder Exstrophy, Branchial Tag, Branchial Vestige, Bronchopulmonary Sequestration, Cervicoaural Fistula, Choledochal Cyst, Cleft Lip, Cleft Palate, Clubfoot, Colonic Atresia, Congenital Abnormalities, Congenital Anomalies, Congenital Cystic Adenomatoid Malformation of Lung, Congenital Diaphragmatic Hernia, Congenital Heart Defects, Congenital Hydronephrosis, Congenital Malformation, Conjoined Twins, Cryptorchidism, Diaphragmatic Eventration, Down Syndrome, Duodenal Atresia, Duodenal Obstruction, Duodenal Web, Epispadias, Exomphalos, Fetal Malformation, Gastroschisis, Hirschsprung's Disease, Hydrocele, Hypospadias, Ileal Atresia, Imperforate Anus, Imperforate Hymen, Indeterminate Sex, Intestinal Atresia, Jejunal Atresia, Jejuno-Ileal Atresia, Malrotation, eural Tube Defects, Oesophageal Atresia, Omphalocele, Orofacial Clefts, Pectus Excavatum, Pes Cavus, Phimosis, Polycystic Kidney Disease, Polydactyly, Preauricular Sinus, Redundant Neck Fold, Spina Bifida, Syndactyly, Tongue Tie, Tracheo Oesophageal Fistula, Umbilical Hernia, Undescended Testicle, Volvulus, Webbed Neck Age: Neonatal Place: Low- and middle-income countries (as defined by World Bank 2019 Classification) Intervention: Surgical or operative interventions.

Information sources: The following databases will be used for the systematic review literature search: PubMed, MEDLINE, EMBASE, and Cochrane Library. The search will include English, French, Spanish, Italian, and Arabic publications articles and will be restricted to human studies. There will be no restrictions on publication date or study design. Published, peer-reviewed journal articles

will be included. Any study without explicit cost data or health outcomes data will be excluded. Case reports, editorials, letters to the editor, and literature reviews will be excluded. Abstracts without available full text will be excluded.

Main outcome(s): 1. Cost of surgical interventions for congenital anomalies in LMICs. 2. Cost effectiveness of surgical interventions for neonates with congenital anomalies in LMICs. * Measures of effect Cost effectiveness: the cost of intervention per quality adjusted life year or disability adjusted life year.

Additional outcome(s): Potential gains in life expectancy * Measures of effect QALYs, HALYs, or DALYs.

Data management: Articles will be uploaded to Covidence software (Melbourne, Australia), duplicate articles will be removed, and remaining articles will be screened by two independent reviewers.

Quality assessment / Risk of bias analysis: The studies will be assessed for their quality of economic evaluations using the Drummond 10 point checklist. The results will be summarized in a table format in the results section.

Strategy of data synthesis: The data will be organized into: author(s), the year of publication, intervention or procedure, country or site of intervention, GDP, cost per outcome, outcome unit, currency. Cost data will be organized into cost to the provider and cost to the patient. The cost will be converted to USD, calculated by the currency year. The effectiveness method of disability adjusted life years, health adjusted life years and quality adjusted life years will be extracted. Any reported incremental cost effectiveness ratio will be extracted. Data reported for different countries or procedures will be extracted as separate results. Quantitative analysis will be undertaken by calculating the median values for the intervention or procedures. Meta-analysis will not be conducted.

Subgroup analysis: None.

Sensibility analysis: No meta-analysis will be undertaken.

Language: English, French, Spanish, Italian and Arabic publications.

Country(ies) involved: Egypt, England, Italy, Palestine, United States of America.

Keywords: congenital anomalies; neonatal surgery; cost-effectiveness; LMICs.

Dissemination plans: On completion of the systematic review, we aim to publish the results in a peer-review journal and apply for conference presentations.

Contributions of each author:
Author 1 - Na Eun Kim - Author 1 drafted the manuscript.
Author 2 - Caris Grimes - The author contributed to the drafting of the manuscript and to the development of the protocol.
Author 3 - Naomi Wright - The author contributed to the drafting of the manuscript and to the development of the protocol.
Author 4 - Dominique Vervoot - The author contributed to the development of the selection criteria, search string, data extraction strategy and provided feedback on the final protocol.
Author 5 - Ahmad Hammouri - The author contributed to the development of the selection criteria, search string, data extraction strategy and provided feedback on the final protocol.
Author 6 - Cristiana Riboni - The author contributed to the development of the selection criteria, search string, data extraction strategy and provided feedback on the final protocol.
Author 7 - Hosni Salem - The author contributed to the development of the selection criteria, search string, data extraction strategy and provided feedback on the final protocol.