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Support: Not applicable.

Review Stage at time of this submission: Preliminary searches.

Conflicts of interest: None.

Adult Cardiac Surgical Cost Variation Around the World: Protocol for a Systematic Review

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Review question / Objective: This review seeks to assess the variation in procedural costs of coronary artery bypass grafting, mitral valve repair, mitral valve replacement, aortic valve repair, aortic valve replacement, and combined coronary-valve procedures between and within countries. Condition being studied: Cardiac surgical conditions requiring coronary artery bypass grafting, mitral valve repair, mitral valve replacement, aortic valve repair, aortic valve replacement, aortic valve repair, aortic valve replacement, and combined coronary-valve procedures. Information sources: The EconLit, Embase, PubMed/MEDLINE, Web of Science, and WHO Global Index Medicus databases will be searched to identify articles published between January 1, 2000, and June 1, 2020. We will further manually review reference lists of all articles that will be

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 July 2020 and was last updated on 01 July 2020 (registration number INPLASY202070001).

INTRODUCTION

Review question / Objective: This review seeks to assess the variation in procedural costs of coronary artery bypass grafting, mitral valve repair, mitral valve replacement, aortic valve repair, aortic valve replacement, and combined coronary-valve procedures between and within countries.

Rationale: Cardiac surgery is expensive and largely inaccessible without insurance or philanthropic support. Substantial cost variation has been reported within cardiac surgery in the United States and among

included after screening.

non-cardiac surgical procedures across the world, but little is known on the global procedural cost variation for common adult cardiac surgical procedures.

Condition being studied: Cardiac surgical conditions requiring coronary artery bypass grafting, mitral valve repair, mitral valve replacement, aortic valve repair, aortic valve replacement, and combined coronary-valve procedures.

METHODS

Search strategy: PubMed/MEDLINE: ("Costs and Cost Analysis"[mh] OR costs[tiab] OR cost effective*[tiab] OR costing[tiab] OR cost-benefit[tiab] OR cost-utility[tiab] OR "Health Expenditures"[Mesh] OR "Direct Service Costs"[Mesh] OR "Hospital Costs"[Mesh] OR "Health Care Costs" [Mesh] OR "Cost of Illness"[Mesh] OR "Cost-Benefit Analysis"[Mesh] OR "Economics, Hospital"[Mesh] OR "Economics, Medical"[Mesh] OR charge*[tiab]) AND ("Cardiovascular Surgical Procedures"[mh] OR "Cardiac Surgical Procedures" [mh] OR "Cardiovascular Diseases/surgery"[mh] OR "Cardiac surgery" [tiab] OR "Cardiac surgical"[tiab] OR "Cardiovascular surgery"[tiab] OR "Cardiovascular surgical"[tiab] OR "Cardiothoracic surgery"[tiab] OR "Cardiothoracic surgical"[tiab] OR coronary artery bypass graft*[tiab] OR "CABG"[tiab] OR valve repair*[tiab] OR valve replacement*[tiab] OR aortic surg*[tiab] OR valvular surg*[tiab]). Embase: (('cost benefit analysis'/exp OR 'cost utility analysis'/exp OR 'cost effectiveness analysis'/exp) OR (cost:ti OR costs:ti OR costing:ti OR cost:ab OR costs:ab OR costing:ab) OR charge*:ab) AND ('cardiac surg*':ti,ab OR 'heart surg*':ti,ab OR 'cardiac surgery'/exp OR 'cardiac surgical'/exp OR CABG:ti,ab OR 'coronary artery bypass graft*':ti,ab OR 'valve repair*':ti,ab OR 'valve replacement*':ti,ab OR 'aortic surg*':ti,ab OR 'valvular surg*':ti,ab) AND (2000:py OR 2001:py OR 2002:py OR 2003:py OR 2004:py OR 2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR

2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py) Web of Science: (TS=(costs OR cost OR cost-effective* OR costing OR cost-benefit OR cost-utility OR charge OR charges)) AND (TS=(cardiac* OR cardio* OR heart OR coronary OR aortic OR valve OR valvular)) AND (TS=(surg*)) EconLit (cost* OR cost-effective* OR charge* OR cost-benefit OR cost-utility) AND (((cardiac* OR cardio* OR heart OR coronary OR aortic OR valve OR valvular) AND (surg*)) OR CABG OR coronary artery bypass graft*) WHO Global Index Medicus: (tw:(cost* OR cost-effective* OR charge* OR cost-benefit OR cost-utility)) AND (tw: (cardiac* OR cardio* OR heart OR valve OR valvular OR aortic OR coronary)) AND (tw: (surg*)).

Participant or population: Adult patients requiring cardiac surgery.

Intervention: Coronary artery bypass grafting, mitral valve repair, mitral valve replacement, aortic valve repair, aortic valve replacement, combined coronaryvalve procedures.

Comparator: Not applicable.

Study designs to be included: All (no exclusion based on study design).

Eligibility criteria: Articles describing other types of cardiac surgery, only describing costs related to non-surgical care, or with incomplete cost data will be excluded from the analysis. No exclusion will be done based on article type or language.

Information sources: The EconLit, Embase, PubMed/MEDLINE, Web of Science, and WHO Global Index Medicus databases will be searched to identify articles published between January 1, 2000, and June 1, 2020. We will further manually review reference lists of all articles that will be included after screening.

Main outcome(s): Procedural costs and cost variation between and within countries for common adult cardiac surgical procedures. Additional outcome(s): Extracted variables: study design, costing method, country, hospital, procedures, costs per procedure and, where available, costs of overall hospital stay, individual (non-medical) expenses, operating time, length of stay, perioperative mortality, and perioperative complications.

Quality assessment / Risk of bias analysis: Due to the variation in study designs (no

exclusion based on study designs (no exclusion based on study design) and the primary outcome of interest (procedural costs), no appropriate quality assessment checklist was identified. Quality assessment will be performed by the authors based on 1) clear description of procedure performed, 2) clear description of cost definitions (procedural costs versus total hospital costs), 3) representativeness of patient population, and 4) completeness of data reporting.

Strategy of data synthesis: Cost variables are assumed to have non-normal distributions. For other variables, normality of data will be assessed using the Shapiro-Wilk's test. Continuous variables will be analyzed using the independent student's ttest (normality) or Mann-Whitney U test (non-normality). Categorical variables will be analyzed using chi-square or Fisher's exact tests. Multi-set comparisons will be performed using ANOVA or Kruskak-Wallis tests. Continuous variables will be reported as mean with standard deviation (if normally distributed) or median with interquartile range (if non-normality). Categorical variables will be reported as counts and percentages. R Statistical Software version 4.0.1 (R Foundation for Statistical Computing, Vienna, Austria) will be used to perform the data analysis. Statistical significance will be accepted at p-values < 0.05.

Subgroup analysis: Cost variation will be assessed between and within countries of different income groups (high-income countries, low- and middle-income countries) as defined by the World Bank Country and Lending Groups classification. Analyses will be performed stratified by procedure (coronary artery bypass grafting, mitral valve repair, mitral valve replacement, aortic valve repair, aortic valve replacement, combined coronaryvalve procedures).

Sensibility analysis: Sensitivity analysis will be performed by excluding studies with outlier values (e.g., very low or very high procedural costs compared to other studies from the same country and comparable patient setting, outcomes, and procedure) and repeating the primary analysis.

Language: No language limits.

Country(ies) involved: United States, India.

Other relevant information: Not applicable.

Keywords: Cardiac Surgery; Global Health; Health Policy; Health Economics.

Dissemination plans: The results of this study will be summarized in English and disseminated by submission for publication in a peer-review journal.

Contributions of each author:

Author 1 - Dominique Vervoort - Dominique Vervoort conceptualized the idea, drafted the search string, and drafted the protocol. Author 2 - Camila Guetter - Camila R. Guetter drafted the search string and drafted the protocol.

Author 3 - Lena Trager - Lena Trager drafted the search string and drafted the protocol.

Author 4 - Priyansh Shah - Priyansh Shah drafted the protocol.

Author 5 - Carlos Diaz - Carlos Eduardo Diaz drafted the protocol.

Author 6 - Eric Etchill - Eric W. Etchill drafted the protocol.

Author 7 - Rawn Salenger - Rawn Salenger drafted the protocol and critically reviewed the protocol.