Directed acyclic graph helps to understand the causality of malnutrition in under-5 children born small for gestational age

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Content

Introduction

Introduction

Small-for-gestational age (SGA)

- Defined as being born with birth weight below 10th percentile for gestational age.

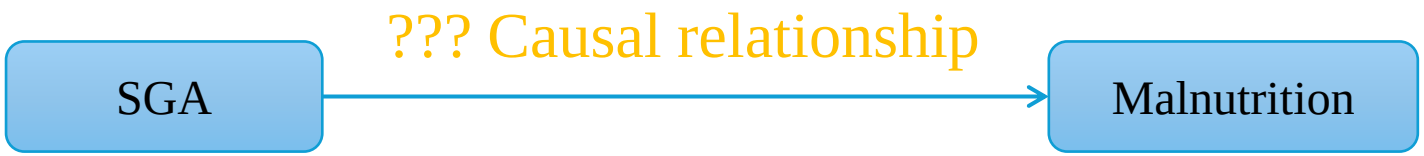
- Approximately 16% of all births are SGA
  - 7% in high-income countries
  - 41.5% in South Asia

- Main cause for SGA infants → Lack of nutrient supply to the fetus
- Other factors → Maternal, environmental, placental, and fetal factors

Introduction

- Although the literature consistently associates SGA/low birth weight with childhood malnutrition, there is no clarity on whether this association is causal.

- WHO and UNICEF list malnutrition as one of the consequences of SGA, but causality is implied rather than proven.



Introduction

Numerous observational studies identify factors related to malnutrition but have limitations.

- ***Causal relationships are often unclear due to:***
  - Lack of differentiation between association and causation.
  - Unclear modelling objectives (to predict or understand causality).
- ***Common methodological errors:***
  - Regression-based adjusting for all covariates without distinguishing confounders, mediators, or colliders (introduce bias).
  - Incomplete factor selection based on available data rather than comprehensive analysis.

Introduction

- Impact → Observational studies are rarely able to provide true estimates of the causal effects of exposure on outcomes.

- DAGs can address this problem by applying causal theory to observational data to provide a model for estimating unbiased effect sizes.

Introduction

Objective

- This study aimed to construct a causal model to estimate the effect of term-SGA on malnutrition
  - ❖ in children aged less than 5 years
  - ❖ belonging to the Indian subcontinent.

Materials and Methods

Systematic review
Causal modelling using DAG

Materials and Methods

Step 1: Systematic review → "rapid narrative review" methodology

- identify the causal factors for malnutrition
- reported following the WHO guidance document on rapid reviews

Step 2: Causal modelling using DAG

- followed the *"Evidence Synthesis for Constructing Directed Acyclic Graphs"* approach proposed by *Ferguson et al*.

Materials and Methods

"Estimand/Estimator/Estimate" framework for study flow

Estimands → Targeting the perspectives of parents, clinicians/ nutrition counsellors, and public health specialists/policymakers.

Estimator → Causal (DAG) models constitute the estimators.

Estimate → The derivation of estimate was beyond the scope of this study.

Step 1: Systematic review

Study eligibility criteria:

- ***Design:*** Original research (observational studies or RCTs) that examined the factors associated with malnutrition
- ***Population:*** Children aged 6 months to 5 years
- ***Setting:*** Indian subcontinent (India, Pakistan, Nepal, Bangladesh, Bhutan, Sri Lanka, and Maldives)
- Studies on human subjects published in English over the last 10 years (January 2014 to December 2023)

Step 1: Systematic review

Literature search:

- Searched 4 databases (PubMed, Scopus, Web of Science, and ProQuest)
- Conducted on December 15, 2023
- References and abstracts were imported into the Rayyan QCRI software.

Step 1: Systematic review

Data extraction:

- Used a pragmatic approach, whereby only the abstracts were reviewed.
  - ❖*Identify risk factors significantly associated with malnutrition.*
- Did not pool the results of the studies or assess their quality.
- A summary table was created for the study characteristics from the included abstracts.
  - ❖*Year of publication, country, research design, sample size, anthropometric indices, and factors associated with malnutrition*

Step 2: Causal modelling using DAG

Three sequential steps:

1. ***Mapping***

   Mapping of the theory from each study produces implied graphs (IGs).

2. ***Translation***

   Each relationship in the individual IGs is then assessed under sequential causal criteria and a counterfactual thought experiment.

3. ***Integration***

   All the translational DAGs are then combined to form one integrated DAG.

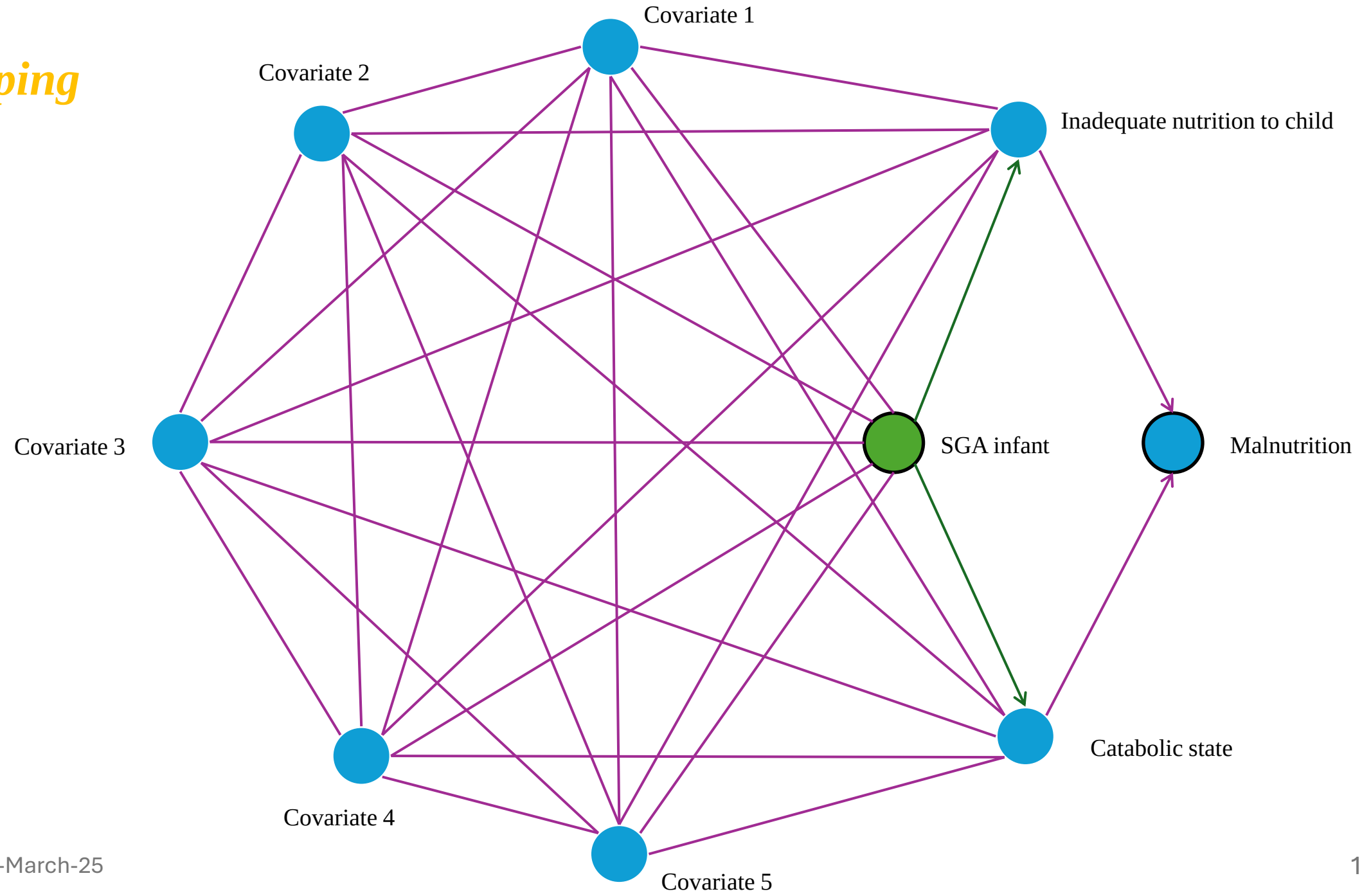
Step 2: Causal modelling using DAG

1. Mapping

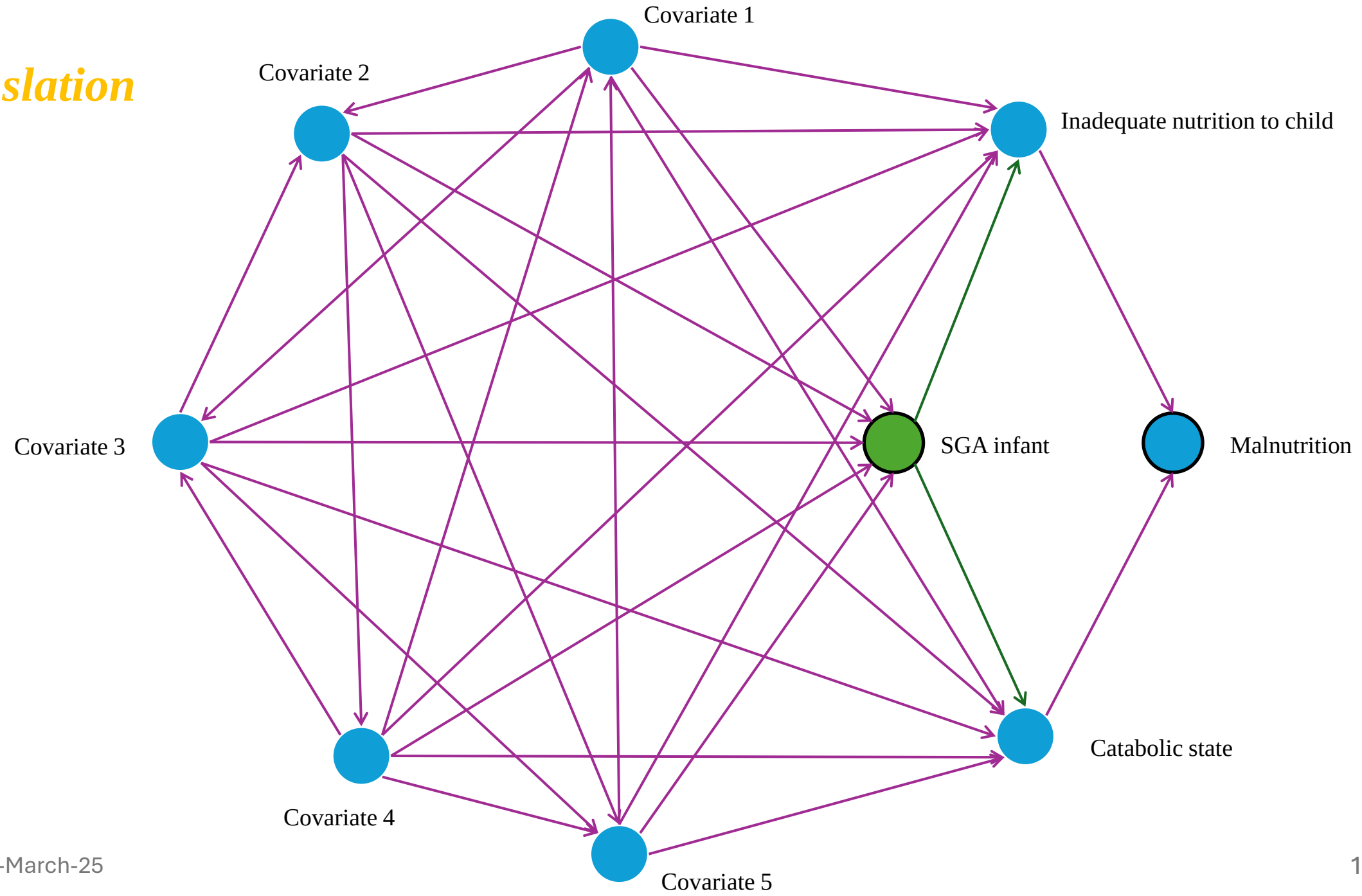
In this review → used pragmatic approach (constructed a single IG by considering all the factors identified)

- Two directed edges were drawn from the exposure, passing through two mediators (‘poor nutritional intake’ and ‘persistent catabolic state’) and terminating at the outcome.
- The remaining causal factors were designated as the unassigned covariates.
- Directed edges were drawn from each covariate to the exposure and outcome (assuming that all were confounders).
- IG was saturated by drawing undirected edges between all confounders.

Mapping


Covariate 1
Covariate 2
Inadequate nutrition to child
Covariate 3
SGA infant
Malnutrition
Catabolic state
Covariate 4
Covariate 5

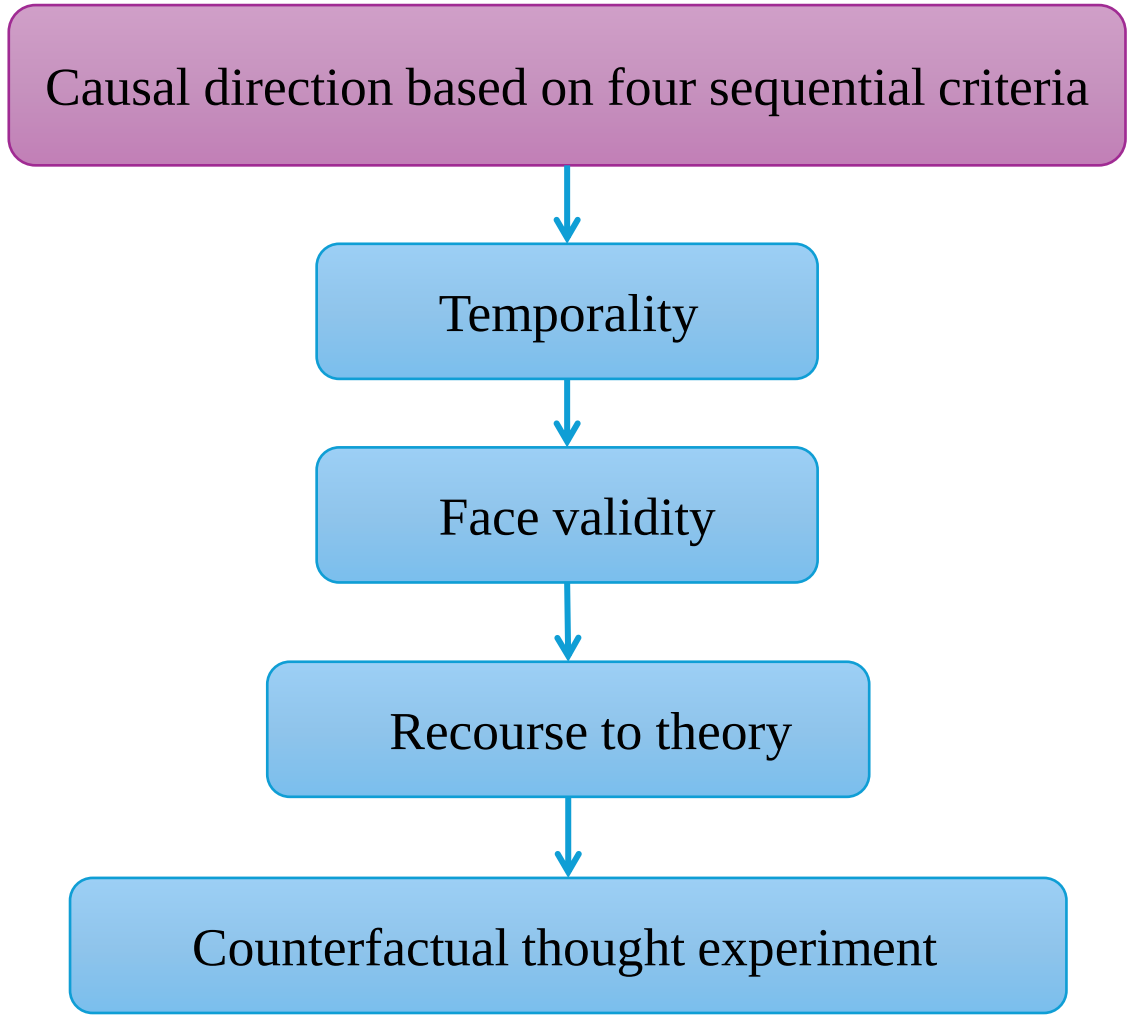
Translation



Step 2: Causal modelling using DAG

2. Translation

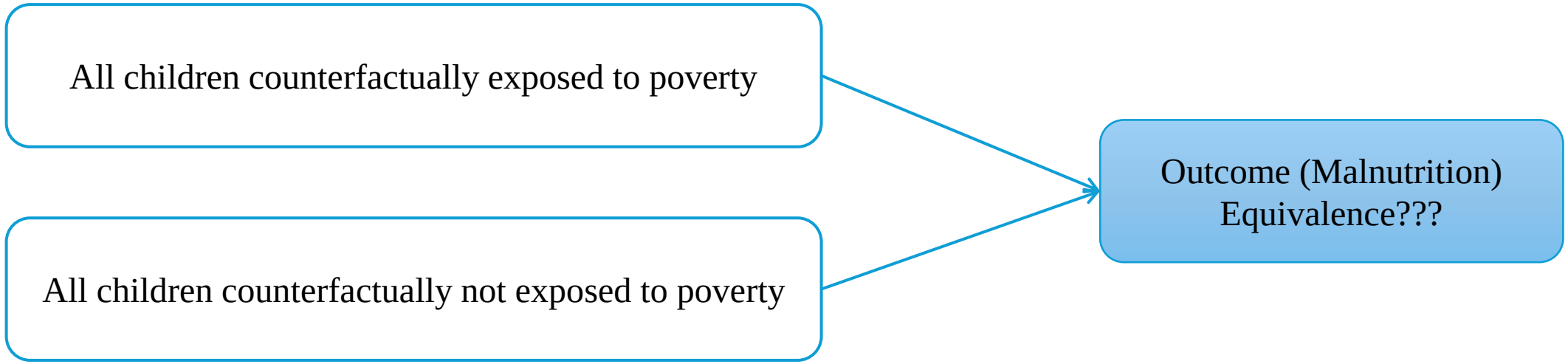
The hypothesized relationship between nodes was assessed forward and reverse directions using four criteria.



Step 2: Causal modelling using DAG

2.1 Counterfactual thought experiment

- Potential outcomes are compared in a scenario in which the entire study sample is exposed vs one in which there is no exposure.



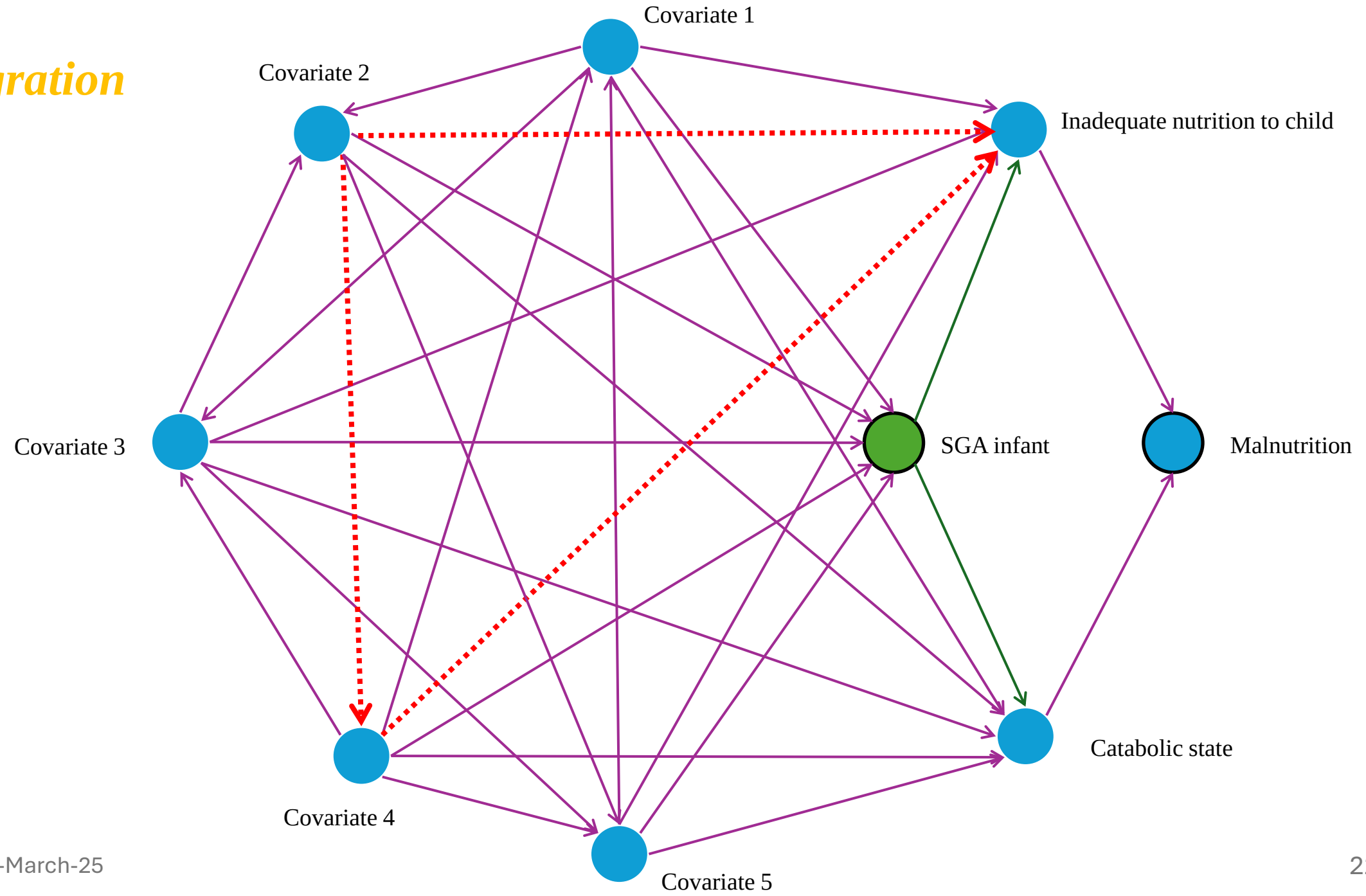
Step 2: Causal modelling using DAG

3. Integration

- Prepared a final DAG by removing edges where a potential relationship could not be conceptualized.

- DAGitty version 3.1 was used for the construction of DAG.
  → Create minimal sufficient adjustment sets

Integration



Results

Results of the literature search
Study characteristics
Factor identification and handling
DAG and minimal sufficient adjustment sets

Result of literature search

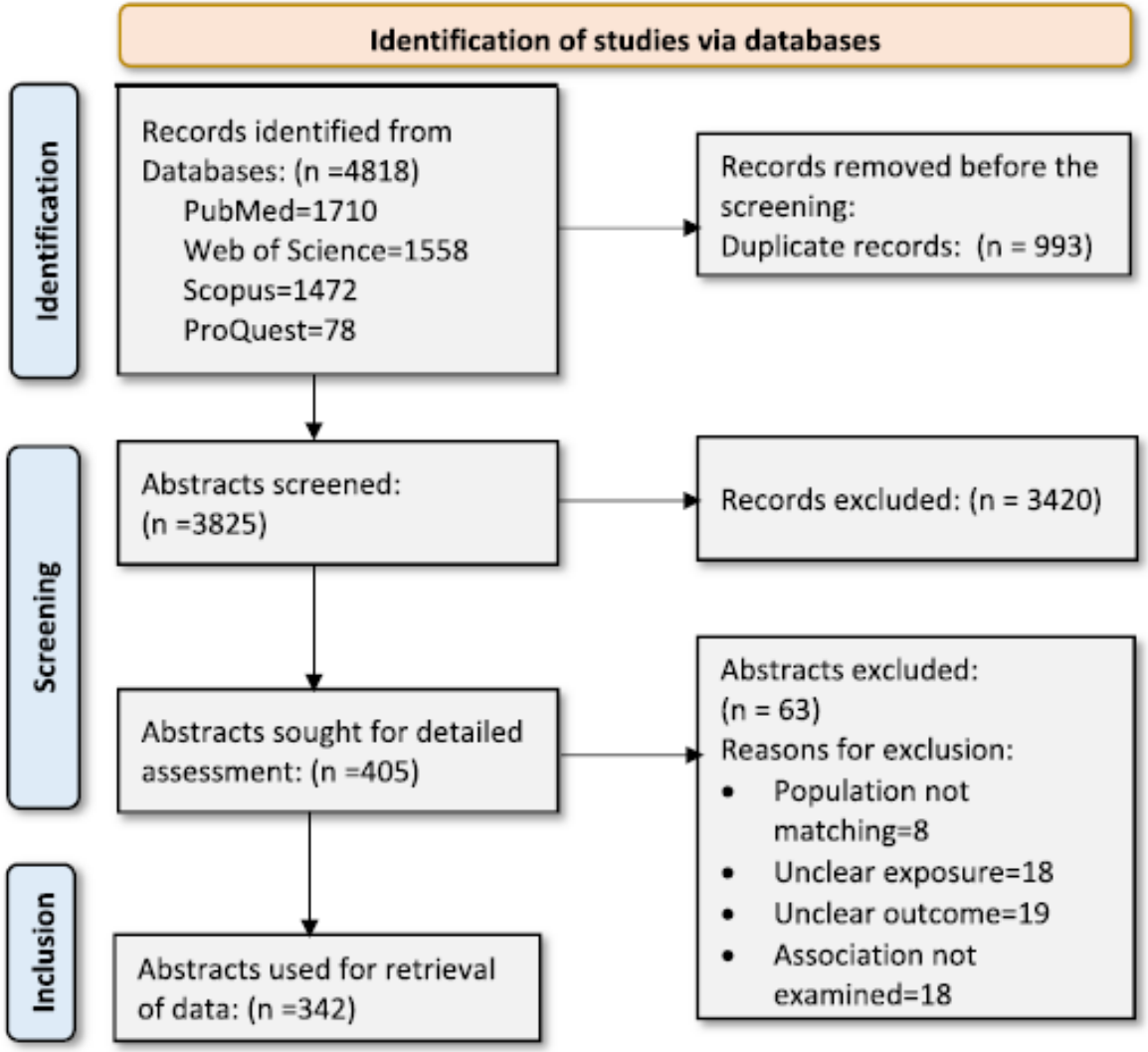
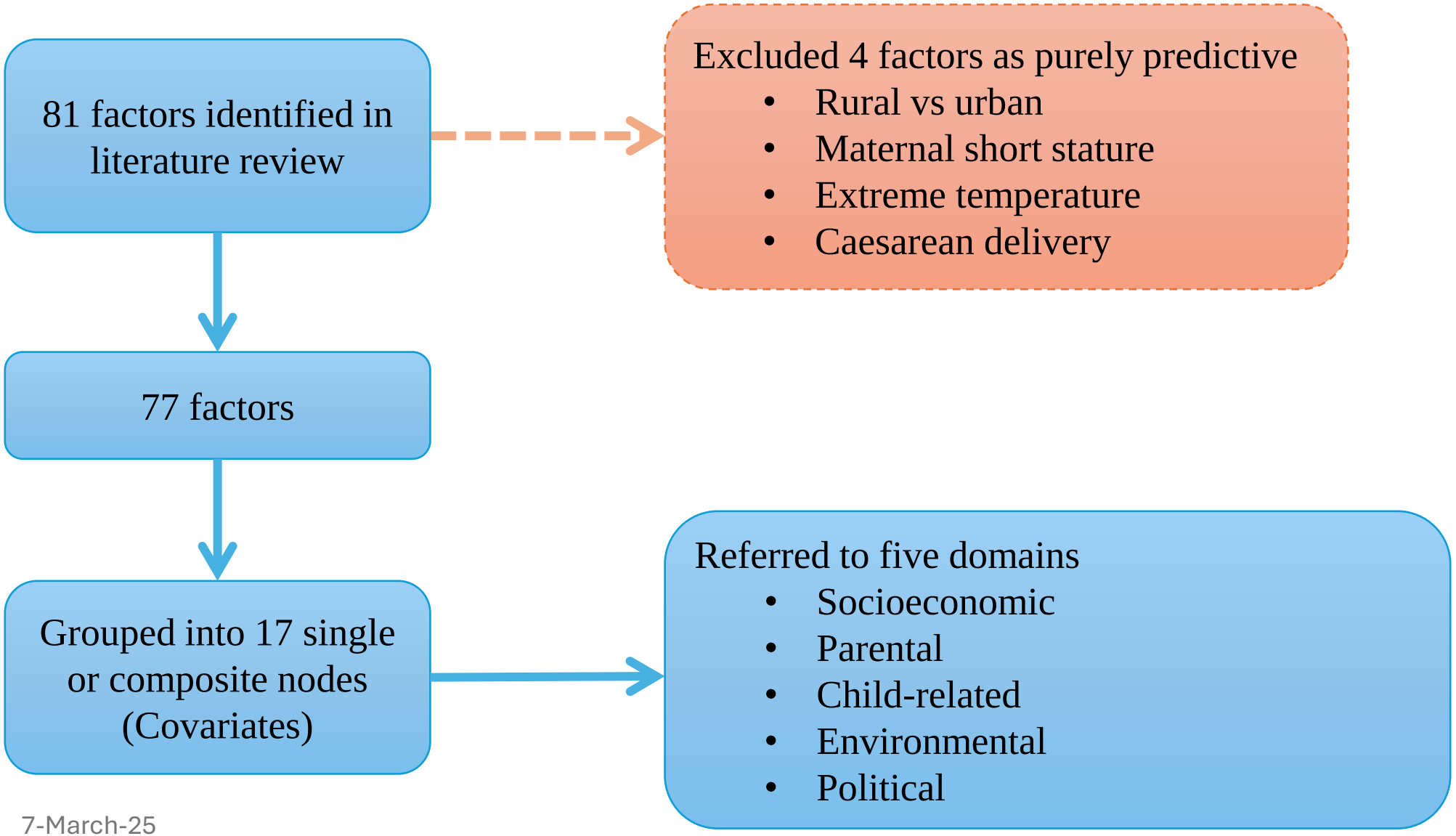


Figure 1. Flow chart showing the result of literature search and selection of abstracts for qualitative synthesis.

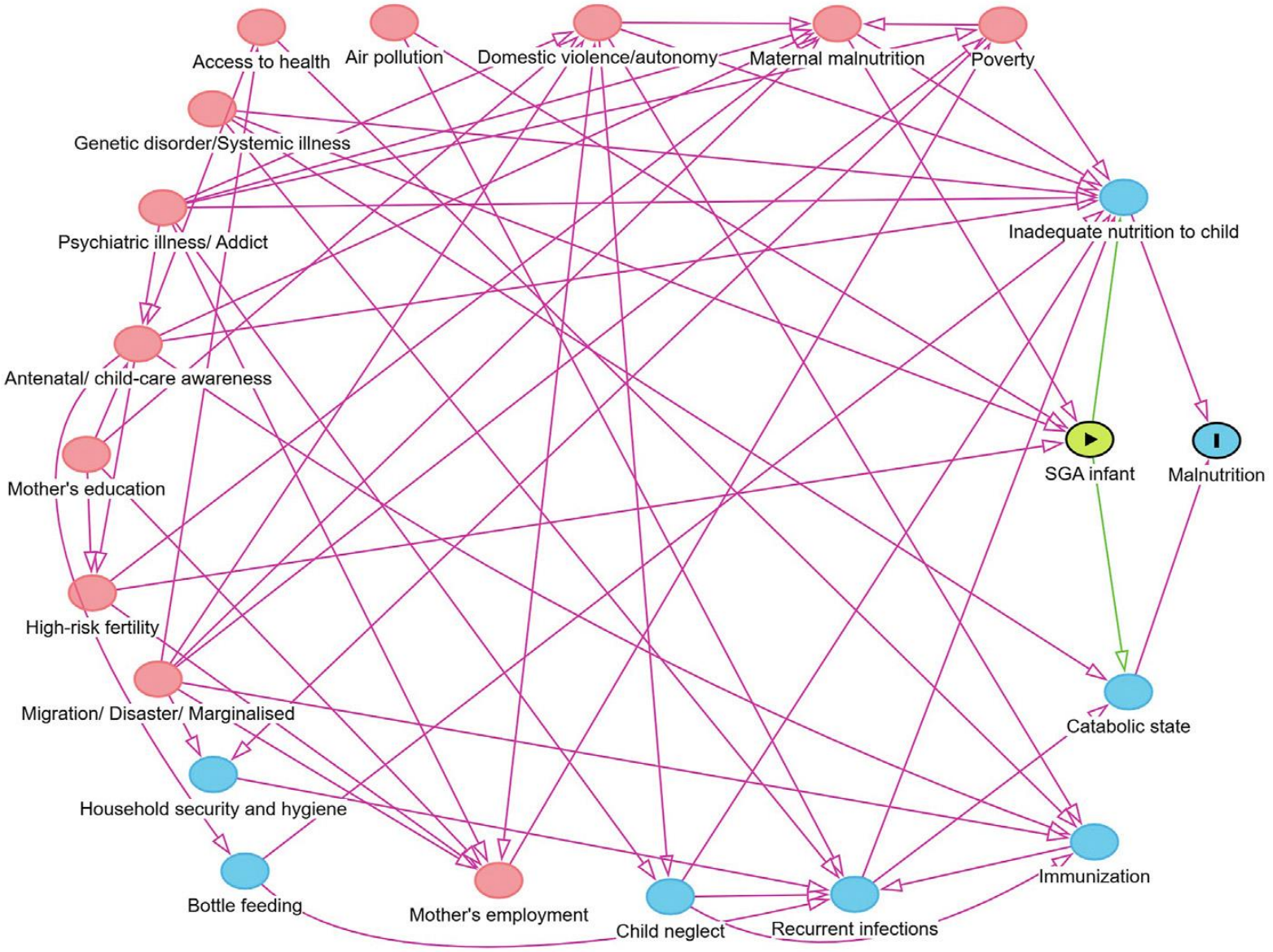
Study characteristics of included abstracts (n=342)

Study variable	No. of studies (%)	Study variable	No. of studies (%)
Country of publication		***Residence***	
Bangladesh	93 (26.9)	Both rural and urban	284 (82.3)
Bhutan	3 (0.9)	Rural	36 (10.4)
India	136 (39.4)	Urban	21 (6.1)
Maldives	2 (0.6)		
Nepal	38 (11)		
Pakistan	45 (13)		
Sri Lanka	7 (2)		
Study design		***Anthropometric index***	
Case-control study	14 (4.1)	Weight-for-age	188 (54.4)
Cohort study	12 (3.5)	Weight-for-height/length	180 (52.1)
Cross-sectional	261 (75.7)	Mid-upper arm circumference	11 (3.1)
Survey	54 (15.6)	Body mass index	2 (0.5)
		Length/Height-for-age	249 (72.1)

Factor identification and handling



DAG and minimal sufficient adjustment sets



- ✓ **21 nodes**
  (primary exposure, outcome, mediators, and covariates)
- ✓ **59 edges**
  interconnecting the nodes
- ✓ **12 minimal sufficient adjustment sets**
  estimate the total effect of SGA on malnutrition

DAG and minimal sufficient adjustment sets

Set 1	Access to health, Air pollution, Antenatal/ child-care awareness, Domestic violence/autonomy, Genetic disorder/Systemic illness, Maternal malnutrition, Migration/ Disaster/ Marginalised, Poverty, Psychiatric illness/ Addict
Set 2	Access to health, Antenatal/ child-care awareness, Bottle feeding, Child neglect, Domestic violence/autonomy, Genetic disorder/Systemic illness, High-risk fertility, Household security and hygiene, Maternal malnutrition, Migration/ Disaster/ Marginalised, Recurrent infections
Set 3	Access to health, Antenatal/ child-care awareness, Bottle feeding, Child neglect, Domestic violence/autonomy, Genetic disorder/Systemic illness, High-risk fertility, Maternal malnutrition, Migration/ Disaster/ Marginalised, Poverty, Recurrent infections
Set 4	Air pollution, Antenatal/ child-care awareness, Child neglect, Domestic violence/autonomy, Genetic disorder/Systemic illness, Household security and hygiene, Immunization, Maternal malnutrition, Poverty, Psychiatric illness/ Addict

DAG and minimal sufficient adjustment sets

Set 5	Air pollution, Antenatal/ child-care awareness, Domestic violence/autonomy, Genetic disorder/Systemic illness, Maternal malnutrition, Migration/ Disaster/ Marginalised, Mother's education, Poverty, Psychiatric illness/ Addict
Set 6	Air pollution, Antenatal/ child-care awareness, Child neglect, Domestic violence/autonomy, Genetic disorder/Systemic illness, Immunization, Maternal malnutrition, Migration/ Disaster/ Marginalised, Poverty, Psychiatric illness/ Addict
Set 7	Air pollution, Genetic disorder/Systemic illness, High-risk fertility, Maternal malnutrition
Set 8	Antenatal/ child-care awareness, Bottle feeding, Child neglect, Domestic violence/autonomy, Genetic disorder/Systemic illness, High-risk fertility, Household security and hygiene, Maternal malnutrition, Migration/ Disaster/ Marginalised, Mother's education, Psychiatric illness/ Addict, Recurrent infections

DAG and minimal sufficient adjustment sets

Set 9	Antenatal/ child-care awareness, Bottle feeding, Child neglect, Domestic violence/autonomy, Genetic disorder/Systemic illness, High-risk fertility, Household security and hygiene, Maternal malnutrition, Migration/ Disaster/ Marginalised, Mother's employment, Psychiatric illness/ Addict, Recurrent infections
Set 10	Antenatal/ child-care awareness, Bottle feeding, Child neglect, Domestic violence/autonomy, Genetic disorder/Systemic illness, Maternal malnutrition, Poverty, Psychiatric illness/ Addict, Recurrent infections
Set 11	Bottle feeding, Child neglect, Genetic disorder/Systemic illness, High-risk fertility, Household security and hygiene, Immunization, Maternal malnutrition, Recurrent infections
Set 12	Bottle feeding, Child neglect, Genetic disorder/Systemic illness, High-risk fertility, Immunization, Maternal malnutrition, Migration/ Disaster/ Marginalised, Poverty, Recurrent infections

Discussion

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Discussion

- Even large sample size datasets from cluster surveys on childhood nutrition cannot mitigate confounding bias, because the list of covariates is often incomplete and selected without causal reasoning.

- This performed a robust systematic review of the literature to identify the causal factors unique to the Indian subcontinent.

- This ensured comprehensiveness in the adjustment set and minimized unmeasured confounding.

Discussion

- This is the first study to integrate causal theory recommendations to develop an evidence-based DAG for malnutrition among SGA infants.
- In a systematic review, *Christian et al* pooled risk estimates of stunting, wasting, and underweight due to SGA and preterm birth.
- OR = 2 to 3 times higher in term-SGA infants than in term appropriate-for-gestational age infants.
- However, the trustworthiness of this effect size is debatable, because the adjustment set was incomplete and not based on a causal model.

Discussion

Strengths

- Formulated estimands that catered to the interests of different stakeholders.
- The availability of 12 minimal sufficient adjustment sets ensures flexibility in selection of confounders.

Discussion

Limitations

- Adopted a pragmatic approach to extract the required information from abstracts but did not review the full texts.
- Adopted a rapid review methodology in which research quality appraisals were not performed.
- This qualitative evidence synthesis is not backed by quantitative analyses as that was beyond the scope of this study.

Conclusion

- This offers an evidence-based DAG that will minimize bias due to improper selection of causal factors in studies focusing on malnutrition in term-SGA infants.

- The availability of different estimands, causal models, and minimum adjustment sets can help researchers design future research and analyze their data.

Thank you…