

## PROSPERO

### International prospective register of systematic reviews

The effects of short-stature-for-age on cardiovascular and metabolic health in children: a systematic review

*Ines Varela-Silva, Emma O'Donnell, Hugo Azcorra, David Oxborough, Susana Monserrat-Revilla, Samantha Sanchez, Nina Mendez*

#### Citation

Ines Varela-Silva, Emma O'Donnell, Hugo Azcorra, David Oxborough, Susana Monserrat-Revilla, Samantha Sanchez, Nina Mendez. The effects of short-stature-for-age on cardiovascular and metabolic health in children: a systematic review. PROSPERO 2019 CRD42019123014 Available from: [http://www.crd.york.ac.uk/PROSPERO/display\\_record.php?ID=CRD42019123014](http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019123014)

#### Review question

How does short stature-for-age in children associate with indicators of cardiovascular and metabolic health?

#### Searches

- NCBI (MeSH and PubMed)

- Scopus

- Web of Science

We are restricting the search to:

1) Studies published in English

2) Studies with human samples only

#### Types of study to be included

Observational studies (longitudinal and cross-sectional) from original articles and short reports.

#### Condition or domain being studied

Short stature has been associated with coronary heart disease in adults (Paajanen et al, 2010), but similar effects have not been established in children. We aim to identify cardiovascular and metabolic health indicators that are associated with height-for-age in children. These consist of any measures of cardiovascular health and metabolic syndrome such as, but not limited to: abdominal obesity; atherogenic dyslipidaemia; hypertension; hyperglycaemia; insulin resistance; body-mass-index, height-adjusted fat mass, pulse rate, insulin-resistance, triglycerides, low density lipoprotein cholesterol, high density lipoprotein cholesterol, and structural and electrical cardiac dysfunction.

Paajaneen et al (2010).European Heart Journal (2010) 31, 1802–1809 doi:10.1093/eurheartj/ehq155

#### Participants/population

Children (male or female) aged 4 to 12 years, without congenital anomalies or known clinical pathologies .

#### Intervention(s), exposure(s)

Metabolic syndrome is defined as a cluster of symptoms that are risk factors for cardiovascular diseases and type 2 diabetes mellitus. The major components of metabolic syndrome include abdominal obesity; atherogenic dyslipidemia; hypertension; hyperglycemia; insulin resistance; a proinflammatory state; and a prothrombotic (thrombosis) state (NCBI-MeSH Definition).

Cardiovascular dysfunction is defined as dysfunction of the heart and the blood vessels (NCBI-MeSH definition).

Early life adverse factors , affecting growth and health in general, may potentiate the onset of one or more one of these outcomes in childhood.

## Comparator(s)/control

We will use:

- a) Cut-off points to define short stature-for-age defined by:
  - i) the WHO standards (children up to 5 years of age) or the WHO references (5+years of age) as -2 standard deviations (SD) of the median value of height-for-age, by sex;
  - ii) NHANES/CDC references as height-for-age below the 5th percentile
- b) Cut-off points for blood pressure, glycemia, and dyslipidaemia reference values set by the American Heart Association.
- c) Cut-off points for body-mass index-for-age (International Obesity Task Force - IOTF, WHO and Centers for Disease Control
- d) Cut-off points for abdominal obesity and other remaining metabolic syndrome reference values set by the WHO.

## Context

All measurement outcomes must have been taken by trained research staff or a medical professional. Studies that rely on any subjective, self-reported data will not be included. Outcomes can be measured in children between ages of 4 and 12 but must be measured before any intervention or treatment. Therefore, only baseline observational studies will be included.

## Main outcome(s)

The primary outcome are cardiovascular and metabolic indicators associated with stature-for-age in children. The secondary outcome consists of any are other measures of metabolic syndrome such as, but not limited to: abdominal obesity; atherogenic dyslipidaemia; hypertension; hyperglycaemia; insulin resistance; body-mass-index, height-adjusted fat mass, pulse rate, insulin-resistance, triglycerides, and high-density lipoprotein cholesterol, ow density lipoprotein cholesterol, and structural or electrical cardiac disfunction.

### *Timing and effect measures*

We will only consider baseline studies in which no interventions have been conducted. We will be narrowing our time search to the last 10 years, which means that it is unlikely that secular trends in height will bias the interpretation of the results.

The mentioning of short-stature or any of the metabolic outcomes are not, per se, a condition for inclusion. The articles must show that they tested for effects of height upon the cardiovascular and metabolic outcomes.

## Additional outcome(s)

None at this stage.

## Data extraction (selection and coding)

Stage I. Ines Varela-Silva (IVS) will screen for title and abstract according to the eligibility criteria. Articles that do not meet the inclusion criteria will be excluded. Articles that do not clearly show they meet the inclusion criteria, from the title and abstract, will pass to stage II. Articles that meet the inclusion criteria will pass to stage II.

Stage II. Potentially eligible full texts will be obtained and screened by IVS against the inclusion criteria. Studies not meeting the inclusion criteria will be excluded at this stage, and the reasons for exclusion will be noted.

Stage III. Nina Mendez (NM) and Emma O'Donnell (EO) will double screen 10% of the full texts included in stage II. If any discrepancies on eligibility occur at this stage these will be discussed and solved by the entire team.

Stage IV. Other key papers identified by the team that have been missed in the searches will be included at this stage. Full-texts of such papers will be obtained and screened against the inclusion criteria by IVS, and those meeting the criteria will be included in the review.

Data to be extracted:

- Citation details (title, year of publication, authors, study ID, country of origin,)
- Study details (design, time, duration, setting, sample size, country/region, study objectives)
- Participant details (baseline participant characteristics)
- Journal of publication
- Outcome(s)
- Methods of statistical analysis used to assess the association of interest
- Key statistical analyses results
- Details on any confounding/mediating factors where adjustments were made, for the association of interest.

Data will be extracted and tabulated by IVS. NM will extract and tabulate information on 10% of the papers included for quality control. If any uncertainty or discrepancies arise after these steps, it will be recorded.

### Risk of bias (quality) assessment

We will design and use a specific rubric (quantitative and qualitative instrument) to reduce the risks of bias. A rubric is a guide that list specific criteria for grading and/or scoring academic papers, projects, or tests. Therefore, the articles will be scored both quantitatively and qualitatively. Specific checklists to score the included papers and to reduce the risk of bias will be developed by the team. As a starting point, higher scores will be given to papers which use the standard/references cut-off points, detailed in question 21. Lower scores will be given to papers that associate stature with any cardiovascular and metabolic syndrome outcomes, but do not use standard/references cut-off points. The lowest scores will be given to papers that include associations between height and any of the markers but whose aim was not primarily focused on this association.

### Strategy for data synthesis

- A narrative synthesis of the findings will be provided and organised around the association found between height and cardiovascular and metabolic syndrome indicators.
- A descriptive synthesis of the outcomes will be tabulated and the quantitative scores regarding the quality of the papers will be provided.
- If suitable (pending the number of articles included for analysis), comparison of the presence/absence of the main outcomes, across studies, will be developed and discussed.

### Analysis of subgroups or subsets

If suitable, analysis will be performed by race/ethnic group, gender, socioeconomic status (SES) or poverty level for any relevant cardiovascular and metabolic syndrome outcomes included in the search criteria.

### Contact details for further information

## PROSPERO

### International prospective register of systematic reviews

Ines Varela-Silva  
m.i.o.varela-silva@lboro.ac.uk

#### Organisational affiliation of the review

Loughborough University  
<http://lboro.ac.uk>

#### Review team members and their organisational affiliations

Dr Ines Varela-Silva. Loughborough University  
Dr Emma O'Donnell. Loughborough University  
Dr Hugo Azcorra. Cinvestav, Ecologia Humana, Merida  
Dr David Oxborough. Liverpool John Moores University  
Dr Susana Monserrat-Revilla. Loughborough University  
Ms Samantha Sanchez. Cinvestav, Ecologia Humana, Merida  
Dr Nina Mendez. Universidad Marista de Merida

#### Anticipated or actual start date

18 February 2019

#### Anticipated completion date

30 September 2019

#### Funding sources/sponsors

None

#### Conflicts of interest

#### Language

English

#### Country

England, Mexico

#### Stage of review

Review\_Ongoing

#### Subject index terms status

Subject indexing assigned by CRD

#### Subject index terms

Cardiovascular System; Child; Dwarfism; Growth Disorders; Humans

#### Date of registration in PROSPERO

14 February 2019

#### Date of publication of this version

14 February 2019

#### Details of any existing review of the same topic by the same authors

#### Stage of review at time of this submission

<b>Stage</b>	<b>Started</b>	<b>Completed</b>
Preliminary searches	No	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

### Versions

14 February 2019

---

#### PROSPERO

This information has been provided by the named contact for this review. CRD has accepted this information in good faith and registered the review in PROSPERO. CRD bears no responsibility or liability for the content of this registration record, any associated files or external websites.