

# INPLASY

## Evidence mapping of metabolic changes in children with growth hormone deficiency (GHD) treated with growth hormone

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### ADMINISTRATIVE INFORMATION

**Support** - Novo Nordisk (China).

**Review Stage at time of this submission** - Other - Not specified.

**Conflicts of interest** - You Wu and Yuning Zhao are the employees of Novo Nordisk, but will not be involved in the process of data generation.

**INPLASY registration number:** INPLASY202450064

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 May 2024 and was last updated on 14 May 2024.

### INTRODUCTION

**Review question / Objective** Population: population with confirmed GHD and less than 18 years old. Intervention: growth hormone (GH) for GHD population, no combined medication for GHD disease, no limitation on the dosage, frequency, treatment duration. Comparison: A: post-treatment versus baseline. B: non-medical therapy. C: matched healthy population. Primary outcomes: Metabolic outcomes: glucose metabolism, lipid metabolism, calcium and phosphorus metabolism, thyroid level. Secondary outcomes: Body composition; Body mass index (BMI); Waist-hip ratio (WHR); New biomarkers; Study design: randomized controlled trial (RCT), cohort study, case-control study, for comparison of post-treatment and baseline only include RCTs.

**Background** Growth hormone deficiency (GHD) occurs as a result of insufficient production of GH by the pituitary glands, resulting in a short stature

as the main symptom. The prevalence of childhood GHD has been reported to range from 1 in 3500 to 1 in 30,000. The treatment for GHD is a supplement of recombinant human growth hormone (rhGH). The effect of GH treatment on increasing the height of patients with GHD has been confirmed. However, the other effects of GH on GHD children, such as metabolic effects, are often overlooked.

**Rationale** Several guidelines underscore the necessity of understanding the current evidence regarding GH treatment on metabolic impacts, particularly on glucose metabolism, lipid metabolism, and bone density. An evidence map is a systematic review of a wide range of studies presented visually or in tables to identify knowledge gaps and/or future research directions. We plan to conduct evidence maps to summarize current research findings in the field to serve as a foundation for guideline developers, identify knowledge gaps, and highlight the need for future research.

## METHODS

**Strategy of data synthesis** The following databases will be searched: PubMed, EMBASE, Cochrane Library, CNKI, Wanfang and China Biology Medicine (CBM), using terms "growth hormone deficiency", "growth hormone" and "pediatrics", with no limitations on time and language.

**Eligibility criteria** Comparative studies focusing on metabolic changes after GH treatment in GHD children, including studies comparing with pre-treatment (RCTs only), GH versus non-pharmacological treatment, and GHD children versus healthy children; studies comparing with healthy children must report differences in metabolic outcomes at baseline as well as post-treatment.

### Source of evidence screening and selection

Two reviewers will screen the literature after reading the titles and abstracts of the search results. All potentially relevant citations will be requested and inspected in detail using the full-text version. Disagreements will be resolved by discussion, with assistance from a third party if necessary. A PRISMA flow diagram will be constructed to show the full study-selection process.

**Data management** Data from each literature will be extracted by one reviewer and double checked by another reviewer by using a standardized data extraction form. Any disagreements will be resolved by discussion, with the assistance from a third party if necessary. A PICOS structure will be used to formulate the data extraction, as follows:

- 1) General study characterizes: the first author's name, the published year, trial registration number, location, centers.
- 2) Participants: sample size, gender and age of patients, waist-hip ratio (WHR), adolescent developmental state and so on.
- 3) Interventions: dosage, mode of administration, frequency and treatment duration.
- 4) Outcomes: definition, measure tool, measure time, conclusion, p value.
- 5) Study design: study type.

**Presentation of the results** Baseline characteristic will summarized in tables, including age, adolescent developmental state, peak GH, nourishment state, causes of GHD, and intervention characteristics. The geographical and publication year distribution will be presented in tables and bar graph.

The metabolic outcomes will be presented in bubble plot. The X axis will present the time of outcomes been measured, Y axis list the outcomes. The color of the bubble will represent the conclusion of outcomes, including "Significant increase", "Significant decrease" and "No difference". The size of bubble will represent the sample size of the studies. For the comparison between GHD and healthy children, the shape of the bubble will represent the baseline differences between GHD and healthy children.

**Language restriction** English or Chinese.

**Country(ies) involved** China.

**Other relevant information** None.

**Keywords** systematic review, pediatric growth hormone deficiency, growth hormone, metabolic.

### Contributions of each author

Author 1 - Wei Wu.

Author 2 - Ningyi Song.

Author 3 - Yue Zhao.

Author 4 - Caiqi Du.

Author 5 - Yuning Zhao.

Author 6 - You Wu.

Author 7 - Xiaoping Luo.