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Long-term effects of an intensive care admission during childhood

Submission date
24/10/2024

Recruitment status
Recruiting

Registration date
07/11/2024

Overall study status
Ongoing

Last Edited
07/11/2024

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Critically ill children are admitted to a pediatric intensive care unit (PICU) where they receive support for vital organ functions. Without this support, their risk of death is significantly high. Fortunately, major advancements in pediatric intensive care have reduced death rates to very low levels. Consequently, research has shifted from finding strategies to decrease death rates to reducing illness, both during PICU stays and after returning to daily life. Many survivors face health issues and problems in physical, emotional, social, and cognitive functioning, collectively referred to as post-intensive care syndrome in children (PICS-p). Previous studies focused on childhood issues, while the longer-term impacts during puberty, adolescence, and young adulthood remain insufficiently explored. This study aims to investigate the effects of critical illness on development during these crucial phases, particularly regarding puberty and body composition.

Who can participate?
Former PICU patients who were critically ill and healthy matched controls

What does the study involve?
The study will involve a comprehensive assessment of the development of former critically ill children 12 years after their PICU admission, comparing their growth, body composition, cardiometabolic risk factors, physical activity, health status, and puberty development with healthy peers. Evaluations will include clinical tests and questionnaires assessing neurocognitive functioning, emotional/behavioral health, and quality of life. Additionally, biological samples such as blood, urine, buccal swabs, and hair will be collected to investigate potential underlying mechanisms, focusing on epigenetic and hormonal/metabolic disruptions.

What are the possible benefits and risks of participating?
Possible benefits include contributing to a better understanding of long-term outcomes for critically ill children, potentially leading to improved preventive measures and management strategies for long-term issues. Risks are minimal but may involve the discomfort associated with biological sample collection and participating in clinical assessments.

Where is the study run from?
University Hospital Leuven (UZ Leuven) (Belgium)

When is the study starting and how long is it expected to run for?
September 2023 to June 2029

Who is funding the study?
Flemish Government Methusalem Program (Belgium)

Who is the main contact?
Prof. Dr Greet Van den Berghe, greet.vandenberghe@kuleuven.be

Contact information

Type(s)
Public, Principal investigator

Contact name
Prof Greet Van den Berghe

ORCID ID
https://orcid.org/0000-0002-5320-1362

Contact details
Herestraat 49
Leuven
Belgium
3000
+32 (0)16 344021
greet.vandenberghe@kuleuven.be

Type(s)
Scientific

Contact name
Prof Ilse Vanhorebeek

ORCID ID
https://orcid.org/0000-0002-5261-5192

Contact details
Herestraat 49
Leuven
Belgium
3000
+32 (0)16 33 05 32
ilse.vanhorebeek@kuleuven.be

Type(s)
Scientific

Contact name
Prof Jan Gunst

ORCID ID
https://orcid.org/0000-0003-2470-6393

Contact details
Herestraat 49
Leuven
Belgium
3000
+32 (0)16 34 40 21
jan.gunst@uzleuven.be

Type(s)
Scientific

Contact name
Dr An Jacobs

ORCID ID
https://orcid.org/0000-0003-2556-4454

Contact details
Herestraat 49
Leuven
Belgium
3000
+32 (0)16348161
an.jacobs@uzleuven.be

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
S69234

Study information

Scientific Title
Post-Intensive Care Syndrome in children (PICS-p): long-term harm extending into puberty, adolescence and young adulthood

Acronym
PICS-pub

Study objectives
Paediatric critical illness evokes a form of Post-Intensive Care Syndrome in children (PICS-p) that extends well beyond childhood, characterised by abnormal development into puberty, adolescence and young adulthood, with vulnerability depending on a priori identifiable risk factors.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 18/10/2024, Ethics Committee Research UZ/KU Leuven (Herestraat 49, Leuven, 3000, Belgium; +32 (0)16 34 86 00; ec@uzleuven.be), ref: S69234

Study design
Long-term follow-up of an interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Other, Quality of life

Health condition(s) or problem(s) studied
Post-intensive care syndrome in children

Interventions
This is a long-term follow-up study of former critically ill children who had been included in the large, multicentre PEPaNIC randomised controlled trial on the impact of early versus late initiation of supplemental parenteral nutrition in the PICU (n = 1440) and of a cohort of age- and sex-matched healthy children as controls (n = 441).

The former PEPaNIC patients will have a standardised assessment of clinical and functional outcomes 12 years after PICU admission, in parallel with similar follow-up of the control cohort. The researchers will collect blood, urine, buccal mucosa and hair samples.

Intervention Type
Other

Primary outcome(s)
1. Clinical assessment of growth (measured height and body weight, calculated BMI, total body fat mass and total body muscle mass as measured via dual-energy X-ray absorption [DEXA] scan) at 12-year follow-up
2. The developmental stage of puberty at 12-year follow-up, as based on interrogation of Tanner stages with the use of a sex-specific questionnaire

Key secondary outcome(s))
All outcomes are measured at the 12-year follow-up:
1. Health status: diagnosis of a somatic illness, diagnosis of a psychiatric illness, and incidence of hospital admission for medical, surgical or psychiatric reasons during the past 12 years for participants in the control group or during the 12 years following admission to the PICU for

PEPaNIC participants. Measured by a structured interview with the parents or caregivers, and/or the participants if competent and old enough.
2. Additional measures of physical growth: measurement of leg length and sitting height, and calculation of the proportion of leg length over total height and sitting height ratio at 12-year follow-up.
3. Additional measures of body composition:
3.1. Total bone mass and localised (arms, legs, and trunk) bone mass, fat mass and lean tissue mass measured via dual-energy X-ray absorption (DEXA) scan at 12-year follow-up
3.2. Surrogate markers of body composition (waist circumference as a measure of central adiposity/obesity, skinfold thickness as a measure of subcutaneous body fat at the triceps and subscapular level (allowing estimation of body fat with the use of the Slaughter equation), a combination of mid-upper arm circumference and triceps skinfold as a marker of muscle mass.
4. Additional measures of pubertal and further development:
With the use of sex-specific questionnaires on pubertal development also interrogates other aspects of puberty development and the time of reaching specific a priori defined stages:
4.1. Development of axillary hair
4.2. Acne
4.3. Menarche
4.4. Growth of facial hair
4.5. First ejaculation of semen
4.6. Voice break
5. During the interrogation of medical history related to the occurrence of somatic illness or hospital admission, health conditions or previous therapies will be documented, including those that may interfere with pubertal development.
6. Where possible, the researchers also aim to evaluate the next crucial developmental stage going in the direction of measures of reproductive health/fertility:
6.1. Female participants will be asked about the heaviness and regularity of their menstruation /menstrual cycle
6.2. For male participants, serum inhibin B levels will be quantified as marker of the level of spermatogenesis, providing a valuable alternative for sperm sample analysis.
7. Biological parents of the participants will be interrogated regarding timing of their pubertal development (“normal”, “delayed” or “precocious” for the father; age menarche for the mother).
8. Bone age as determined by hand X-ray at 12-year follow-up
9. Cardiometabolic risk factors: systolic and diastolic blood pressure, glycated haemoglobin (HbA1c), insulin, glucose, high-molecular-weight adiponectin, leptin, triglycerides, LDL- and HDL-cholesterol at 12-year follow-up
10. Physical activity: daily physical activity assessed with an activity-tracking device (Actigraph accelerometer), measured for 7 days following the 12-year follow-up appointment.
11. Neurocognitive functioning at 12-year follow-up:
11.1. General intelligence measured using the Wechsler Intelligence Scale for Children or Adults
11.2. Visuo-motor integration measured using the Beery-Buktenica Developmental Test of Visual-Motor Integration
11.3. Attention and executive functions measured using the computerised tasks of the Amsterdam Neuropsychological Tasks system
11.4. Immediate and delayed verbal-auditory and visual memory measured using Children /Wechsler Memory Scales
11.5. Executive functioning measured using the Behaviour Rating Inventory of Executive Function questionnaire, with use of different informant-specific versions (parents/caregivers or participant self-report)
12. Emotional and behavioural problems will be assessed with internationally recognised and validated questionnaires:
12.1. Child Behaviour Checklist (CBCL) or Adult Behaviour Checklist (ABCL) to be completed by

the parents/caregivers
12.2. Youth (YSR) or Adult Self Report (ASR) to be completed by the participants if competent
13. Daily life impact:
13.1. Interrogation of the participants' school participation, highest level of education and/or employment status, leisure-time spending, ability to participate in social roles and activities, relationships, and use of follow-up services (semi-structured interview combined with PROMIS ability to participate in social roles and activities questionnaire items).
13.2. Subjective evaluation of physical, emotional, and social functioning of the participants in daily life: health-related quality-of-life questionnaires. For participants up to 17 years, the PROMIS Short Forms will be used.

Completion date
01/06/2029

Eligibility

Key inclusion criteria
1. Participated in the PEPaNIC trial as a critically ill patient or having been recruited as a healthy child within the control group for a longitudinal follow-up in parallel with the PEPaNIC patients
2. Survival up to the 12-year follow-up time point

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
12 years

Upper age limit
30 years

Sex
All

Key exclusion criteria
No informed consent

Date of first enrolment
04/11/2024

Date of final enrolment
31/12/2027

Locations

Countries of recruitment
Belgium

Netherlands

Study participating centre
UZ Leuven
Herestraat 49
Leuven
Belgium
3000

Study participating centre
Erasmus MC
Dr. Wolewaterplein 40
Rotterdam
Netherlands
3015

Sponsor information

Organisation
Universitair Ziekenhuis Leuven

ROR
https://ror.org/0424bsv16

Funder(s)

Funder type
Government

Funder Name
Vlaamse regering

Alternative Name(s)
Flanders, Flemish Government, Flandre, Flandern, Vlaanderen

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Belgium

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publicly available repository (RDR; https://rdr.kuleuven.be/).

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes