Towards lifelong healthy LUNGS: a multidisciplinary follow-up framework for preterm infants.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON52324

Source
ToetsingOnline

Brief title
LONG LOVE

Condition

- Respiratory tract infections

Synonym
Lower Respiratory Tract Infections; Bronchiolitis

Research involving
Human

Sponsors and support

Primary sponsor: Franciscus Gasthuis & Vlietland
Source(s) of monetary or material Support: BeterKeten (stichting),Revenio Research LTD, Finland

Intervention

Keyword: eHealth, Neonatology, Paediatric Pulmonary Health, Prematurity, Preventive Healthcare, Pulmonary Diseases

Outcome measures

Primary outcome

Total number of physician diagnosed lower RTI and wheezing episodes in the

first 18 months of life.

Secondary outcome

time to first lower RTI or wheezing episode

total number of RTI

total number of wheezing episodes

distribution of viruses (in case of hospital admission)

medication use (bronchodilators, corticosteroids, antibiotics)

lung function as measured by expiratory variability index and relation with

LRTI/wheezing

comparison of expiratory variability index in moderate/late prematurity

compared to term cohort (reference cohort from other center)

correlation between expiratory variability index and other pulmonary function

analyses

association between expiratory variability index and number of RTI/wheezing

outdoor air quality

indoor air quality

association between air quality and number of RTI

quality of life

classification of high-risk patients

costs- and cost-effectiveness

Study description

Background summary

Approximately 8% of all births occur between 30-36 weeks of gestation (moderate-late prematurity). Respiratory tract infections (RTI) and wheezing illnesses disproportionally affect preterms, resulting in a 1.5-2 fold higher hospitalisation rate during the first years of life compared to term born children. Besides prematurity, several other modifiable influencing factors are associated with increased risk of respiratory morbidity and impaired pulmonary development. These factors include rapid weight gain and obesity at early age, tobacco smoke exposure, air pollution, microbiome composition and recurrent RTI.

To promote optimal lung health and development in moderate-late preterm infants, increased respiratory health surveillance and protection against RTI in early life might be crucial. Previous research has shown that the introduction of a multidisciplinary follow up framework in children with bronchopulmonary dysplasia resulted in a significant reduction of hospital readmissions.

Despite the burden of respiratory disease, moderate to late preterms do not currently receive standardised respiratory follow-up care. With LONG LOVE we introduce a novel follow-up framework tailored for preterms and designed to improve respiratory health. As the risk of the onset of pulmonary disease is further increased by postnatal factors such as tobacco smoke exposure, air pollution and RTI, our main focus is the detection and treatment of these modifiable influencing factors. LONG LOVE incorporates eHealth and new technology in order to measure pulmonary function and air quality. Intervention strategies include counselling on nutrition, lifestyle, medication and improving indoor air quality.

Study objective

The project*s overarching aim is to diminish respiratory disease burden in moderate-late preterm born infants in their first 18 months of life.

We have formulated the following specific objectives:
1. Determine whether the introduction of our follow-up framework will reduce the number and/or severity of RTI and wheezing episodes in the first 18 months of life

2. Analyse the predictive value of nocturnal impedance pneumatography on lower respiratory symptoms in premature born infants < 1 year of age. Further, correlate this novel tool to other forms of pulmonary function analyses such as the Lung Clearance Index and Hypoxic Challenge Test.
3. Conduct a cost-benefit analysis after the implementation of our framework.

Study design

We intend a quasi-experimental design based on a non-randomized cluster trial, in which moderate-late preterm born infants will be allocated to the intervention or control group based on location of birth. This design was chosen based on the limited amount of participating clusters and feasibility. As a quasi-experimental design can result in confounding by cluster and to increase internal validity, subjects of the control and intervention groups will be demographically matched at baseline[54,55]

Cluster 1
Consists of participants born in Franciscus Gasthuis (FG) and/or Vlietland (FV) and will be allocated to the intervention group, receiving additional (in addition to current standard of care) follow-up in accordance with our newly developed framework to identify modifiable influencing factors compromising pulmonary health using validated questionnaires, weekly monitoring of respiratory symptoms as reported by parents using an app, in- and outdoor air quality measurements and non-invasive pulmonary function measurements based on impedance pneumatography.
In case of any modifiable influencing factors, appropriate lifestyle and/or medical interventions will be undertaken.

Cluster 2 (control)
Consist of participants born in Maasstad Ziekenhuis (MSZ) and Albert Schweitzer Ziekenhuis (ASZ) and will receive standard of care follow-up.
Parents are requested to provide informed consent for the registration of outcome measurements and requested to complete validated questionnaires. Data on utilization of medical services will be inquired to avoid recall bias.

Intervention

Follow-up regimen after premature birth using the LONG LOVE framework:

Identification of modifiable influencing factors
Five study visits are scheduled to monitor health status on 1-1.5*, 3, 6, 12 and 18 months of age. These visits are planned in conjunction with regular follow-up examinations. Well-being and other potential risks will be determined by: growth, nutritional problems, feeding mode, pets, maternal stress (Edinburgh Postnatal Depression Scale questionnaire), sleep (Infant Sleep Questionnaire (ISQ)), tobacco smoke exposure, day-care attendance, existence of

siblings.

Air quality measurements
Outdoor air analysis will be obtained using national and regional air measurement networks (RIVM Luchtmeetnet; DCMR Milieudienst Rijnmond). This network consists of a large number of air quality measurement sites, measuring harmful substances: nitric oxides (NOx, NO2), particulate matter (PM2.5, PM10) and ozone. Measurements will be taken from a station located nearest to the home address of the participant. Measurements are provided as publicly accessible data by the Dutch government.

Indoor air quality will be analysed using a commercially available environment monitor. This device offers real-time monitoring of air quality factors such as temperature, humidity, particulate matter (PM1, PM2,5, PM10), carbon dioxide(CO2), and volatile organic compounds (TVOCs). Readings are exported using the AirThings web platform. Air quality measurements will be taken from the living room for a total duration of 12 months. All recorded data is encrypted using 128-AES end-to-end encryption.

Pulmonary function analysis
Pulmonary function analysis using impedance pneumatography will be measured at 3, 6 and 12 months age during two consecutive nights using the Ventica recorder.

eHealth
All parents are requested to install a newly developed application on their phones when enrolled in the study. The app is used for a weekly evaluation of respiratory symptoms. The following clinical parameters/variables will be monitored throughout the study: Respiratory health will be determined as follows: physician-diagnosed lower RTI- and wheezing episodes, hospitalizations for respiratory problems, clinical variables such as other respiratory episodes, common colds, medication use (bronchodilators, corticosteroids, antibiotics).

Interventions
Aside from identification of potential health risks, our framework is designed to offer interventions if required. At baseline, all participants receive verbal and written information (App) defining potential hazardous factors regarding pulmonary development and overall health. In the event of pulmonary symptoms, parents are requested to consult a doctor.
In case of modifiable influencing factors, the following lifestyle and medical interventions will be performed:

In the case of 1.5 SDS weight gain or loss (based on birth weight), nutritional advice is provided by a paediatrician and follow-up by primary infant health care services.
In case of EPDS-scores >=12 (stress-depression mother) consultation by lifestyle

coach or community worker (Kleine Heldenhuis). If required, referral to general practitioner or psychologist/psychiatrist.
If sleep quality is affected (ISQ): medical advice and sleep training is provided by a paediatrician and/or primary infant health care services
In the case of pulmonary symptoms: clinical assessment by general practitioner or paediatrician. Administration of antibiotics according to Dutch board of Paediatricians guideline, optionally C-reactive protein measurement to prevent unnecessary antibiotics use
If one or both caretakers are smoking: consultation by general practitioner and primary infant health care services to provide stop smoking services
In case of inferior indoor air quality: visit by PhD-student or pulmonary care nurse to instruct how to improve air quality
Optimal identification and treatment of comorbidity: gastro-oesophageal reflux disease, vitamin D deficiency, iron deficiency anaemia by paediatrician
Active consultancy and treatment of nasal congestion using saline and-or xylometazoline by paediatrician
Bronchodilator/broncholytic (salbutamol) trial by pediatrician in event of recurrent clinical bronchial obstruction and/or abnormal expiratory variability index using impedance pneumatography. If bronchodilator therapy is regularly required (a minimum of 2 episodes 2-3 days of week for a minimal duration of two weeks), inhaled corticosteroids can be prescribed.

These interventions are performed by both primary and secondary healthcare professionals (including the PhD-student who has an active role in patient management). Primary infant healthcare services operating in the Rijnmond region will fulfill an important role and are directly involved with the implementation of this framework.

Study burden and risks

Safety is important in paediatric studies. All subjects will receive standard of care follow-up after preterm birth as specified by the directive *Te vroeg en/of small for gestational age (SGA) geboren kinderen'' of the Dutch Primary Infant Health Care Services (Jeugd Gezondheidszorg). However, subjects enrolled in cluster 1 and using our novel framework will experience better surveillance of pulmonary condition with an expected reduction of healthcare consumption (e.g. hospitalization and medication usage). Lung function analysis based on expiratory variation index is a non-invasive form of measurement and requires placement of four individual skin-friendly chest electrodes (as used for EKG and respiratory monitoring) near the armpits. A special bodysuit or shirt made from certified toxic-free Ökotex100 material is used to house the recorder. Measurements are taken at night and do not require cooperation. All other lung function analyses are non-invasive. Additonal (voluntary) lung test in Sophia Children's hospital are non-invasive and offer high success rates. There are no serious AEs anticipated in relation to pulmonary function testing.

The burden of participation in this study is expected to be minor. A total of 5

study visits are planned in conjunction with routine follow-up visits. s. Optional additional pulmonary function analysis requires an extra visit. Using the app to file a weekly report will take no more than 5 minutes.

Based on the assessment of benefits and risks, it is considered justified to perform this study. Any alleged risk to the subject is outweighed by potential near- and long-term benefits associated with better pulmonary surveillance and health.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Babies and toddlers (28 days-23 months)
Newborns
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

Moderate-late preterm infants (GA 30+0 - 35+6 weeks) without any other

significant underlying morbidity

Exclusion criteria

Underlying other severe respiratory diseases such as bronchopulmonary dysplasia (BPD); diaphragmatic hernia, other serious cogenital pulmonary disorders; hemodynamic significant cardiac disease; immunodeficiency; severe failure to thirve; birth asphyxia with poor neurological outcome; syndromic or serious congenital disorders

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-07-2022
Enrollment:	330
Type:	Actual

Medical products/devices used

Generic name:	Luscii Remote Patient Monitoring
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	27-01-2022

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-06-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-03-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-11-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL78984.100.22
Other	NL9688