# Rotavirus vaccinatie voor zuigelingen met een medisch risico

No registrations found.

| | |
|---|---|
| **Ethical review** | Positive opinion |
| **Status** | Recruiting |
| **Health condition type** | - |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON21569

**Source**
NTR

**Brief title**
RIVAR

**Health condition**

RV vaccine coverage rates and timeliness among qualifying high-risk infants
RV related hospitalizations among high-risk infants.
(severe) RV gastroenteritis among high-risk infants up to 18 months of age.

### Sponsors and support

**Primary sponsor:** UMC Utrecht
Heidelberglaan 100
3508 GA Utrecht
The Netherlands
**Source(s) of monetary or material Support:** ZonMw
Postbus 93245
2509 AE Den Haag
The Netherlands

UMC Utrecht
Heidelberglaan 100
3508 GA Utrecht
The Netherlands

Innovatiefonds Zorgverzekeraars
Sparrenheuvel 16
Postbus 304, 3700 AH Zeist
The Netherlands

GlaxoSmithKline
Huis ter Heideweg 62
3705 LZ Zeist
The Netherlands

## Intervention

## Outcome measures

### Primary outcome

• The impact of the RV vaccination program on number of hospitalizations due to RV gastroenteritis and symptomatic nosocomial RV infections among high-risk infants in the first and second year after implementation. Occurrence is expressed as cumulative number of children with at least one hospitalization due to RV gastroenteritis or symptomatic nosocomial RV infection in one of the participating hospitals per number of children at risk.

• Vaccine effectiveness in reducing episodes of severe RV gastroenteritis between 2 and 18 months of age among high-risk infants included in the follow-up study. Occurrence is expressed as number of events per 1000 person-years.

• Proportion of eligible high-risk children receiving a full 2-dose course of RV vaccination after implementation of RV vaccination program.

### Secondary outcome

Program evaluation

• Vaccine coverage among eligible high-risk infants at 6 and 12 months post-implementation and number and causes for missed or delayed RV vaccine doses.

• Number and characteristics of serious vaccine adverse events in the 30 days following administration of each dose of oral RV vaccine among high-risk infants. Occurrence is expressed as the number of events per 100 vaccine doses administered.

• Proportion of eligible high-risk children receiving at least 1-dose of RV vaccination after implementation of RV vaccination.

• Satisfaction and experience among involved physicians and parents with the RV vaccination program concerning organization, information, vaccine deliverance and administration.

• Cost-effectiveness of the RV vaccination program and net costs or savings from the healthcare payer perspective.

Effectiveness

• Vaccine effectiveness in reducing hospitalizations due to RV gastroenteritis and symptomatic nosocomial RV infections among high-risk infants up to 18 months of age. Occurrence is expressed as cumulative number of children with at least one event per number of children at risk.

• Vaccine effectiveness in reducing episodes of RV gastroenteritis of any severity between 2 and 18 months of age among high-risk infants. Occurrence is expressed as number of events per 1000 person-years.

• RV disease symptoms, severity, related quality of life lost and disruption of family life among high-risk infants and their parents between 2 and 18 months of age.

• Anti-rotavirus IgA antibody seroconversion rates at 30-90 days after the complete vaccination series and geometric mean concentrations (GMCs) in vaccinated high-risk infants and at similar time-points in unvaccinated high-risk infants and persistence of anti-rotavirus IgA antibodies at 12-18 months of age.

• Effectiveness in reducing nosocomial RV infections in the first and second year after implementation of RV vaccination in participating hospitals. Occurrence is expressed as the number of infections per 1,000 patient-days.

Epidemiology
• Number of hospital admissions for acute gastroenteritis and nosocomial gastroenteritis episodes among children 0-2 years old, including high-risk children, in each participating hospital and the number and proportion RV positive.
• Number and proportion of different RV genotypes present in stool samples positive for RV from children 0-2 years old, including high-risk children, hospitalized for acute gastroenteritis or suffering from nosocomial gastroenteritis.

# Study description

**Background summary**

BACKGROUND AND MOTIVATION

Children with underlying medical conditions, prematurity and low birth weight are at increased risk of hospitalizations due to rotavirus (RV) gastroenteritis, RV related complications and mortality. In a recent Dutch study it was demonstrated that high-risk

infants had increased risks of requiring hospitalization due to RV (1.7 to 4.4), of ICU admission (RR: 4.2 to 7.9) and of acquiring nosocomial RV infection (OR: 3.2 to 3.6) compared to healthy infants. High-risk infants also experienced prolonged hospitalization (1.5 to 3.0 excess days) and generated higher healthcare costs (€648 to €1533 per patient). Most importantly, it was estimated that on average 6-7 high-risk infants succumbed due to direct and indirect consequences of RV infection annually in the Netherlands. No mortality was observed among healthy infants. A subsequent cost-effectiveness analysis demonstrated that RV vaccination of high-risk infants would be very cost-effective and potentially cost-saving from the healthcare payer perspective.
The results demonstrate that prevention against RV gastroenteritis is urgently needed for high-risk infants. Yet, there is no RV vaccination program in the Netherlands. Organizing a successful RV vaccination program within the Dutch infant immunization framework generates additional challenges concerning adequate reach-out to high-risk infants because of the strict age-window indicated for RV vaccine administration. The first dose of RV vaccine should be administered between 6 and 14 weeks of age and vaccination completed no later than 24 or 32 weeks of age, depending on the vaccine. Secondary and tertiary pediatric care would provide an excellent environment for RV vaccination in order to reach optimal RV vaccine coverage rates in high-risk infants and to ascertain timely vaccination, because high-risk infants are closely followed here during their first month of life. There is however little experience in the Netherlands with organizing immunization programs for target groups through secondary and tertiary pediatric care.
Furthermore, there is a lack of data on RV vaccine performance among the special populations of high-risk infants, although these patients require protection most. Further data on vaccine effectiveness are needed to improve vaccination guidelines pertaining to high-risk infants.

This project will study the feasibility and impact of implementing a RV vaccination program for high-risk infants organized through secondary and tertiary care.
This study will also determine RV vaccine effectiveness among high-risk infants.

PRIMARY OBJECTIVES
• To evaluate the feasibility of RV vaccination of high-risk infants organized through secondary and tertiary pediatric care as measured by vaccine coverage and timeliness of vaccination.

• To evaluate the impact of RV vaccination of high-risk infants organized through secondary and tertiary pediatric care on rotavirus related hospitalizations among this patientgroup.

• To evaluate the protective effectiveness of at least 1 dose of RV vaccine against severe RV gastroenteritis up to 18 months of life.

RV VACCINATION PROGRAM
Dutch Hospitals with Neonatal Intensive Units and associated post IC/HC hospitals will be approached for participation in an implementation project of a hospital-based RV vaccination

program for high-risk infants. The RV vaccination program consists of offering a 2-dose course of the oral monovalent RV vaccine free of charge to all high-risk infants receiving care in one of the participating hospitals at discharge or during routine clinic visits and will be accompanied by a RV active surveillance program within the participating hospitals.

STUDY DESIGN
An observational study accompanying the program will assess occurrence of gastroenteritis among high-risk infants pre- and post-implementation, RV epidemiology within hospitals, vaccine coverage rates and timeliness of vaccination among RV vaccine eligible high-risk infants. A step-wedged design is used to account for inter-season variability of RV epidemics. Occurrence of (RV) gastroenteritis among high-risk infants will be studied by recruiting high-risk infants, both pre- and post-implementation, for an individual follow-up study until 18-months of age. Follow-up includes parental reporting of gastroenteritis, symptom and severity scoring and collection of stool samples.

STUDY POPULATION
Hospitals and eligible high-risk infants receiving care at these hospitals.

PRIMARY ENDPOINTS
• RV vaccine coverage rates, timeliness of vaccination and impact of the RV vaccination program in reducing RV related hospitalizations among high-risk infants.

• Vaccine effectiveness against severe RV gastroenteritis among high-risk infants up to 18 months of age.

**Study objective**

Children with underlying medical conditions, prematurity and low birth weight are at increased risk of hospitalizations due to rotavirus (RV) gastroenteritis, RV related complications and mortality. In a recent Dutch study it was demonstrated that high-risk infants had increased risks of requiring hospitalization due to RV, of ICU admission and of acquiring nosocomial RV infection compared to healthy infants. High-risk infants also experienced prolonged hospitalization and generated higher healthcare costs.

The results demonstrate that prevention against RV gastroenteritis is urgently needed for high-risk infants. Yet there is no RV vaccination program in the Netherlands.

Furthermore, there is lack of data on RV vaccine performance among the special populations of high-risk infants. Further data on vaccine effectiveness are needed to improve vaccination guidelines pertaining to high-risk infants.

This project will 1)

study the feasibility and impact of implementing a RV vaccination program for high-risk infants organized through secondary and tertiary care, and

2) determine RV vaccine effectiveness among high-risk infants.

**Study design**

Program impact is measured 1 and 2 years post-implementation. Vaccine effectiveness is measured based on follow-up of each enrolled infant up to 18 months of age.

**Intervention**

No randomized interventions. This is a step-wedged implementation project of a rotavirus vaccination program for high-risk infants in participating hospitals combined with and observational before-after cohort study measuring rotavirus gastroenteritis occurrence in a pre- and post-implementation cohort of high-risk infants.

## Contacts

**Public**
Research Support Unit Julius Centrum - UMC Utrecht

Lydeke Zwart
Heidelberglaan 100 - PO Box 85500

Utrecht 3508 GA
The Netherlands
phone: +31 (0) 6 5012 4901
**Scientific**
Research Support Unit Julius Centrum - UMC Utrecht

Lydeke Zwart
Heidelberglaan 100 - PO Box 85500

Utrecht 3508 GA
The Netherlands
phone: +31 (0) 6 5012 4901

## Eligibility criteria

## Inclusion criteria

1. Infants 6 weeks 0 days to 13 weeks 6 days of age who receive medical care in hospital or through outpatient clinics at the time of the first vaccine dose administration in one of the participating hospitals and

2. Diagnosed with at least one high-risk condition:

• Gestational age less than 36 weeks and 0 days

• Birth weight less than 2500 grams

• A qualifying diagnoses of severe congenital malformation or perinatal morbidity

## Exclusion criteria

• Known hypersensitivity to any of the vaccine components.

• Previous intussusception or an uncorrected congenital condition predisposing to intussusception (such as Meckel's diverticle).

• A diagnosis of severe (congenital) immunodeficiency syndrome.

# Study design

## Design

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| Study type: | Observational non invasive |
| Intervention model: | Other |
| Allocation: | Non controlled trial |
| Masking: | Open (masking not used) |
| Control: | N/A , unknown |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 01-12-2014 |

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|---|---|
| Enrollment: | 2000 |
| Type: | Anticipated |

## Ethics review

Positive opinion

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| Date: | 13-08-2015 |
| Application type: | First submission |

## 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 |
|---|---|
| NTR-new | NL5213 |
| NTR-old | NTR5361 |
| Other | 80-83600-98-20129 : ZonMW |

## Study results