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Immunological response after early extra and regular MMR immunization: 10 years follow-up

Submission date
11/07/2023

Recruitment status
No longer recruiting

Registration date
05/10/2023

Overall study status
Completed

Last Edited
19/12/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
From May 2013 until March 2014, a measles epidemic occurred in the Netherlands. During this epidemic, the Dutch Ministry of Health decided to offer infants between 6 and 12 months of age, living in the measles outbreak area, an early extra MMR (MMR-0) immunization during this outbreak, to protect children below 1 year of age in areas with lower immunization coverage (less than 90%) and thus with higher risk of exposure to measles virus. Researchers previously investigated the immunological response to early vaccination in a group of these children and a control group. Blood samples were taken at 14 months, 15.5 months, 2 years, 4 years and 6-7 years of age. About 12% of the children who received MMR-0 between 6 and 8 months of age had no detectable antibodies at 14 months of age before MMR-1. All other children had MMR-0-induced antibody levels above the protective threshold and were regarded as protected against measles during the epidemic. After the regular MMR-1 vaccination at 14 months of age, all children had developed protective measles antibody levels. However, 3 years later, measles antibody levels had dropped below the protective threshold in 11% of children, particularly children who received MMR-0 between 6 and 8 months of age. At 6-7 years of age, this percentage had increased to 68%. Among the children who received MMR-0 between 9 and 12 months of age and the children of the control groups who only received their regular MMR-1 at 14 months of age, 21% and 11% had dropped below the threshold of protection, respectively. The aim of this study is to analyse the levels of measles-specific antibodies in children who participated in the EMI study or BMR-nul-study at about 11 years of age, which is 2 years (+/- 2 months) after having received the regular MMR-2 vaccination. The proportion of children who have gained protective antibody levels through MMR-2 vaccination compared to the ones who haven't will be assessed. Finally, the levels and the quality of antibodies will be compared between children who had received an MMR-0 at 6-12 months of age and the children of the control group who only received the regular MMR-1 vaccination at 14 months of age.

Who can participate?
Children aged 10 to 12 years who previously participated in the EMI clinical study on the immunological response after MMR-0 immunization or the epidemiological questionnaire study BMR-nul.

What does the study involve?
One blood sample is obtained by fingerstick and one short questionnaire is completed.

What are the possible benefits and risks of participating?
The children have no direct benefit from participating in the study. Blood collection will be done using a finger stick, which poses no risk.

Where is the study run from?
Dutch National Institute of Health and the Environment (RIVM) (Netherlands)

When is the study starting and how long is it expected to run for?
June 2023 to November 2024

Who is funding the study?
The Dutch Ministry of Health, Welfare and Sport (Netherlands)

Who is the main contact?
bmr-nul-emi@rivm.nl

Study website
https://www.rivm.nl/mazelen/onderzoek#BMR-0

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IIV-628

Study information

Scientific Title
Observational study on immunological response 2 years after MMR-2 vaccination in children that received early extra or regular MMR immunization as infants to assess long-term effect of early extra MMR immunization

Acronym
EMI-3

Study objectives
Previously the immunological response to early vaccination was investigated in a cohort of children with the last blood sample obtained at 6-7 years of age, which is 6 years after the MMR-1 vaccination (NL45616.094.13/IIV-273 and NL69434.100.19/IIV-411). A large part of the early extra MMR-0 vaccinated children had protective measles levels at the age of 14 months. However, the decline in antibody levels was steeper than in children who received the regular MMR-1 vaccination and for some children antibody levels dropped below seroprotective levels at 4 and 6-7 years of age. This study will monitor the effect of MMR-2 on these children.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/09/2023, Dutch Medical Ethics Committee MEC-U (Postbus 2500, Nieuwegein, 3430 EM, Netherlands; +31 (0)88 320 8784; info@mec-u.nl), ref: NL84855.100.23 (R23.050)

Study design
Observational case-control study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Home, Internet/virtual

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Measles immunization in children

Interventions

In this follow-up study, a single small blood sample will be collected by finger-stick of children who previously were immunized with an MMR-0 vaccination between 6-12 months of age and children of a control group who only received the regular MMR-1 at 14 months of age. Blood sampling through a finger-stick will be performed at 2 years (+/- 2 months) post MMR-2 vaccination. Parents can perform the finger-stick on their child themselves and mail the blood sample to the RIVM. If parents do not feel comfortable performing the finger-stick themselves, an alternative can be arranged. Furthermore, a digital questionnaire is filled out with questions about the health of the child and other vaccinations.

Intervention Type
Other

Primary outcome measure
Measles-specific serum IgG measured by Luminex multiplex-based serology and virus-neutralizing antibodies by Plaque Reduction Neutralization Test (PRNT) 2 years (+/- 2 months) after MMR-2 vaccination

Secondary outcome measures
Serum IgG antibody concentrations against mumps and rubella measured by Luminex multiplex-based serology 2 years (+/- 2 months) after MMR-2 vaccination

Overall study start date
01/06/2023

Completion date
26/11/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 30/01/2024:
1. Participation in the study on the immunological effects of early extra measles vaccination, as described in a separate study protocol (NL45616.094.13/IIV-273) or participation in the BMR-nul-study on epidemiological effects of early extra measles vaccination as described in a separate study protocol
2. The parents/legal representatives accept participation in the trial according to the described procedures
3. Presence of an informed consent signed by both parents/legal representatives
4. Children must have received the MMR-2 vaccination

Previous inclusion criteria:
1. Participation in the study on the immunological effects of early extra measles vaccination, as described in a separate study protocol (NL45616.094.13/IIV-273)
2. The parents/legal representatives accept participation in the trial according to the described procedures
3. Presence of an informed consent signed by both parents/legal representatives
4. Children must have received the MMR-2 vaccination

Participant type(s)
Healthy volunteer

Age group
Child

Lower age limit
10 Years

Upper age limit
12 Years

Sex
Both

Target number of participants
80

Total final enrolment
88

Key exclusion criteria
1. Presence of a serious disease that requires medical care that can interfere with the results of the study
2. Known or suspected immunological disorder
3. Bleeding disorders

Date of first enrolment
09/10/2023

Date of final enrolment
18/07/2024

Locations

Countries of recruitment
Netherlands

Study participating centre
Rijksinstituut voor Volksgezondheid en Milieu
Antonie van Leeuwenhoeklaan 9
Bilthoven
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Sponsor information

Organisation
National Institute for Public Health and the Environment

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mensgebonden-onderzoek@rivm.nl

Sponsor type
Research organisation

Website
http://www.rivm.nl/en/

ROR
https://ror.org/01cesdt21

Funder(s)

Funder type
Government

Funder Name
Ministerie van Volksgezondheid, Welzijn en Sport

Alternative Name(s)
Dutch Ministry of Health, Welfare and Sport, VWS

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Netherlands

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/09/2025

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date