Personalised Risk assessment in Febrile illness to Optimise Real-life Management across the European Union (PERFORM)

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This study aims to improve the diagnosis and management of febrile children across Europe and West Africa through the development of simple diagnostic tests to discriminate febrile illnesses in children, including bacterial and viral infection and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Observational non invasive

Summary

ID

NL-OMON43233

Source
ToetsingOnline

Brief title
PERFORM

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
febrile illness

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Het is een Horizon 2020 project;goedgekeurd door de Europese Unie. EU funding - GA668303

Intervention

Keyword: bacterium versus virus, diagnosis, febrile children, infectious diseases

Outcome measures

Primary outcome

Biomarker discovery study (BIVABI):

the identification of a minimal discriminatory biomarker signatures that define febrile diagnoses, including infection (bacterial vs viral), or inflammatory illness.

MOFICHE:

Primary outcomes: Antibiotic prescription, hospitalization and number/type of investigations. Number of children re-attending within 5 days of the first hospital presentation.

BIVA-studies:

The identification of (serious) bacterial or viral infection (confirmed by culture and/or molecular microbiology), or inflammatory disease by using new clinical, proteomic and transcriptomic biomarkers. Sensitivity and specificity of the new biomarkers and the added value of new biomarkers to usual clinical signs and diagnostic work up to discriminate viral and bacterial infections in children, including diagnostically challenging groups (immunocompromised patients, patients with inflammatory/rheumatological disorders , severe ill patients at intensive care departments).

Airway device:

Percentage of children in which collection and analysis of exhaled air using

the Aeonose device was successful.

Secondary outcome

BIVABI study: identification of minimal biomarker signatures that discriminate

children with febrile illness on the basis

of their severity

MOFICHE:

Secondary outcome: number of prescriptions of broad spectrum antibiotics versus

the number of prescription of narrow spectrum antibiotics (dose in 24 hours).

Clinical and general characteristics of antibiotic prescription,

hospitalization duration of stay and investigations.

BIVA-studies:

Secondary:

The identification of biomarkers predictive of disease severity in children

with bacterial and viral infection, using a combination of clinical phenotypic

markers and proteomic and transcriptomic biomarker signature discovery.

Study description

Background summary

The management of febrile patients is one of the most common and important problems facing healthcare providers. Distinction between bacterial infections and trivial viral infection on clinical grounds is unreliable, and as a result innumerable patients worldwide undergo hospitalization, invasive investigation and are treated with antibiotics for presumed bacterial infection when, in fact, they are suffering from a self-resolving viral infection.

With this study we aim to improve diagnosis and management of febrile children through the development of simple diagnostic tests to discriminate febrile illnesses in children, including bacterial and viral infection and inflammatory diseases.

Sophisticated phenotypic, transcriptomic (genomic, proteomic) and bioinformatic approaches will be used to well characterised large-scale, multi-national patient cohorts already recruited with EU funding. Our aim is to identify, and validate promising new discriminators of bacterial and viral infection including transcriptomic and clinical phenotypic markers. The most accurate markers distinguishing bacterial and viral infection will be evaluated in prospective cohorts of patients reflecting the different health care settings across European countries. By linking sophisticated new genomic and proteomic approaches to careful clinical phenotyping, and building on pilot data from our previous studies we will develop a comprehensive management plan for febrile patients which can be rolled out in healthcare systems across Europe.

Study objective

This study aims to improve the diagnosis and management of febrile children across Europe and West Africa through the development of simple diagnostic tests to discriminate febrile illnesses in children, including bacterial and viral infection and inflammatory diseases.

The whole project will:
• Assess current management of febrile illness across Europe and West Africa using quantitative and qualitative methods (including cost-effectiveness analysis).
• Identify personalized discriminators of bacterial and viral infection and inflammatory diseases, and diagnostic signatures that distinguish severe and mild disease, using a combination of clinical phenotypic markers, host genetic markers, and biomarkers derived using transcriptomic, proteomic, and bioinformatic approaches.
• Develop simple proof-of-concept personalized tests for application at the point of care. The new biomarkers will be validated in samples of new prospective inclusions. This part of the study is described in this protocol.
• Model the impact of the introduction of optimised management strategies for febrile children, in the varied healthcare settings of Europe, thus providing the evidence necessary for European and international health systems to adopt

new management strategies for febrile children.
• Investigate if collection and analysis of exhaled air in children with and without a lower respiratory tract infection using the Aeonose device is possible and reliable. This might be a useful diagnostic tool to recognize viral and bacterial VOC patterns at the bedside.

Study design

PERFORM consists of 3 parts using clinical data and/or samples of patients:

1. Biomarker discovery using pre-existing sample collections (Biomarkers of Viral and Bacterial Infection (BIVABI))
The BIVABI study is a retrospective observational study which will use transcriptomic, proteomic and metabolomic approaches to discover biomarkers that distinguish the different phenotypes of childhood febrile illness, including children with infection (viral, bacterial, mycobacterial, other) and inflammation (including Kawasaki disease, juvenile idiopathic arthritis). For this part no new patients will be included.

2. Prospective observational study of patient management and outcome, using large, aggregated datasets and not involving sample collection (Management and Outcome of Fever in children in Europe (MOFICHE))
MOFICHE is a prospective observational study assessing the management and outcome of children presenting to Emergency Departments (ED) with fever across Europe. This study will use large departmental datasets to collect information on nearly 50,000 febrile episodes in 12 ED*s in 8 European countries. In the Netherlands we aim to collect 5.000 febrile episodes. This study will use large-scale, pseudo-anonymized departmental data to safeguard identity of participants and will not involve consented patient recruitment; nor will it use patient samples. Data included in MOFICHE will be based on that collected as part of routine clinical care. No tissue samples will be taken for research use, and informed consent will not be taken for the MOFICHE study. This ABR-form contains the WMO-part of the study (BIVA) mentioned below at point 3.

3. Biomarker validation using prospectively recruited patients and patient samples (Biomarker Validation studies (BIVA))
Prospective, observational studies will recruit a validation group of children with infectious and inflammatory conditions. Research blood samples will be taken and analysed in order to validate biomarker findings identified in the BIVABI discovery study. There are 5 related prospective studies. The BIVA-ED study will recruit the majority of the children. The other studies will target harder-to-reach groups who will not be adequately recruited in an ED study, in order to increase numbers. The studies are:

• Biomarker Validation in Emergency Department (BIVA-ED)
• Biomarker Validation in Paediatric Intensive Care (BIVA-PIC)
• Biomarker Validation in High Risk patients (BIVA-HR)

• Biomarker Validation in Inflammatory patients (BIVA-INF)

Airway device study: exhaled air will be collected and analysed with a portable Aenose..

Study burden and risks

Blood samples will be collected during a routine diagnostic blood sampling. It is possible that a fingerstick blood collection will be changed in a venapunction. In addition a nasopharyngeal swab or throat swab will be obtained. When urine of stool is left over, these will also be collected.
It is estimated that in this way the burden for the child is very low and without any risks.

In the majority of the inclusions there will be only 1 timepoint for blood collection. But, if at 48-72 hours or at 28 days after the hospital visit or at discharge a routine diagnostic blood sampling will be done, then we also want to collect blood for this study. At 48-72 hours and (if necessary) at 28 days after the hospital visist the parents will be asked by a text message about the illness/recovery of the child.

Bij kinderen op de PICU worden er nog additionele bloedsamples afgenomen op t=24h, t=48h en daarna 1x per week met een maximum van 5 research samples.

Airway device study:
The exhaled breath sampling technique is non-invasive, safe and without risks. The sampling will be tested in 1 visit and will not exceed 10 minutes.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

All children <18y presenting to the Emergency department or paediatric intensive care unit or other appropriate wards with fever, or a history of fever <72h, or a suspected infection, in whom the attending clinician determines the need for blood sampling. ;Healthy control children: • afebrile control children who are having blood tests for reasons other than for investigation of infectious or inflammatory illness.

Exclusion criteria

Participation may not lead to an earlier need for blood transfusion.

Study design

Design

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

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-02-2017
Enrollment:	1600
Type:	Actual

Ethics review

Approved WMO Date:	14-12-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-04-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-10-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL58103.091.16