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Observational study of blood transfusions in European preterm infants

Submission date	Recruitment status	[_] Prospectively registered
29/11/2022	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
02/12/2022	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
27/01/2025	Neonatal Diseases	

Plain English summary of protocol

Background and study aims
The aim of this study is to learn more about the use of blood transfusions in the neonatal intensive care unit. Most premature babies in the neonatal intensive care unit receive a blood product during their admission. Unfortunately, there are no international transfusion guidelines for this patient group that are used by Europe as a whole. There may be a great deal of variation between doctors when they decide to administer a blood product. To investigate this, researchers are collecting information on how many preterm babies receive a blood transfusion and why they did or did not receive a blood transfusion. The results of this study will help to improve the use of blood transfusion in preterm babies in Europe.

Who can participate?
Babies born below 32 weeks of gestation who are admitted to a participating center during the 6 weeks of the study

What does the study involve?
All participating neonatal intensive care units will collect information on blood transfusions for a period of 6 weeks. The study requires the collection and use of the participating child's medical and personal data. This is necessary to answer the research questions of the study. The researchers will only collect data from the child's (electronic) patient record, including gender, gestational age, date of birth and birthweight, and data on any blood transfusions the child may receive during admission. The researchers will only collect information from laboratory tests that are part of the regular treatment in the neonatal intensive care unit. To protect the child's privacy, each child will be given a study code that will appear on the data. The personal data that can identify the child will be converted. Only the local researcher knows which study code the child has. The key to the study code remains with the local researcher. The study data will be safely stored in an encrypted (coded) electronic database to ensure proper use and data protection. The researchers will store the data for 15 years.

What are the possible benefits and risks of participating?
Participating will contribute to more knowledge on the blood transfusions given during

admission to the neonatal intensive care unit. The study does in no way influence the care the child receives. No additional measurements will be taken during this study. There are no negative consequences, other disadvantages, or risks for the child participating in this study.

Where is the study run from?
Leiden University Medical Center (Netherlands)

When is the study starting and how long is it expected to run for?
January 2021 to September 2023

Who is funding the study?
1. Sanquin Blood Supply Foundation
2. European Society for Pediatric Research (ESPR)
3. European Blood Alliance (EBA)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
G21.207

Study information

Scientific Title
International Neonatal tranSfusion PoInt pREvalence study

Acronym
INSPIRE

Study objectives
Premature neonates are a highly transfused patient group, though robust evidence supporting neonatal transfusion practice is scarce. Two randomized trials indicated no benefit in long-term outcomes of liberal compared to restrictive thresholds for red blood cell (RBC) transfusions. Another randomized trial, comparing a high and low platelet transfusion threshold, even reported evidence that transfusions can cause harm. No neonatal transfusion guidelines have been implemented by Europe as a whole, resulting in significant variation in transfusion practice. Detailed contemporary data on neonatal transfusion practice in Europe is lacking.

Ethics approval required
Old ethics approval format

Ethics approval(s)
On 31/03/2022 the Medical Research Ethics Committee Leiden Den Haag Delft (2300 RC Leiden, the Netherlands; +31(0) 71 – 5265106; metc-ldd@lumc.nl) confirmed that the research protocol "INSPIRE-study: International Neonatal tranSfusion PoInt pREvalence", reference number G21. 207 does not apply to the Medical Research Involving Human Subjects Act (Dutch abbreviation: WMO). Therefore, it is exempt from review by the Committee.

Study design
International multicenter prospective observational point prevalence study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
The use of blood transfusion in European preterm infants

Interventions
In this international, multicenter, prospective, observational point prevalence study, the researchers will include neonates with gestational age at birth <32 weeks admitted to a participating tertiary-level neonatal intensive care unit (NICU). Data will be collected over a 1-year period, in which each NICU will collect data for 6 weeks. Data will be collected from the hospital’s written or electronic patient record files, recorded imaging reports, hospital blood bank records, and nurses’ records.

Intervention Type
Other

Primary outcome(s)
1. The prevalence and incidence of RBC, platelet, and plasma transfusions in neonates with a gestational age of less than 32 weeks at birth, admitted to a tertiary-level NICU:

1.1. The prevalence is calculated by dividing the number of transfusions of the respective transfusion type by the total sum of neonate study days
1.2. The incidence of receiving at least one transfusion, both for any transfusion as per transfusion type, is calculated by dividing the number of neonates receiving at least one transfusion by the total sum of neonate study days

Each participating center will collect data during a 6-week period, in which they will screen all 7 days of these weeks for the study outcomes in the included neonates. For neonates already admitted at the start of the study, the start of patient follow-up in the study is equal to the first day of the study period in the participating center. For all other included infants, the start of patient follow-up equals the day of admission. The end of patient follow-up in the study is equal to the day of death, the day of transfer, the day of discharge, or the last day of the study period in the center (whichever occurs first).

Key secondary outcome(s))

1. Variations in prevalence rates of RBC, platelet, and plasma transfusions. Data analysis will be predominantly descriptive, comparing both participating countries and different types of NICUs. Types of NICUs will be defined based on unit size and whether surgical procedures are being performed.
2. Indications for transfusion: the primary indication for which the transfusion is prescribed by the treating physician will be collected. If applicable, the secondary and tertiary indications will also be registered, as clinicians may consider multiple factors when deciding to give a transfusion. For each transfusion, the prescribing physician must choose from a list of predefined indications (up to three options can be selected, ranked primary to tertiary indication). The primary indication is the indication that has the most weight in the decision to prescribe a transfusion. If the indication for transfusion is registered by someone other than the prescribing physician, the prescribing physician must confirm the correctness of these data.
3. Duration, volume, and transfusion rate of the prescribed RBC, platelet, and plasma transfusions
4. Guideline use: data is collected on whether centers have guidelines in place regarding RBC, platelet, and plasma transfusion for neonates. Following the implementation model by Wensing and Grol, information is gathered on the implementation of transfusion guidelines. Additionally, the researchers will ask centers with established guidelines to provide the guidelines in place at the start of data collection. The researchers will analyse how many of the RBC and platelet guidelines have already incorporated the results of recent clinical trials. They will categorize the existing RBC guidelines into “TOP and/or ETTNO incorporated” and “TOP and/or ETTNO not incorporated”. They will categorize the existing platelet guidelines into “PlaNeT-2/MATISSE incorporated” and “PlaNeT-2/MATISSE not incorporated”. They will assess to what extent centers follow their own local and/or national guidelines.
5. Evidence-basedness of practice: before the start of data collection, the researchers will collaborate with various experts to define what they view as high-quality evidence regarding RBC and platelet transfusion practices in neonates, using the best available evidence including the TOP, ETTNO, and PlaNeT-2/MATISSE trials. They will assess if the RBC and platelet transfusions were prescribed following the best available evidence, by categorizing the prescribed transfusions into different levels of certainty in evidence. They will assign a panel review by three ‘blinded’ experts to discuss cases where there may be ambiguity on the certainty of evidence to support transfusion practice. Transfusion events in clinical scenarios that were not addressed in randomized trials will not be assessed.
6. Transfusion-associated adverse effects: in the absence of clear definitions of transfusion-associated side effects in neonates, the researchers will ask participating centers to register any perceived transfusion-associated adverse effects if the local investigators consider the adverse

event to be potentially associated with the preceding transfusion. With this they hope to gain insight into what adverse effects neonatologists identify in clinical practice, despite the lack of well-defined descriptions.
7. Component specifications: the researchers will perform an online survey among transfusion experts in which they explore variations in transfusion component characteristics. They chose this strategy because neonatologists may not be aware of all relevant component specifications. The survey will be sent to transfusion experts in all countries participating in this study during the data collection period. The researchers will record the blood banks from which each participating NICU receives their blood products, which will allow them to link the NICU clinical data to the component specifications reported by the transfusion specialists. They aim to include all blood banks that provide blood products to participating NICUs in the survey.
8. Transfusion with blood products other than RBC, platelet, and plasma or agents that promote or reduce coagulation. The researchers will collect data on transfusions of blood products other than RBC, platelet, and plasma transfusions or agents that promote or reduce coagulation, such as erythropoietin. They will describe these treatments and the indications for which they were prescribed.

Each participating center will collect data during a 6-week period, in which they will screen all 7 days of these weeks for the study outcomes in the included neonates. For neonates already admitted at the start of the study, the start of patient follow-up in the study is equal to the first day of the study period in the participating center. For all other included infants, the start of patient follow-up equals the day of admission. The end of patient follow-up in the study is equal to the day of death, the day of transfer, the day of discharge, or the last day of the study period in the center (whichever occurs first).

Completion date
30/09/2023

Eligibility

Key inclusion criteria
A potential subject who meets both of the following criteria can be included in this study:
1. Admission to a participating tertiary level NICU during the study period (note: this also includes neonates who are admitted to the NICU prior to the start of the study period, born outside the NICU institute of admission and/or readmitted to the NICU)
2. Gestational age at birth below 32 weeks (note: the postmenstrual age [PMA; gestational age + chronological age] at admission can be ≥32+0 weeks, however the PMA at inclusion cannot exceed 44+0 weeks)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Total final enrolment
1143

Key exclusion criteria
Does not meet the inclusion criteria

Date of first enrolment
26/09/2022

Date of final enrolment
31/08/2023

Locations

Countries of recruitment
England

Austria

Bosnia and Herzegovina

Croatia

Czech Republic

Denmark

France

Germany

Hungary

Ireland

Italy

Netherlands

Norway

Poland

Portugal

Romania

Slovakia

Slovenia

Spain

Sweden

Switzerland

Study participating centre
Leiden University Medical Center
Albinusdreef 2
Leiden
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2333 ZA

Study participating centre
A list of all the European participating centers is available upon request from the coordinating investigator (email: INSPIRE@lumc.nl).
Netherlands
2333ZA

Sponsor information

Organisation
Leiden University Medical Center

ROR
https://ror.org/05xvt9f17

Funder(s)

Funder type
Charity

Funder Name
Stichting Sanquin Bloedvoorziening

Alternative Name(s)
Sanquin Blood Supply Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Netherlands

Funder Name
European Society for Pediatric Research (ESPR)

Funder Name
European Blood Alliance (EBA)

Results and Publications

Individual participant data (IPD) sharing plan
The coded datasets generated during and/or analyses during the current study are not expected to be made available. The dataset will be exclusively accessible for the involved researchers and restrictions apply to the availability of these data as underlined in the data sharing agreement. The database shall be jointly owned by the parties involved, and participating centres have the right to apply to use the dataset for their own research proposal(s). External applications for access will be assessed by the principal investigators after the prior written consent of all parties involved. The dataset will be stored in a Leiden University Medical Center ProMISe Datasafe. ProMISe meets the requirements for data safety and privacy as set by international law and the security conditions as demanded by GCP. The ProMISe Datasafe automatically makes back-ups twice a day. Data will be stored for the length of the study and 15 years afterwards.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		03/09/2024	27/11/2024	Yes	No
Results article	Platelet transfusion	10/10/2024	27/11/2024	Yes	No
Results article	Plasma transfusions	19/01/2025	27/01/2025	Yes	No
Protocol file			30/11/2022	No	No
Protocol file	version 3	11/03/2022	30/11/2022	No	No
Statistical Analysis Plan	Red Blood Cell Transfusion Paper version 6	21/12/2023	26/01/2024	No	No
Statistical Analysis Plan	Plasma Transfusion Paper version 1	19/04/2024	08/07/2024	No	No

Statistical Analysis Plan	Platelet Transfusion Paper version 1	29/01/2023	08/07/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes