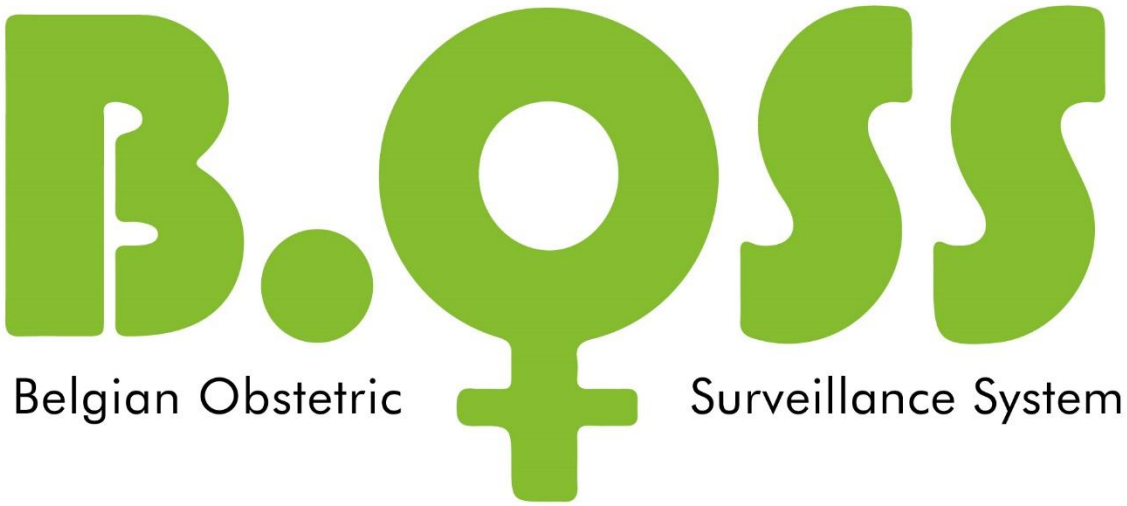

Study protocol

Version 1.0 dd 08/01/2021

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SUMMARY

Study title and specifics

Title: B.OSS: Belgian Obstetric Surveillance System
B670201526875
EC(UZ Gent)/2015/1470

Study type

National surveillance system
Multicentre epidemiological study
Observational study, non-interventional

Aim of the study

Evaluation of obstetrical care in Belgium and international comparison of obstetrical care, by the registration and analysis of collected data of obstetric complications in Belgium, to **improve maternal care** and decrease severe maternal morbidity and mortality.

Primary objectives

- To investigate the incidence of rare obstetric complications in Belgium
- To collect data on these complications on a national level
- To identify risk factors and contributing factors
- To describe and evaluate management
- To compare with international studies and guidelines

Secondary objectives

- To formulate recommendations for primary prevention (based on risk-factors)
- To formulate recommendations for secondary prevention (based on management and substandard care)
- To translate these recommendations into national guidelines

Patient population

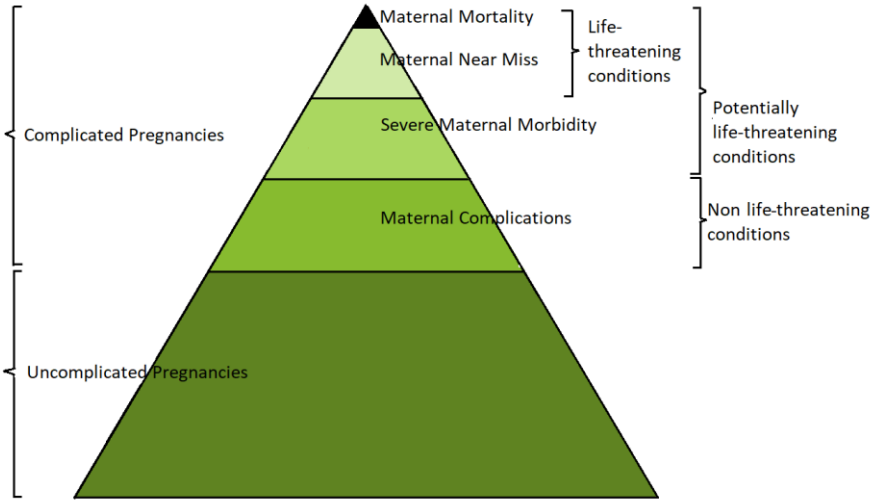
All women in Belgium who are pregnant and until 42 days after delivery.

Study duration

The B.OSS registry is a long-term registry that started in 2012 and is on-going.
Each year 1 or 2 complications are registered for a certain period of time (2 to 4 years).

INTRODUCTION

In obstetric medicine we know several diseases and complications that can result in so-called near-miss events: severe life-threatening obstetric complications necessitating urgent medical intervention in order to prevent likely death of the mother. Many of these obstetric complications cannot be anticipated by risk factors or tests. Obstetricians will be challenged by these complications at the most a few times along their clinical career, therefore individual expertise is scarce. It is challenging to investigate rare diseases and severe complications to find robust evidence on incidence, risk factors and pathophysiology as basis for evidence-based guidelines on prevention and management.



The United Kingdom was a pioneer when developing the UK Obstetric Surveillance System (UKOSS) in 2006 (1), a nationwide survey to identify and study 'near-miss' events and rare diseases of pregnancy. Collaboration of all maternities nationwide to collect data enables identification of a relatively small number of women. This allows to conduct descriptive epidemiologic studies, case-control and parallel cohort studies (https://www.npeu.ox.ac.uk/ukoss/completed-surveillances). Gathering experience and knowledge on incidence, risk factors, pathophysiology and management, results in better understanding, better patient information and care by practical improvements in prevention and treatment of these uncommon conditions (2).
Similar surveillance systems have been set up in other countries and the International Network of Obstetric Surveillance Systems (INOSS) was constituted in July 2010. Current member countries of INOSS include Australia, Austria, Belgium, Denmark, Finland, France, Germany, Iceland, Italy, the Netherlands, New Zealand, Norway, Portugal, Slovakia, Spain, Sweden and the United Kingdom. The mission of INOSS is to co-operate, share information and enable cross-national comparisons and analyses (https://www.npeu.ox.ac.uk/inoss) (3).

The Belgian Obstetric Surveillance System was constituted in 2011 supported by the College of physicians for the Mother and Newborn, a consultative body of the Federal Public Service of Health, and started its registration in the whole of Belgium in January 2012 (4). Meanwhile B.OSS has proven to be successful in monitoring severe maternal morbidity (5-10). Belgian gynaecologists are willing to participate in order to receive advice based on own data, because practice in Belgium and certainly the organization of medical care differs from neighbouring countries.
Whereas Peristat (http://www.europeristat.com) develops valid and reliable indicators that can be used for monitoring and evaluating perinatal health in the EU, the purpose of B.OSS in Belgium and of

INOSS internationally is trying to analyse and explain the figures obtained and to establish the best possible treatment to avoid maternal near misses and deaths. The results of the first studies suggest the need to develop nationally adopted guidelines and invite to critically evaluate the current organisation of obstetric health care in Belgium.

STRUCTURE OF B.OSS

Funder

Federal Public Service (FPS) Public Health

The B.OSS study was established in 2011 as an initiative of the College of Physicians for Mother and Newborn, an agency of the FPS Public Health.
Mieke Walraevens, in name of Minister Maggie De Block, approved funding for the maintenance of B.OSS and the development of BAMM (Belgian Analysis system for Maternal Mortality) in 2019 as a pilot project for 18 months. This funding allowed the recruitment of a national coordinator for B.OSS and BAMM, by means of a B-4 contract at the Ghent University Hospital. The pilot project started in January 2020.
Aim is to consolidate both B.OSS and BAMM into long-term national registration systems.

Scientific committee of B.OSS and BAMM (alphabetical order)

- Anne Clercx – FPS Health, Collge Mother and Newborn
- Caroline Daelemans – Erasme ULB, CEpiP
- Charlotte Leroy – CEpiP
- Frédéric Chantraine – CEpiP, CHU Liège
- Frédéric Debième – CEpiP, College Mother and Newborn
- Griet Vandenberghe – UZ Gent, B.OSS, BAMM
- Ilse Peeters – Sciensano
- Kristien Roelens – UZ Gent, College Mother and Newborn, SPE, B.OSS, BAMM
- Laura Cornelissen – Sciensano
- Leen Verleye – KCE
- Monika Laubach – UZ Brussel, SPE
- Régine Goemaes – SPE
- Roland Devlieger – UZ Leuven, SPE
- Sophie Quoilin – Sciensano
- Virginie Van Leeuw – CEpiP

Supervisory committee

The supervisory committee stands for the follow-up and evaluation of the project and exists of:

- A representative of the current Minister of Public Health
- Isabelle Van Der Brempt as representative of the FPS Health, Food chain safety and Environment
- Margareta Haelterman as representative of the FPS Health, Food chain safety and Environment (retired since April 2020)
- Omer Vanhaute as representative of the Ghent University Hospital
- Frédéric Debième as representative of CEpiP and the College of Mother and Newborn
- Roland Devlieger as representative of SPE and the College of Mother and Newborn

- Kristien Roelens as representative of the Ghent University Hospital, SPE and the College of Mother and Newborn
- Julie Belhomme as representative of the BAMM working group and the College of Mother and Newborn

B.OSS-team for daily work

- B.OSS officer: Karolien Benoit – FPS / Ghent University Hospital (B4-contract)
- Principal investigator: Dr. Griet Vandenberghe / Ghent University Hospital
- Investigators current studies:
    - Intrahepatic Cholestasis in Pregnancy: Laura De Luca ; Audrey Francinetti
    - COVID-19 during pregnancy: Dr. A. Vercoutere
    - Complications of Bariatric Surgery in Pregnancy: Paulien Demulder

Local investigators

In every Belgian maternity unit, B.OSS has a contact person who voluntarily collaborate by receiving a monthly call through mail and by registering cases. This is a gynaecologist in most cases, a senior midwife or an administrative person. See Contact persons | B-OSS (b-oss.be).

AIM of B.OSS

B.OSS aims to **evaluate obstetrical care** in Belgium by the registration and analysis of collected data of obstetric complications in Belgium, and by international comparison of obstetrical care.
B.OSS aims to **improve the quality and safety of obstetric care** in Belgium by practical recommendations based on the results.

STUDY OBJECTIVES

Primary objectives

- To investigate the incidence of rare obstetric complications in Belgium
- To collect data on these complications on a national level
- To identify risk factors and contributing factors
- To describe and evaluate management
- To compare with international studies and guidelines

Secondary objectives

- To formulate recommendations for primary prevention (based on risk-factors)
- To formulate recommendations for secondary prevention (based on management and substandard care)
- To translate these recommendations into national guidelines

STUDY POPULATION

All women in Belgium who are pregnant and until 42 days after delivery.

STUDY DESIGN

Type of study

B.OSS is

- a nationwide multicentre epidemiological study
- a national surveillance system
- an enhanced web-based registration and data collecting system of rare obstetric complications

Study period

The B.OSS registry is a long-term registry that started in 2012 and is on-going.
Each year 1 or 2 complications are registered for a certain period of time (2 to 4 years).

Study period of ongoing B.OSS studies: please consult Current studies | B-OSS (b-oss.be).
Study period of the completed studies,, see Completed studies | B-OSS (b-oss.be).

Inclusion criteria

The website can be consulted to find inclusion criteria for each complication that is being registered within B.OSS,..
See Definitions | B-OSS (b-oss.be).

Methodology

i. B.OSS contact person

In every Belgian maternity unit a responsible contact person is appointed: a gynaecologist in most cases, or a senior midwife or an administrative person. This local B.OSS investigator takes care of the B.OSS registration on a monthly basis by checking the occurrence of B.OSS complications at his maternity. Further this B.OSS contact person takes care of the local Ethical Committee approval in case of a new study. This contact person gets information on the ongoing studies on a regular basis: which complications, during which time period, in- and exclusion criteria, …

ii. Informed consent

Before registration in the B.OSS study, the patient is informed by her gynaecologist / by the local B.OSS contact person. An informed consent letter is handed to the patient. A signed informed consent is necessary and is guarded by the local B.OSS contact person.

iii. Monthly mailing

The B.OSS contact person is invited by monthly mailing to report a selected number of rare obstetric complications that occurred in the preceding month or alternatively to state that there was 'nothing to report', as is mostly the case.
In the event of a case being reported, the contact person is asked to complete an extensive data collection form. In case of incomplete reporting or incomplete data collection forms, the contact person is encouraged repeatedly by email and phone to provide the missing data.
Access to the website is restricted to the B.OSS-contact person, by using 1) an IP address of the hospital and 2) by a login and password. The contact person has only access to the reporting forms and data collection forms of his maternity unit.

iv. Notification of a case

When the B.OSS contact person reports a case for a certain complication, the platform asks to give name and date of birth. An irreversible HASH-code and a questionnaire is generated for this case. Name and date of birth are not saved, nor stored on the platform.
The B.OSS contact person receives an email with the generated HASH-code for the case and a link to the online questionnaire on the B.OSS platform.

v. Online data collection form

The contact person completes the data collection form, asking for data available in the medical file of the patient.
Access to the B.OSS platform is restricted to the B.OSS contact person.

vi. Data control

Completed questionnaires are checked by the B.OSS -team (cfr supra). When data are missing or questions are interpreted incorrectly, the B.OSS-team gets in contact with the local B.OSS-investigator and kindly asks to check or complete the answers.

DATA MANAGEMENT

Data collection

A detailed data collection form is drawn up for each complication registered by B.OSS. Most DCF are based on the DCF of the United Kingdom Obstetric Surveillance System (UKOSS) or other similar studies within the INOSS (International Network of Obstetric Survey Systems). Core data are requested in a similar way to optimize and enable international comparison.
The following pseudonymised data are collected by the data collection forms:

- Socio-demographic characteristics: age, weight, length, ethnicity, smoking status
- Medical history and obstetrical history
- Details on the current pregnancy
- Circumstances and the progress of the current obstetric complication
- Management of the complication
- Outcome for mother
- Outcome for the foetus or newborn

All the data collection forms (completed and current studies), can be consulted on the website: Data Collection Forms | B-OSS (b-oss.be).

Data pseudonymisation

An irreversible HASH-code is generated for every registered case, based on a name and date of birth introduced by the B.OSS contact person. The platform does not save or store the name and date of birth. The local B.OSS contact persons need to keep a list of registered patients of their maternity unit with the assigned HASH-codes.

Data storage

For the duration of the registry of a certain complication, all data gathered are saved **electronically on the B.OSS platform on the secure servers of Nestor**.

Nestor is a cvba, with whom there is a good and ongoing cooperation since 2013 for the B.OSS project https://nestor.coop/ .

The decision to work with Nestor is broadly supported by the DPO UGhent, DPO Ghent University Hospital, ICT head of department Ghent University Hospital, IT Security Officer UGhent, Legal Service Ghent University Hospital, following presentation and discussion on 23/10/2019 and 2/09/2020. A data processing agreement is set up between Ghent University Hospital and Nestor.

The Ghent University Hospital is involved in B.OSS through the B-4 contract by the FPS of Public Health (see Structure of B.OSS - Funder) and as the central Ethical Committee.

Once the registry of a certain complication is finalised, the data will be removed from and no longer archived on the servers of Nestor.

Archiving data

The data of the completed registries will be archived on the secure servers of the University Hospital of Ghent, for the duration of 20 years.

Access to data

Access to the data of B.OSS **for current studies** (data on the B.OSS platform) is restricted

- to the **B.OSS team**, by a login and password and by IP-address.
- to the **contact persons**, also by a login and password and by IP-address, with only access for their own hospital forms and cases.

Access to the data of B.OSS **for completed studies** (archived data) is restricted

- to the B.OSS officer and principal investigator

Use of data

The data collected by the B.OSS registry will be used for

- scientific purposes, by drawing up a B.OSS-report, national and international publications
- epidemiological purposes, by providing data to national instances (such as STATBEL, SPE, CEpiP) and international instances (such as Europeristat, WHO).
- quality improvement purposes, by formulating recommendations based on results of data analysis. Recommendations can lead to the development of guidelines, to (proposals of) policy changes.
- (inter)national comparison, e.g. initiatives to compare maternal morbidity within the International Network of Obstetric Survey System (INOSS). International comparison can contribute to better insight in a country's quality of (obstetric) care.

ETHICS & LEGAL ASPECTS

Ethics Committee approval

At the beginning in 2012, the B.OSS methodology was approved by the Medical Ethics Committee of Ghent University Hospital (EC UZG 2012/734; B670201215359) and by the Medical Ethics Committee of the Erasme University Hospital, Brussels (EC ULB 2012/111; B406201213660).

In 2015 the Medical Ethics Committee of the Ghent University Hospital became central Ethics Committee **(EC UZG 2015/1470; B670201526875).** Ethics Committees of the participating maternities were informed, asked for approval and included in the multicentre B.OSS study following approval.

Application for approval by the central EC of changes to the study protocol or the start-up of a new study by B.OSS, can be done through an amendment. The local ethical committees are informed by the central EC following approval.

Good Clinical Practice

The study is conducted in accordance with the guidelines of good clinical practice (ICH/GCP) and the Helsinki Declaration, written to protect those involved in clinical studies.

Confidentiality & data protection

In accordance with the Belgian law of August 22, 2002, relating to the rights of the patient, the General Data Protection Regulation (or GDPR) (EU) 2016/679 of April 27, 2016 (that is in force since May 25, 2018) and the Belgian law of July 30, 2018, on the protection of individuals related to the processing of personal data and on the free movement of such data, the privacy of the patients will be respected.

The collection of medical data by the data collection forms, will be limited to those data necessary to fulfil the objectives of the B.OSS registry. All data will be collected and processed with adequate precautions to ensure the utmost confidentiality. This processing of data is provided by law on the basis of Article 6, § 1 (e) and Article 9, § 2 (j) of the General Data Protection Regulation.

A signed informed consent must be obtained before collecting the medical data. These informed consent forms are guarded in the proper hospitals by the local B.OSS contact person, so that cases remain anonymous for the B.OSS research team.
When a new complication is registered by B.OSS, the informed consent form is adapted by the researchers of B.OSS; and submitted for approval by the central ethical committee.
With the start of each new registration period, the local ethical committees are informed by the central ethical committee and by their local investigators, of the start of the new study period with the approved data collection form and the informed consent form.
The form can be consulted on the website in 3 languages: Patient information letter | B-OSS (b-oss.be).

Appropriate technical and organisational measures are taken, to guarantee confidentiality of data, to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or alteration:

- All information collected during this study will be pseudonymised. An irreversible HASH-code is generated for every registered case. Only pseudonymised data will be used for analysis.

- A data processing agreement is set up between Ghent University Hospital and Nestor, the company that develops and maintains the safe B.OSS platform.
- Data access to the B.OSS platform and the servers of University Hospital Ghent: restricted in time and restricted to individuals (see Acces to data).
- Access will only be possible with authentication (username and password) and via IP address.

The controller of the data is the principal investigator of the study. In the context of data protection, the data will only be processed by personnel belonging to the research team and designated by and under the responsibility of the principal investigator, including internal employees with a non-healthcare profession.

Remuneration

There are no remunerations for participation or contribution to the study. All collaborators cooperate on a voluntary basis.

Insurance

Insurance for participants in the B.OSS project is provided by the Ghent University Hospital: Allianz Global Corporate & Specialty - Policy Number: BEL001889.
The Ghent University Hospital is involved in the B.OSS project through the B-4 contract by the FPS of Public Health (see Structure of B.OSS - funding) and as central Ethical Committee.

B.OSS AUTHORSHIP POLICY

Authors will be documented according to the B.OSS authorship policy:

1. The investigators in charge of the study and part of the writing group will be mentioned as 'personal author names' as the first and last authors listed
2. One author from each maternity that contributed to the B.OSS registry, will be listed as 'B.OSS research group'. This B.OSS research group will be mentioned as 'group author name' between the first and last author.
3. All other contributors will be listed under "Acknowledgements".

Authorship in MEDLINE (nih.gov)

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