SCUOLA DI DOTTORATO
UNIVERSITÀ DEGLI STUDI DI MILANO-BICOCCA

Department of Medicine and Surgery

PhD Program in Public Health Cycle XXXII

Curriculum in Biostatistics and Clinical Research

Obstetric Near Miss in Italy:

Sepsis, Eclampsia, Amniotic Fluid Embolism and Spontaneous Haemoperitoneum in Pregnancy

Candidate: Colciago Elisabetta

Registration number: 073784

Tutor: Professor Maria Grazia Valsecchi

Co-tutor: Professor Laura Antolini

Coordinator: Professor Guido Grassi

ACADEMIC YEAR 2020/2021

TABLE OF CONTENT

INTRODUCTION

This thesis describes two research projects carried out during my Ph.D. at the University of Milano - Bicocca.

The FIRST PART of the thesis will present the main project that was conducted using a quantitative methodology regarding **maternal near miss** cases in Italy.
A near miss event is defined as "*A woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy*''.
Near miss episodes represents very rare life-threatening obstetric complications, and they are approximately between 9 and 16 every 1000 births across Europe [1]. In socially advanced countries, it is estimated that about 50% of maternal deaths could be prevented and severe maternal morbidity could be reduced by improving healthcare standards [2].
A prospective population-based study will allow to estimate, for the first time in Italy, the incidence rates of severe obstetric conditions and to collect data that may contribute to prevent avoidable severe morbidity.
This study considers four near miss events: Eclampsia, Sepsis, Amniotic Fluid Embolism (AFE) and Spontaneous Hemoperitoneum in Pregnancy (SHiP). These complications, together with haemorrhagic emergencies, account for about 75% of maternal deaths in Italy.

In Chapter 1 I will introduce the near miss concept and definition, I will provide a rationale for its selection and explain the contribution this research may give to the evidence.
Chapter 2 will present the literature review concerning the methods to analyse near miss cases and the evidence regarding the obstetric complications under surveillance.
In Chapter 3 the research design is outlined, with the description of data collection approach, data collection forms and data analysis method.
Results regarding Eclampsia and Sepsis will be presented in Chapter 4.
Discussion with a comparison with the existing evidence will be offered in Chapter 5.
A brief conclusion is given in Chapter 6, together with limitations of the research and suggestion for further studies.

The SECOND PART of the thesis will describe the project developed during the Visiting period at the University Of Surrey (United Kingdom -UK) between February and June 2018. This study was conducted using a qualitative methodology and it focused on parental expectations of childbirth, aiming to explore maternal and paternal expectations of birth and whether these are being fulfilled.

Qualitative research enables the understanding of behaviours, interactions, attitudes, beliefs, experiences and opinion of individuals or groups of people [3]. This methodology usually starts with a broad research question, in regard to the topic that the researcher wants to consider, and it is suitable to explore phenomena about which little is previously known or reported [4]. Studies using a qualitative methodology usually involve small, relevant samples. Non-probability sample methods are used and participants are recruited because they have lived an experience of interest that the researcher is exploring [5] .

An overview of the study will be presented in Chapter 1.

Chapter 2 will focus on the literature review concerning the existing evidence regarding the expectations of birth, both of women and their partners.

Chapter 3 will present the research proposal developed, which includes the research design, the methodology, the data collection approach and the data analysis method.

Potential findings, limitations of the research design and implications for the future of Midwifery practice are described in Chapter 4.

I PART | NEAR MISS PROJECT

ABSTRACT

Background: Data on maternal mortality offers valuable information to improve women's health. In countries such as Italy maternal mortality is a rare event. For each death, many other women survive serious complications during pregnancy, birth and the post-natal period that lead to different degree of sequelae. Life-threating conditions, defined as near miss, could provide additional information on disease risk factors, prevention and treatment for promoting best practices, improving quality of care and achieving better health for mothers and babies. The Italian Obstetric Surveillance System (ItOSS) was set up to monitor the maternal morbidity rate in Italy. In 2017 ItOSS activated a project to collect maternal near miss cases due to sepsis, eclampsia, amniotic fluid embolism (AFE) and spontaneous haemoperitoneum in pregnancy (SHiP) in 9 Italian Regions.

Aim: To estimate the incidence rate of eclampsia, sepsis, amniotic fluid embolism and spontaneous haemoperitoneum in pregnancy and to describe the care provided during the near miss episode.

Method: A Population-based descriptive study was conducted, a case-control design was applied only on post-partum sepsis cases to evaluate risk factors associated to the complication. Data were obtained through a prospective active collection of cases by a monthly call according to the principle of nothing-to-report, along with data collection forms that confirm the diagnosis and gather detailed information. Data collection occurred web-based since November 2017 through http://www.salutedonnabambino.it/ITOSS/login.aspx and was completed on the 31st of October 2019 for the sepsis cases, while the remaining complications were investigated until the 31st of March 2020. Statistical analysis was performed on eclampsia and peripartum sepsis cases; data collected on AFE and SHiP will be used to participate into a multi-national study promoted by INOSS, with the aim to give a stable incidence about this extremely rare conditions. For this reason this thesis will present findings regarding Eclampsia and Sepsis, of which there are sufficiently enough cases to give a useful feedback to healthcare professionals.

Results: Our study achieved good participation and response rates. A total of 109 near misses of eclampsia were identified, representing an estimated incidence rate of 0.15 cases per 1,000 births. Findings indicated that there is space to improve the use of magnesium sulphate as prophylactic treatment in women diagnosed with pre-eclampsia and underlighted the importance of population risk stratification to administer low-dose aspirin to high risk women and at the appropriate time.

More than 3 women in 10 developed sever complications after the eclamptic episode, this could be due to an inappropriate stabilization before birth.
Sepsis estimated incidence rate was 0.87 cases per 1,000 births. The high rate of women who developed severe complications, might reflect the inappropriate time of diagnosis and treatment prescribed to our population. Findings reported different major criticisms during the care of women with sepsis: delayed diagnosis and treatment, the administration of inappropriate antibiotic therapy, the high number of vaginal examinations in labour and the need of correct aseptic technique during all procedures. This might reflect the high rate of women, 1 in 4, with severe complications after sepsis.
Conclusions: This research developed significant information concerning obstetric disorders related to the Italian population, prior to this project no Italian data were available. The present study offers an unique source of information and allows to identify the Italian system or clinical practice related-failures, in order to address strategies and strengths to improve the quality of maternal health care and promote an evidence-based practice.

Keywords: Maternal Near Miss; Severe Maternal Morbidity; Obstetric Surveillance System; Sepsis; AFE; SHiP; Eclampsia; population-based.

CHAPTER ONE: NEAR MISS CONTEXT

1.1 Context study

Traditionally, maternal mortality is considered an indicator of economic development and of the quality of midwifery and obstetric care. Although studies on maternal mortality improve women's health, this event in countries such as Italy is rare. The study on Near Miss could help developing a new indicator of the quality of perinatal care, which, in turn, could provide additional information on disease risk factors, prevention and treatment for promoting best practices, improving quality of care and achieving better health for mothers and babies. Furthermore, women who survive life-threatening conditions arising from complications related to pregnancy and childbirth, have many common aspects with those who die of such complications. This similarity led to the development of the near miss concept in maternal health.

In fact, for each death, many other women survive serious complications during pregnancy, birth and the post-natal period that lead to different degree of sequelae. In the majority of cases, these complications are consequences of the same factors that cause death [6], for every woman who dies, it is estimated that 20 others suffer severe morbidity or disability [7]. The higher rate of near miss cases compared to the low rate of maternal death, allows to generate more reliable estimates, in a shorter time, and will develop valuable knowledge to improve the appropriateness of clinical practice. Near misses offer a rich source of information that can inform error prevention strategies and are a learning opportunities for healthcare professionals. Near miss events represent clinical achievements, as they involve women who survive life-threatening conditions, the good outcome facilitate the investigation, the case review and the audit process, which are hard to do in case of maternal death. Maternal near miss audits give an opportunity to study the cases which were almost similar to those where maternal deaths occurred; thus, the study of near miss cases will increase the understanding of the weakness of the perinatal care within the healthcare systems, improve the quality of midwifery and obstetric care and, further, may help to reduce and avoid a maternal death or a life-threatening complication.

The aim of this thesis is to estimate the incidence rate of near miss cases due to sepsis, eclampsia, amniotic fluid embolism (AFE) and spontaneous hemoperitoneum in pregnancy (SHiP) at the Maternity Units involved into the Project, where there is 75% of all births in Italy.
Furthermore, the study will describe the care provided to the women, including the cascade of events that could lead to a maternal death and will analyse the characteristics of the Maternity Units where the near miss occurred.

1.2 Definition of near miss cases

Near miss and severe acute maternal morbidity (SAMM) are two interchangeable terms for a severe, life-threatening obstetric complication. The term near miss was borrowed from the airline industry, that defines these events such as “successes realized because of good fortune rather than good processes” [8]. In healthcare it generally describes a condition that is not an illness, however in the field of maternal health, the term near miss has been used to define a severe complication, where a woman nearly died, but survived [9–13]. Considering that the term ‘‘maternal near miss’’ best reflects the concept of ‘‘nearly dying but surviving’’, the World Health Organisation (WHO) working group on Maternal Mortality and Morbidity classifications, advocates the use of this term instead of SAMM [14]. The WHO has recommended investigating near misses as a benchmark practice for monitoring maternal healthcare. However, routine implementation of this concept has been limited due to the lack of a standard definition and of a uniform approach to identify cases.

In 2007, WHO established a technical working group of obstetricians, midwives, epidemiologists and public health professionals from low and high income countries, the WHO working group on Maternal Mortality and Morbidity classifications, to develop a maternal death classification system, due to the inconsistence in the way maternal deaths were classified. The working group also reached consensus on how to define a maternal near miss: ‘‘A woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy’’ [14]. Signs of organ dysfunction that follow life-threatening conditions are used to identify maternal near misses so that the same classification of underlying causes is used for both maternal deaths and near misses.

However, also criteria used for diagnosis to classify near miss cases varied widely across studies with three main approaches; disease-specific (specified criteria for common conditions); management-specific (specified criteria related to response to disease); and organ-system dysfunction/failure based (specified criteria for dysfunction or failure related to each organ system) [14]. A World Health Organization systematic review found that, internationally, the prevalence of severe acute maternal morbidity ranged from 0.80 to 8.23% in studies that use a disease-specific approach, it is from 0.01 to 2.99% when using a management-based approach and the rate changes from 0.38% to 1.09% when the organ-system dysfunction/failure based approach is adopted [11].

The disease-specific approach could classify a woman with a post-partum haemorrhage as a maternal near miss case, however the same threshold to identify a severe haemorrhage could have different consequences in women with normal level of haemoglobin or those with severe anaemia. The woman with good haemoglobin levels won’t be close to death, therefore according to the near miss definition, she will not be a case to include.

The management-based approach could identify a near miss case when a woman is admitted to Intensive Care Unit (ICU) or Stroke Unit or when performing an hysterectomy. However, it involves variables such as presence of ICU, availability of ICU beds or indications for hysterectomy, that could vary widely.

The organ-system dysfunction based approach represents the most promising frame for establishing a standard set of criteria [11]. The criteria emphasize the presence of organ dysfunction or failure that is identified using three groups of elements (clinical, laboratory, and management).

According to this approach a set of criteria should be developed in order to identify a near miss case.

The WHO working group on Maternal Mortality and Morbidity classifications proposed a list of potential life-threatening conditions to optimize surveillance efforts for the identification of maternal near miss cases and a list of criteria to identify an organ dysfunction [14]. This list is not definitive as a women could present a different condition that may escalate to a life-threatening event, that should be define as well as near miss.

Table 1 shows the WHO list of life-threatening conditions that has been proposed [14].

Haemorrhagic disorders	• Abruptio placentae • Accreta/increta/percreta placenta • Ectopic pregnancy • Postpartum Haemorrhage • Ruptured uterus
Hypertensive disorders	• Severe pre-eclampsia • Eclampsia • Severe hypertension • Hypertensive encephalopathy
Severe Management Indicators	• Endometritis • Pulmonary oedema Respiratory failure • Seizures • Sepse Shock • Thrombocitopenia <100.000 • Thyroid crisis
Other Systemic disorders	• Blood transfusion • Central venous access • Hysterectomy • ICU admission • Prolonged hospital stay (>7 postpartum days) • Non anaesthetic Intubation • Return to operating room • Surgical intervention

Table 1. WHO list of life-threatening conditions

The criteria used to identify organ dysfunction derived from the Sequential Organ Failure Assessment score (SOFA Score), a tool that has not been validated in obstetrical populations but is largely used in the assessment of severely ill patients [15].

A woman who developed one of the criteria that describes an organ dysfunction/failure and survived during pregnancy, childbirth or within 42 days of termination of pregnancy, should be classified as a maternal near miss case.

Table 2 shows the WHO list of organ dysfunction criteria [14].

Clinical criteria	• Acute cyanosis • Gasping • Respiratory rate >40 or >6/min • Shock • Oliguria non responsive to fluids or diuretics • Clotting failure • Loss of consciousness lasting ≥ 12 hours • Loss of consciousness and absence of pulse • Stroke • Uncontrollable fit/total paralysis • Jaundice in the presence of pre-eclampsia
Laboratory-based criteria	• Oxygen saturation <90% for ≥ 60 min • PaO_2/FiO_2 <200 mmHg • Creatinine ≥ 300µmol/L or ≥ 3.5mh/dl • Bilirubin> 100 µmol/L or > 6.0mg/dl • pH< 7.1 • Lactate >5 • Acute thrombocytopenia (<50 000 platelets) • Loss of consciousness AND the presence of glucose and ketoacids in urine
Management-based criteria	• Use of continuous vasoactive drugs • Hysterectomy following infection or haemorrhage • Transfusion of _5 units red cell transfusion • Intubation and ventilation for _60 minutes not related to anaesthesia • Dialysis for acute renal failure • Cardio-pulmonary resuscitation (CPR)

Table 2. WHO list of organ dysfunction criteria

The WHO technical working group recommends that the new maternal death classification system be adopted by all countries and the maternal near miss approach be considered in national plans for improving maternal health [14]. By using the same classifications, reliable comparisons can be made within and between countries and regions. Applying this classification should help to identify the health system weakness and failures that countries need to address in order to reduce complications and fatal outcomes of pregnancy and childbirth [16].

1.3 The Italian Obstetric Surveillance System (ItOSS)

Severe conditions developed during pregnancy, childbirth and the post-natal period are individually rare, however together represent a considerable burden to the women they affect and for the Healthcare Systems. Women with a rare disease present unique challenges for the Healthcare System because there is often a lack of knowledge about their condition and clinical practice is not sufficiently evidence based. When dealing with severe complications, there are many elements to consider before conducting studies. When a disease is rare it is difficult to conduct studies and to obtain a high number of cases, because they would take a long period of time to be collected. Moreover, these particular complications usually occur in emergency situations when documentation could be less accurate and retrospective studies may result having information biases [17]. Randomized controlled trials are unreasonable to conduct. In addition, cases should be identified using uniform definitions between studies, in order to collect comparable data and provide guidelines across different countries. Also the methodology adopted could have a major impact on the findings of each study [17]. For this reasons a single, shared, reporting system could avoid all these problems.

The first Obstetric Surveillance System (OSS) was set up in the United Kingdom (UK) in 2005 with the aim to study rare obstetric complications, including near miss episodes. This model was adopted also by other countries and in 2010 an international body was established with the purpose to bring together the various national and regional Obstetric Survey Systems. This international System was called “International Network of Obstetric Survey Systems” (INOSS). INOSS is a multinational collaboration of organisations conducting prospective population-based studies of serious illnesses in pregnancy and childbirth.

The INOSS network promotes a collaborative working between countries, providing numerous advantages. A commentary by Marian Knight published in 2013 described the numerous benefits of multi-country studies of severe and uncommon maternal morbidities [17].

Multi-national studies provide a clear advantage in terms of the number of cases which can be included in any study, they use the same definitions to identify cases, collecting common variables, allowing international comparisons and investigation of variations in incidence and management [17]. In addition, they have the opportunity to investigate different risk factors that could change from country to country. A very important advantage is the ability to investigate the replicability of observational findings across different population [17]. Observational study do not demonstrate causality, however replication of findings across similar populations make the associations that have been found stronger. In fact, INOSS member countries have generated evidence to inform aspects of management of many severe pregnancy complications [18–21].

Multi-national studies with uniform case definitions, common methodology, shared variables collected, allow for the conduct of reliable studies less subject to many of the biases attributed to

typical single-center observational studies. For very rare conditions, such collaborative studies may provide the only route to high quality evidence to guide practice [17].

The Italian Obstetric Surveillance System (ItOSS), coordinated by the National Centre for Epidemiology, Surveillance, and Health Promotion - Unit of Women's Health – of the Italian National Institute of Health, is the national system set up to study rare disorders of pregnancy and to monitor the maternal morbidity rate in Italy. In 2012 ItOSS was included into the INOSS network.

The co-operation and collaboration with existing population-based Obstetric Survey Systems allows ItOSS to describe the epidemiology of a variety of uncommon disorders of pregnancy and to collect evidence aiming to improve outcomes for women with serious and rare diseases in pregnancy.

The Obstetric Survey Systems included into INOSS are:

- United Kingdom Obstetric Surveillance System (Ukoss)
- Australasian Maternity Outcomes Surveillance System (Amoss)
- Austrian Obstetric Survey System (Auoss)
- Belgian Obstetric Surveillance System (Boss)
- Épidémiologie de la Morbidité Maternelle Sévère (Epimoms)
- German Obstetric Surveillance System (Geross)
- Italian Obstetric Surveillance System (Itoss)
- Nordic Obstetric Surveillance Study (Noss - Svezia, Islanda, Finlandia, Norvegia, Danimarca)
- Netherlands Obstetric Surveillance System (Nethoss)
- Slovak Obstetric Survey System (Soss).

The Italian Surveillance System works to achieve the Sustainable Development Goals (SDGs) 2016-2030 established by the United Nation, a call for action by all countries, to promote prosperity while protecting the planet. Especially important is Goal 3 "Ensure healthy lives and promote well-being for all at all ages" aiming to guarantee healthy lives and to promote well-being at all ages, this includes the prevention of maternal mortality and the need to ensure the highest level of women's and infants health (https://www.un.org/sustainabledevelopment/health/).

1.4 Rationale of the study

ItOSS conducted different projects to estimate the maternal mortality rate (MMR) in Italy.

Data collected by ItOSS allowed to know the causes of maternal death and to address the priority of interventions.

Data were initially collected for 7 years in 10 Italian Regions (Lombardia, Piemonte, Friuli Venezia Giulia, Emilia-Romagna, Toscana, Lazio, Campania, Puglia Sardegna e Sicilia), between 2006 and

2012, throughout a record-linkage procedure, using the Mortality Registers and the Hospital Discharge Database. A total of 320 women died in pregnancy or within 42 days after giving birth, accidental causes were excluded, giving 277 maternal deaths [22] with a Maternal Mortality Ratio (MMR) of 9.2 per 100.000 live births. The leading cause of direct maternal death was post-partum haemorrhage, followed by hypertensive disorders in pregnancy and thromboembolism, these contributed together to the 70% of all maternal deaths. Whereas 5% of women died due to sepsis, that was the fourth cause of direct maternal death [22].
Between 2013 and 2016, ItOSS adopted also the methodology based on the Confidential Enquiry into Maternal and Child Health Report generated by the United Kingdom and started in 1952. This approach consists to collect data on deaths prospectively, using a specific data collection form completed by clinicians involved into the care of the woman who died. From this Surveillance, post-partum haemorrhage continued to be the leading cause of maternal death, followed by sepsis, which resulted to be the second cause of direct maternal death [22].

These data gave the opportunity to plan the first prospective population-based study to evaluate the incidence of severe post-partum haemorrhage and other serious conditions such as invasive placenta, uterine rupture and peripartum hysterectomy, since these are the leading cause of maternal mortality and the most common contributors to maternal morbidity in Italy. Findings allowed to understand the process of care and to identify system or clinical practice related-failures, this facilitated preventive interventions and provided guidelines to support healthcare professional, improving the quality of maternal health care.

The next step would be to investigate the incidence of the remaining disorders responsible of maternal deaths, thus the need to plan a new prospective population-based study to estimate the near miss cases due to Sepsis, Eclampsia, Amniotic Fluid Embolism (AFE) and Spontaneous Hemoperitoneum in Pregnancy (SHiP).

1.5 Contribution of the research

There is a knowledge gap that needs to be urgently filled regarding the incidence of these complications in Italy.
Surveillance on Sepsis, Eclampsia and AFE have already been completed by the Uk Obstetric Surveillance System and by the Surveillance Systems of other countries. This would give the opportunity to make cross-national comparisons of incidence, aetiology, management, prevention and outcomes.
Data collected on AFE and SHiP will be used to participate into a multi-national study promoted by INOSS, with the aim to give a stable incidence about this extremely rare conditions. For this reason

this thesis will present findings regarding Eclampsia and Sepsis, of which there are sufficiently enough cases to give a useful feedback to healthcare professionals.

In high income countries preventable maternal mortality is estimated to be 50% [2]. The Italian data would offer precious information to implement evidence-based prevention strategies and effective treatment in order to reduce the incidence of maternal mortality and morbidity due to maternal near miss cases.

The present study regarding four obstetric near misses in Italy, integrated into the INOSS researches, has been conducted with the aim to make recommendations for best practice and improve outcomes for women with severe and rare complications in pregnancy, childbirth and during the post-natal period.

The final goal of this projects is to enable the lessons learnt to improve future care to be identified more quickly and to reduce preventable maternal severe morbidity and mortality.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

The evidence regarding methods to review near miss cases and the four conditions under analysis (Sepsis, Eclampsia AFE and SHiP) will be presented taking into account all the studies conducted by the members of the INOSS network and all the existing reliable research.

The following Chapter will present different diagnostic tools and the WHO near miss approach to identify and analyse maternal near miss cases. The methodology adopted by the Obstetric Surveillance Systems will be described. Evidence exploring women's experience of a near miss will be considered. In addition, evidence regarding the four obstetric conditions under investigation will be appraised and each disease will be discussed throughout the following sessions: *definition, diagnosis, epidemiology, risk factors, etiology and management*.
Rare obstetric events are, by virtue of their rarity, difficult to study. However researches conducted throughout INOSS helped to better understand the incidence, risk factors, diagnosis and management of these severe and uncommon disorders.

2.2 The WHO methods to review near miss cases

The Sustainable Development Goals (SDGs), also known as the Global Goals, were adopted by all United Nations Member States in 2015 as a universal call to action to end poverty, protect the planet and ensure that all people enjoy peace and prosperity by 2030. Under Goal n. 3 WHO is committed to ensure healthy lives and promote well-being for all at all ages (https://www.undp.org/content/undp/en/home/sustainable-development-goals/goal-3-good-health-and-well-being.html). This Goal includes also the promotion of maternal well-being, supporting the reduction of maternal mortality and morbidity by 2030. For this to happen, high quality reproductive, maternal and newborn health care must be available, accessible and acceptable to all in need. There are numerous strategies to improve the quality of maternity care, one of these are the review and audit of maternal death cases. However, in view of the new evidence, there are various advantages when review and audit are applied also on maternal near miss cases [23].

In 2004 the WHO released a document entitled "*Beyond the Numbers - Reviewing maternal deaths and complications to make pregnancy safer*" [24], where the review of maternal deaths and near misses is promoted through different diagnostic tools, to retrospectively analyse cases. The WHO underlined the need for every country to estimate maternal mortality and to implement a system to

monitor and review cases, in order to understand why women die. The final aim should be to avoid preventable maternal mortality and near miss episodes.

The term “audit” has been used to define a wide range of methods adopted to review cases, however there are two main types of audit involved in the evaluation of maternal and child health: critical incident or adverse event audit and clinical audit [25]. The first one includes the confidential enquiries and the facility-based case review of deaths or near miss cases, which have the aim to assess any aspect of care, experts are often involved to evaluate the structure and the process components of care. Clinical audit comprises mainly the criterion-based clinical audit, peer review is encouraged to evaluate the care and the outcomes, using agreed standards, in order to change clinical practice when needed [25].

Deciding which of the approaches to use, is influenced by two considerations:

1. which level is appropriate for the review
2. what kind of cases will be studied.

In terms of level, there are different options, such as community, health care facility, district, regional or national level. In choosing which cases to study, a decision needs to be taken whether these will be outcomes or processes [24].

2.2.1 Confidential enquiries

The confidential enquiry approach on national level is the most hard to conduct, as it requires important efforts to be planned and innovative data collection systems to be run. For these reasons are recommended in countries with an advanced healthcare system, with a support by the State and with healthcare professionals who are committed to improve the quality of care [26].

Data are collected confidentially and then anonymized, to allow a multidisciplinary team of independent experts, to examine the quality of care of individual cases against national guidelines or accepted best practice. Confidentiality and anonymization is paramount to allow healthcare professionals involved within the care, to report without bias all the events [24].

The longest running example of a confidential enquiry into maternal deaths (CEMD) is that of the United Kingdom, which has operated continually since 1952.

A further recent advance is the introduction of confidential reviews of the care of women with severe morbidity, the Confidential Enquiries into Maternal Morbidity, which are topic specific. The enquiry is conducted in exactly the same manner as for maternal deaths, with the exception that the care of only a stratified random sample of women with a specific morbidity, is reviewed. Women with specific morbidities are identified through different sources depending on the topic; the majority to date have been identified by sampling from the women included in UK Obstetric Surveillance System studies [27]. The enquiry of near miss cases allows to evaluate the incidence,

risk factors, care and outcomes of numerous maternal complications, to identify the failure and weakness of the system, with the aim to make recommendations to improve clinical practice [28].
Population based prospective surveillance systems aim at generating the information required to outline realistic and practical actions with the final goal to reduce preventable maternal severe morbidity and mortality.

2.2.2 Criterion-based clinical audit (CBCA)

According to the WHO document "Beyond the numbers" [24], the clinical audit is a process aiming to improve the quality of care, it is a cycle iterative process, which is repeated until practice meets agreed standards.
The CBCA of near miss allows to evaluate the quality of maternity care in life-threatening conditions, making comparisons between death women and survivors. This might underline elements of care that allows women with the same complication to have different outcomes, contributing to the identification of best practice [29].
According to WHO [24] the CBCA comprises 5 steps:

1. established criteria of best practice;
2. measure current practice;
3. feedback practice and set local standards;
4. implement change;
5. re-evaluate practice and feedback.

The established criteria are standard of clinical practice, that could be measured.
The CBCA are also an opportunity to involve healthcare professionals giving them proper feedback to improve their practice, facilitating changes of the care [14]. This audit gives a standardized method to analyse the data. On the contrary, some professionals may be unfamiliar with concepts such as evidence-based or best practice [24], data retrospectively collected could have selection bias [14], moreover professionals should be committed to implement at least one change within the audit cycle.

2.2.3 Facility-based maternal near miss case review (NMCR)

The facility-based maternal near miss case review (NMCR) involves an in-depth knowledge of the process of care including administration and management aspects, as well as the lived experience of the women [30]. The NMCR consists of a discussion between all the staff members involved into the care of the woman. Obstetricians, Midwives and Midwife Care Assistants together examine the care provided against guidelines, local protocols and standards [31]. Data are collected throughout the "gate to gate" method, describing care from the admission until the discharge of the woman. In addition, women's experience is considered and face-to-face interviews are conducted to understand their evaluation of care received [30]. The interview should be conducted before or just

after discharge to minimize the recall bias, which occurs when participants do not remember previous events or experiences accurately [32].
The aim of the NMCR is to appraise the care, the management and attitudes of the professionals, in order to identify areas that could be improved, implementing appropriate solutions to the issues emerged.
One of the strengths of this method is the “bottom-up” approach, it means that professionals who provided care to the women are committed to make a change [31], promoting a reorganisation of staff activities, such as better specification of roles and responsibilities, task shifting and improved communication [33]. The WHO [24] underlined the importance to collect the women's views, to develop recommendations to improve the quality of care.

All this methods described in “Beyond the Numbers” [24] share the same fundamental principles of ensuring confidentiality, and not apportioning blame in their attempts to understand the factors contributing to poor outcomes and to learn lessons for the future. Behind successful review and audit, there should be a positive cultural environment at personal, institutional and national level, based on fostering of professionalism and focused on learning, as a crucial part to improve services and quality of care [26]. Midwives and Obstetricians would develop a culture of continuous improvement and transparency, would see adverse outcomes, errors and omissions as learning opportunities, would mature a philosophy of no blame, whereas the audit and review methodologies will be included in their training curriculum [34].

2.3 The WHO near-miss approach for maternal health

In 2011, when the definition of near miss has been developed, the WHO realized a document focus on near miss audit, where surveillance recommendations on maternal near miss were further updated. A systematic process for assessing the quality of care with a standard approach to monitor the implementation of critical interventions in maternal health care, has been proposed [35]. This generic guide is based on the concept of criterion-based clinical audit. The WHO suggested to adopt this approach routinely to evaluate and improve the quality of care provided to the women, their babies and families. The ultimate purpose of the near-miss approach is to improve clinical practice and reduce preventable morbidity and mortality through the use of best evidence-based practices. Hence, this guide should be used in conjunction with evidence-based clinical guidelines [35].

In any setting, women who develop severe acute complications during pregnancy share many features and characteristics. While death is very rare, near miss cases are more frequent. The document reported that around 7.5 cases per 1000 births are expected to be severe maternal

outcomes. By evaluating cases of near miss episodes, in addition to maternal death reviews, much can be learnt in order to improve quality of maternal care [35].
The WHO recommended to use this approach in any healthcare facility, a database should be constituted to collect women records, then data should be stored and managed.

The process to assess, monitor and improve the quality of care should follow 3 steps (Figure 1).

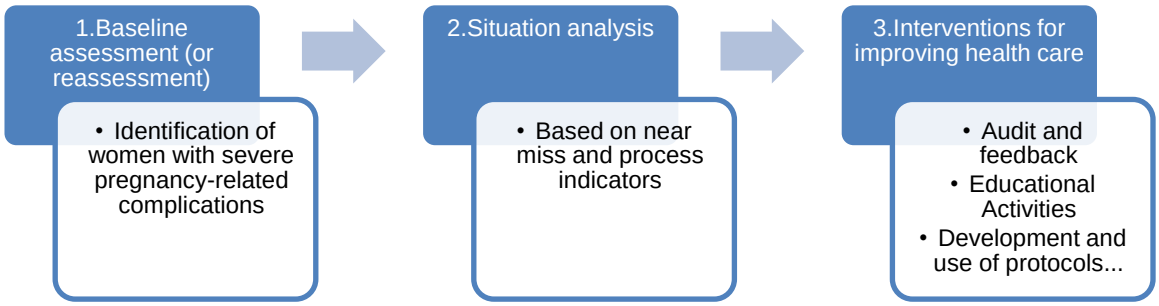


Figure 1. Implementation of the WHO near miss approach

The first step should be done considering two assumptions described by the WHO document: all maternal death involve at least one life-threatening condition and women who will be classified as a near miss case will have one or more severe pregnancy-related complication or are the ones who will receive critical interventions. For this reason, all women who are pregnant, in labour, or who had a miscarriage up to 42 days with any potential life-threatening condition or with an organ dysfunction, would be eligible to be included for the assessment.
The second step should involve the adoption of the near miss indicators, as proposed by the WHO document (such as: Maternal near-miss (MNM)= woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy; MNM ratio (MNMR)= number of maternal near-miss cases per 1000 live births (MNMR = MNM/LB). This indicator gives an estimation of the amount of care and resources that would be needed in an area or facility, and the use of process indicators to analyse if the management of the condition occurred was appropriate and in accordance with the guidelines.
During the third step, strategies should be activated in order to improve the quality of care.
The approach should be performed periodically, otherwise data could be collected continuously after the initial assessment.

The WHO has the final expectation to facilitate health systems to understand patterns of maternal mortality and morbidity, strengths and weaknesses of the clinical practice and of the organization and to evaluate whether evidence-based practice is provided. Finally, publications of data are suggested, adding evidence to the literature and improving the quality of maternity care worldwide.
Since their publication, the WHO maternal near-miss criteria and the audit tool have been applied in over 30 countries [23,36–39].

2.4 The Obstetric Surveillance System

Overall, maternal death and near-miss audits generate valuable information, but this is not enough to create and sustain a change in clinical practice. To 'activate' the information, a systems approach of surveillance is advised, prospective identification of severe morbidity cases is responsible for the generation of actionable information that effectively guides immediate and longer-term actions [23].

In 2005 the United Kingdom Obstetric Surveillance System (UKOSS) was launched to investigate uncommon disorders of pregnancy. The need to generate a national Obstetric Surveillance System had different reasons. Before UKOSS, information request regarding rare complications arrived from multiple sources, this might represent a burden for clinicians involved into the reporting activities. Many uncommon disorders are difficult to study and even if large collaboration are organized, very few cases could be identified. Furthermore, the 50 years' experience of Confidential Enquiries into UK maternal deaths have led to many important changes in care, but evidence have suggested that study of near miss events may be more useful [40,41].
The UKOSS started the Surveillance taking as example the British Paediatric Surveillance Unit (BPSU), which since 1985 has developed a method to study rare paediatric diseases (https://www.rcpch.ac.uk/work-we-do/bpsu).
Since then, many countries around the World, implemented an Obstetric Surveillance System, included Italy, to improve the quality of maternity care and reduce preventable maternal morbidity and mortality.

INOSS supports to conduct a clinical audit each time a case has been identified, in order to promote peer review and to develop a "no blame" culture.

2.4.1 Data collection

The Obstetric Surveillance System of each country included into INOSS has adopted the methodology for case reporting developed by UKOSS. Each maternity unit involved into a study coordinated by the Obstetric Surveillance System (OSS), will nominate a contact person (obstetrician or midwife), who will deal with all the activities regarding the project. This contact person will mainly be sent a monthly mailing reminder, to report a selected number of rare obstetric complications, currently under surveillance, that occurred in the preceding month. Only rare complications will be investigated, and thus the most common response will be "nothing to report".
If a case needs to be reported, the contact person will complete an on-line data collection form. In case of incomplete reporting, the contact person is encouraged repeatedly by email and by phone calls, to provide the missing data. If a women will have a complication under surveillance followed

by a fatal outcome, the event will be reported by the contact person named for the study and by the one who is responsible for the surveillance of maternal death.
Data collection forms will be developed individually for each condition and should be easily completed using the women's case notes.
Some Obstetric Surveillance Systems decided to collect data throughout a website created specifically for the study they are currently running. Instead, UKOSS, for example, has a page where all the studies currently collecting data are shown. Reporters should go down the list of studies and add the number of cases (or 0 for nothing to report) to the text box for each study. If a clinician submits a case, the UKOSS team will send out (via post) the data collection form of the case, that will be completed and returned.

2.4.2 Variables collected

Data collection forms seek confirmation of the appropriate case definition and additional data on maternal characteristics, medical and obstetric history, details of the current pregnancy, details regarding birth, circumstances of the adverse event, its management, the outcome for mother and newborn and a box to use any other addition information the contact person wants to send. Women's personal information will not be collected, as anonymous data will be analyse.

2.4.3 Data analysis

Data are exported, then cleaned and analysed using a software for statistical analysis. The incidence of the obstetric cases is estimated using as denominator the total number of births occurred during the study period into the Maternity Units that included into the study or nationally if this is the case.

2.4.4 Projects conducted by the Italian Obstetric Surveillance System

ItOSS is involved in different projects, which will be listed below.

- Since 2012: prospective surveillance on maternal mortality;
- 2020 ongoing: currently ItOSS is conducting a study to monitor the Sars-CoV-2 infection in pregnancy and during the post-natal period, in all the 20 Italian regions;
- 2017 ongoing: prospective population-based study on stillbirths;
- 2017 – 2020: prospective population-based study on maternal obstetric near miss due to Sepsis, Eclampsia, Amniotic Fluid Embolism and Spontaneous Haemoperitoneum in Pregnancy;
- 2016 – 2018: prospective population-based study on maternal mental health;
- 28/11/2017 – 04/12/2017: Global Maternal Sepsis Study (coordinated by WHO);
- 2014 – 2016: prospective population-based study on maternal near miss due to postpartum haemorrhage.

2.5 Early and long-term effects on women who had experienced a near-miss

Little is known about the early and long-term consequences of a near miss on maternal health, especially about the emotional impact this episodes might have either on the woman and on her family. This paragraph would deserve an entire chapter to explain the feelings that women may have after such a crucial event in their life. This would require the exploration of all the qualitative research present in the literature and would need further studies to better understand women's and partners perceptions, which is not the aim of this thesis. However, it appeared important to mention the main findings published in regard of this issue, giving an idea about women's experiences and how much more should be done to help them to go beyond this critical event.

In UK up to 8000 women and their families each year have to cope with a life-threatening pregnancy complication and its aftermath [42].

Women who suffered severe morbidities during pregnancy and childbirth may present clinical and psychological disorders that may last for long time [43]. Thus, these conditions may lead to deterioration of quality of life and adverse effects on maternal, infant and family well-being Evidence show that in addition to their physical recovery, women may experience anxiety, isolation and flashbacks in the aftermath [44]. Complicated pregnancy can also impact negatively on early breastfeeding behaviours and rates [45,46]. Although critical illness in pregnancy, childbirth and the post-natal period may be uncommon, it is a potentially devastating complication. Women may have to recover from a major surgery, emergency treatment or time in Intensive Unit and some may have to cope with the grief for the loss of their baby or with babies who need to spend long time in Neonatal Intensive Unit. These experiences are far from normal birth and maybe from what women would expected.

Women who survived a life-threatening complication report to have been lucky, to be grateful to the healthcare professionals, but most of all they report the feeling of loss [47]. Loss of their baby, loss of body integrity and well-being, loss of strength, with physical, economic and social consequences [47]. The proportion of physical consequences is higher among women who experience a near miss, with higher probability to have hypertensive disorders, urinary incontinence, prolapse, haemorrhoids, anaemia [48], urinary infections and fever [49].

There is a high variability regarding the coping strategies women may have to manage their feelings and how they feel their life has changed. Women who participated in a qualitative study in UK [50], reported symptoms of anxiety, panic attacks, and post-traumatic stress disorder. In some cases the partner's mental health was also affected. Women often described feeling isolated. Their experiences can have a profound impact on their relationships, family life, career, and future fertility [50]. In addition, also symptoms of pain, insomnia, irritability and struggling to cope with the

loss of their baby were described [51]. Other feelings such as fear, frustration, altered state of consciousness, perception of the imminence of death and the transitoriness of life, sometimes with chest pain and dyspnoea, were stated [52,53]. Frustration comes as women feel unable to perform the physiological process of pregnancy and childbirth, they feel useless and incompetent [53].
The risk of depression is significantly higher among women who survived a near miss, especially if a perinatal death occurred [48].

However, some women may describe also positive changes, such as feeling more mature, improved family relationships and need to pay more attention to their health [51].

Furthermore women described feeling of isolation, feeling distanced from family, friends who shortly forgot about the critical episodes, and from other pregnant women who could not understand their lived experience [50,53]. In low income countries, or in countries where the healthcare needs to be payed, the cost of the healthcare resulted in an economic burden for all the family members. As a consequences women become isolated, the economic and social stresses involved in managing the care of such complications increases their vulnerability. After a life-threatening condition, women's health issues last for long and could compromise their productive and reproductive capacity, leading to a loss of income and marital stability [47].
Women's relationships with their partners could became complicated and additional support may be required [42].

Also the partners had been deeply affected by the women's experience [42]. For some, this event had an impact on their long-term mental health, with financial, practical and emotional consequences [42]. They often report that support from staff and family member was very helpful, however they would appreciated more frequent updates during the emergency because sometimes they stayed hours without having news about the partners, with the joy to have a baby with them, but the worries for their partners. This was described as very traumatic [42,47].

In view of all the symptoms felt by women who experienced a near miss event, the hypothesis of a "maternal near miss syndrome" was considered. This may be explained as an acute stress disorder that may be associated with the occurrence of severe maternal complications [53].
Addition care to women and their family might be needed in order to help to alleviate the impact that severe maternal complications have on women, including physical, emotional and social support.

2.6 Near misses under surveillance

This paragraph will discuss the evidence regarding the four obstetric complications under surveillance, each one will be described going throughout the following sections: *definition, diagnosis, epidemiology, risk factors, aetiology and management.*

The main challenge researchers face in conducting studies on rare severe maternal morbidities, is the absence of uniform definitions. The importance to have shared definitions would facilitate the identification of these rare obstetric diseases with the aim to enable international comparisons, improving the quality of maternal care. In addition, a uniform definition together with a common research method, would allow to find stable incidences of the obstetric complications under surveillance.

At this purpose, the International Network of Obstetric Survey System conducted a study applying the Delphi method to arrive at unified definitions of eight conditions of maternal morbidity [54]. The eight complications were choose based on the multi-national studies INOSS was planning to conduct. The Delphi study was conducted using an online survey tool with the participation of 103 experts from 13 countries. The experts panel agreed on the definition of: Eclampsia, Amniotic Fluid Embolism, Pregnancy-related Hysterectomy, Severe primary postpartum haemorrhage, uterine rupture, Abnormally invasive placentation, Spontaneous Haemoperitoneum in Pregnancy, cardiac arrest in pregnancy.

The present study used some of the definitions successfully developed using the Delphi process.

Data collected regarding AFE and SHiP, two of the four complications under surveillance, will allow to participate in a multi-national study, coordinated by INOSS. AFE and SHiP are two extremely rare conditions, for this reason the number of cases collected in our country would not be enough to make a useful statistical analysis, therefore data require to be pooled with the ones collected in other countries.

2.6.1 Sepsis

The Italian Minister of Health within the Recommendations regarding the prevention of maternal death or severe maternal morbidity associated to labour and birth, reported that sepsis is one of the leading cause of maternal death in high income countries [55].

Although considerable progress regarding diagnosis and treatments, infections during the childbearing continuum account for about one tenth of the global burden of maternal death [56].

Worldwide sepsis is estimated to be the third cause of direct maternal death, following post-partum haemorrhage and hypertensive disorders in pregnancy, at childbirth and during the post-natal period [57]. Even though the improvement of treatment and antibiotics, in high income countries, sepsis has been observed to increase [58–60]. It should be emphasised the high risk of lethality of

sepsis to promote a prompt diagnosis. When a delay in diagnosis and treatment occurs, maternal infections could lead to sepsis, maternal morbidity and death, in addition to a higher risk of foetal and neonatal poor outcomes [61,62].
Sometime maternal sepsis may present without specific risk factors. Furthermore, physiological changes of pregnancy, which mimic those of sepsis, often delay recognition and optimal management [62].
In UK the absolute risk of maternal death due to sepsis is 2 per 100'000 live births [63], however maternal morbidity due to this complication is 50 times higher [64].

2.6.1.1 Definition of Sepsis

Sepsis is a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection [65]. It is a worldwide emerging condition and due to his high lethality rate, has been already internationally studied throughout a research coordinated by the World Health Organization, the Global Maternal Sepsis Study (GLOSS). The aim of the study will be to improve the standard of maternal care and to reduce the preventable cases.

In 2016, a task force of recognized experts, supported by the European Society of Intensive Care Medicine and by the Society of Critical Care Medicine, after a year of work, proposed a new definition of sepsis, termed Sepsis-3 [65]. The new definition defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection [62,66]. The definition emphasizes the presence of infection together with an organ failure. The new definition abandoned the use of host inflammatory response syndrome criteria (SIRS) in identification of sepsis and eliminated the term severe sepsis.
The organ failure is evaluated using a score denominated Sequential sepsis related Organ Failure Assessment (SOFA) based on vital signs and laboratory exams [62]. This score is adopted in critical care wards, because it would be hard to use it in normal wards. For this reason a score called quick SOFA (qSOFA) has been proposed, which have the advantages to be simpler and quicker to calculate throughout the assessment of blood pressure, respiratory rate and conscious state. The difference between the two scores is that the SOFA allows the diagnosis of organ failure and then sepsis, while the qSOFA consents to identify patients with infection or suspected infection.
However it is crucial to mention that both scores are not validated for the obstetric population.

2.6.1.2 Definition of Maternal Sepsis

In 2015, during the conference Enhancing the Focus on Maternal Sepsis the need to focus on this important cause of maternal and newborn mortality and morbidity has been recognized. The World Health Organization (WHO) and Jhpiego have launched the Global Maternal and Neonatal Sepsis

Initiative, with the aim to develop new strategies to promote prevention, diagnosis, early detention and appropriate treatment of this complication [67]. The Definitions for Sepsis and Septic Shock [65] has been generated for an adult population, which has very different characteristics compared with maternal features. In April 2016, WHO convened a multidisciplinary international panel of 48 experts to discuss, develop and propose a new global definition for maternal sepsis [67]. The new definition of maternal sepsis reflects the thinking embedded in the 2016 Third International Consensus Definitions for Sepsis and Septic Shock and it is: “Maternal sepsis is a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or postpartum period.”[67].

Sepsis definition involves [68]:

- genital tract infection
- urinary tract infection
- breast infection
- respiratory tract infection
- cardiac infection
- central nervous system infection
- gastrointestinal infection
- skin and soft tissue infection

Figure 2 shows what is the rationale of the sepsis definition: clinicians should always consider sepsis when in front of a suspected or sure infection and searching for an potential organ failure; vice versa when an organ failure occurs, a potential infection should always be considered.

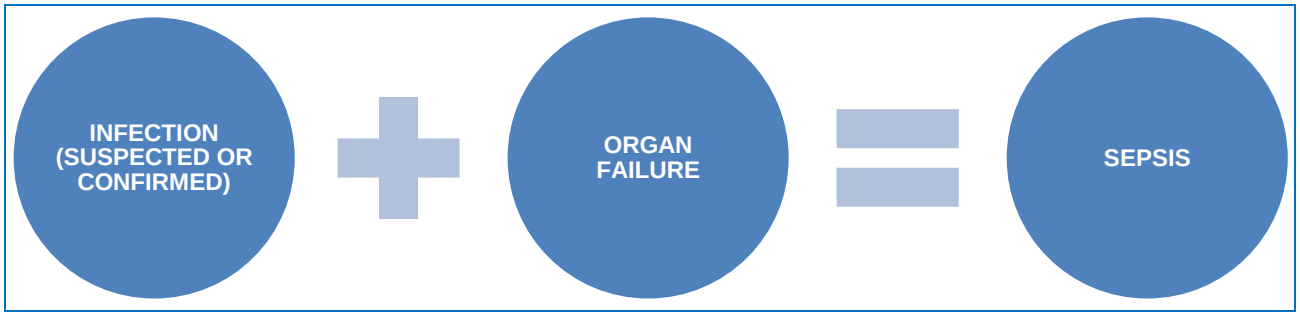


Figure 2. Sepsis definition [67]

The use of the SOFA score was not supported by WHO. Due to normal body changes in pregnancy, vital signs and features observed during maternal sepsis, are different from the ones founded in the general population.

For this reason, a multinational Study denominated GLOSS (Global Maternal Sepsis Study) within the Global Maternal and Neonatal Sepsis Initiative, has been promoted and coordinated by the WHO in 54 countries, with the aim to better understand the incidence and the risk factors of maternal infection, but also to define and validate a set of criteria to facilitate the appropriate and prompt diagnosis of maternal sepsis [69].

2.6.1.3 Diagnosis

As already said, the ranges of vital signs and laboratory exams elaborated during the Consensus Sepsis 3 [66] are not validated in the obstetric population and could not be used to diagnose maternal sepsis. ItOSS proposed a set of criteria to diagnose an infection and an organ failure, to help clinicians to start a prompt treatment and avoid the overuse of antibiotics.

The set of criteria defined by the Consensus Sepsis 3, have been considered, taking into account the physiological changes due to the pregnancy and are shown in table 3.

Infection	Organ failure
Fever ≥ 38°C	Cardiovascular: SBP<90mmHg or MAP<65mmHg
Headache and/or nuchal rigidity	Respiratory: oxygen to maintain SpO_2>95%
Respiratory symptoms (frequency ≥ 20/min; SpO_2<95%)	Renal: creatinine>1.2 mg/dl
Urinary symptoms	Hepatic: bilirubin>1.2 mg/dl
Abdominal pain/pelvic pain	Central Nervous System: altered state of consciousness
Diarrhoea or vomiting	Haematological: platelets<100.000mm^3 or ↓ 50% of normal levels
Rash	

Offensive vaginal discharge	
Pre-term labour/ Pre-term Rupture Of Membranes	
Malodorous amniotic fluid	
Foetal or neonatal signs of infection	

Table 3. ItOSS criteria to diagnose a perinatal sepsis

SpO_2: oxygen saturation; SBP: systolic blood pressure; MAP: mean arterial pressure

2.6.1.4 Epidemiology

Worldwide maternal sepsis in the third leading cause of direct maternal death [67], representing 11% of all maternal deaths [57]. Sepsis is estimated to cause 9.7% of maternal deaths in Africa, 11.6% in Asia and 7.7% in Latin America and the Caribbean combined [57].

Although less frequent, maternal death from sepsis appears to be increased in countries with advanced health-care system and although the absolute mortality rate is low, the maternal morbidity rate due to this complication, appears significant. Available data on maternal sepsis from high-income countries report an incidence of 9 to 49 per 100,000 birth-year, depending on the definition and population used [70].

In 2006–2008, the UK maternal mortality rate from sepsis was 1.13/100'000 maternities, a rate not seen since the early 1970s [71,72]. This trend was due to an increasing number of maternal deaths from group A streptococcal infection, accounting for 50% of direct maternal sepsis deaths. Recent work has suggested an approximate doubling of the incidence of maternal sepsis in the United States since 2003 [60]. For each maternal death due to sepsis, there are much more cases of near miss episodes, which could leave women with several health sequelae. A UKOSS case-control study conducted between 2011 and 2012, enrolled 214 UK hospitals with a 100% participation rate and collected 365 confirmed cases of severe sepsis with 757 controls out of 780'537 maternities, representing an incidence of 4.7 per 100'000 maternities (95% CI 4.2–5.2) [61].

Another study with an appropriate research methodology from the Netherland, conducted nationwide between 2004 and 2006 found 78 cases of maternal sepsis, with an incidence of 2.1 per 10'000 births [73]. There were 44 cases of obstetric sepsis (58%) and 34 cases of non-obstetric sepsis (42%), among all cases 79% were admitted to Intensive Care Unit (ICU). The variability in the incidence rate of sepsis could be due to the lack of a uniform definition to identify cases and to a different methodology approach which often uses retrospective studies providing disadvantages in terms of number of cases.

The eighth report of the confidential enquiries into maternal deaths of the United Kingdom [74] reported an MMR due to sepsis of 1.13 out of 100'000 maternities between 2006 and 2008, which went down to 0.67 in 2009-2011 [75] and to 0.43 between 2013 and 2015 [76]. However, the authors of the report published in 2014, within the chapter dedicated to maternal sepsis wrote that

between 2009 and 2012 the direct maternal deaths due to sepsis of the genital tract represent less than a quarter of all indirect maternal deaths due to an infection in pregnancy, childbirth or post-natal period. The sum of direct and indirect maternal deaths gives an MMR due to sepsis of 2.04 out of 100'000 maternities [74]. Both direct, cases due to genital tract infection, and indirect maternal deaths, cases due to respiratory infection or influenza, should be included in order to examine the phenomenon in its entirety.

In Italy, the maternal death surveillance conducted throughout a record-linkage procedure between 2006 and 2012 within 10 regions (Lombardia, Piemonte, Friuli Venezia Giulia, Emilia-Romagna, Toscana, Lazio, Campania, Puglia Sardegna e Sicilia) and including 77% of all Italian births, estimated and MMR of 9.2 out of 100'000 live birth [77]. Sepsis was the fourth source of direct maternal death, causing 7% of all deaths, with an MMR due to sepsis of 0.31 out of 100'000 live births, including direct and indirect maternal deaths within 42 days from birth [77].
Using the prospective maternal death surveillance procedure, conducted between 2013 and 2016, sepsis was observed to be the second cause of maternal death, with 10 women who died out of 48 direct maternal deaths, and 10 out of 32 indirect maternal deaths [22]. Among women died due to sepsis, 4 happened in pregnancy, 1 following a uterine cavity instrumental revision due to miscarriage, 1 due to complication following a termination of pregnancy, 1 following an amniocentesis, 1 after receiving a cervical cerclage. A total of 4 women died due to a septic shock following a caesarean section (C/S) (1 planned C/S, 1 emergency C/S and 2 crash C/S) and 1 women died due to septic shock after an infected wound. The Confidential Enquiries into Maternal Death stated that 8 deaths out of 10 were preventable because a substandard quality of care was provided. This is consistent with the evidence, in fact the lethality of maternal sepsis is often due to a substandard care and, in the majority of cases, to a late diagnosis [61,64,72]. Among the 10 women who died, 5 were complication of H1N1 influenza, 3 women had an infection disease (Tuberculosis and malaria) and 2 had a respiratory infection.
More recent data collected by the prospective maternal death surveillance system and involving 8 Italian regions between 2013 and 2017, found 110 direct and indirect maternal deaths among 1 455 545 new-borns [12] were counted, corresponding to a MMR of 7.56/100 000 live births. The leading causes of the 106 direct and indirect maternal deaths were maternal sepsis (23 cases, 21.7%) and obstetric haemorrhages (22 cases, 20.8%), followed by hypertensive disorders of pregnancy (9 cases, 8.5%) and cardiovascular diseases (9 cases, 8.5%) [78].

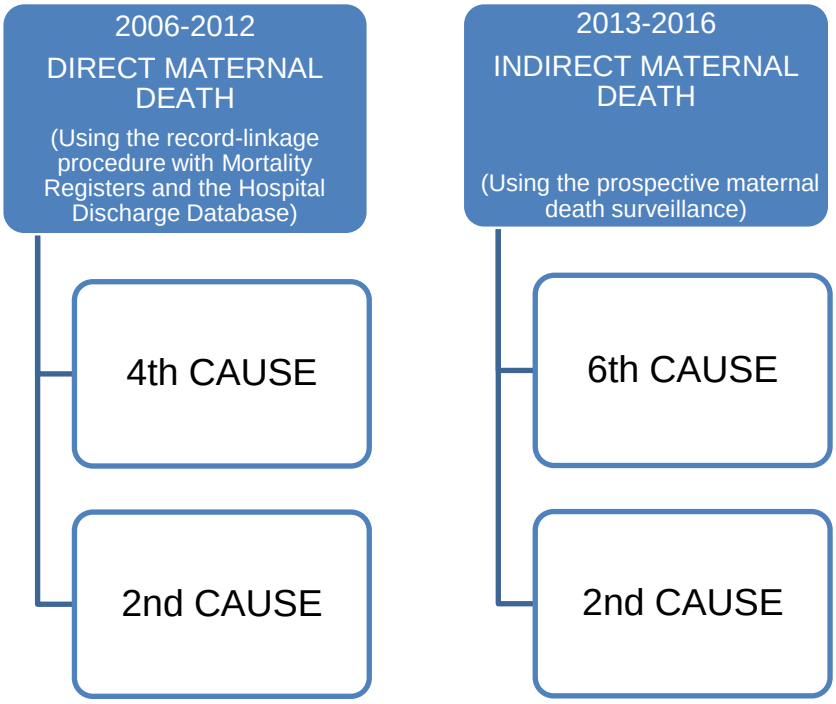


Figure 3. Direct and Indirect maternal death caused by sepsis in Italy

In a study by Chantry et al. [79] the Hospital Discharge Databases were used to assess the feasibility of monitoring life-threatening complications using common definitions across Europe. Eight European countries participated: Finland, France, Italy, Portugal, Switzerland, and three nations of the United Kingdom (England, Scotland, Wales). Maternal sepsis was one of the indicator that the authors decided to investigate. Number of births were 2,826,868, rate of sepsis are reported in table 4.

Finland	France	Italy	Portugal	Switzerland	United Kingdom	Scotland	Wales
2.2/1000	2.4/1000	0.5/1000	2.2/1000	5.0/1000	5.1/1000	6.8/1000	10.8/1000

Table 4. Rate of maternal Sepsis across Europe [79]

The Hospital Discharge Database's codes adopted to report a maternal sepsis, should not be used as a reliable method to assess the incidence rate of this maternal complication.

2.6.1.5 Risk factors

A population-base case-controls study conducted retrospectively using data from the University of Aberdeen, Aberdeen Maternity Hospital, a tertiary-care maternity hospital for the NHS North of Scotland region, described the risk factors associated to maternal sepsis [80]. After controlling for mode of birth and demographic and clinical factors, obesity (OR 2.12; 95% CI 1.14–3.89), Age <25 years (OR 5.15; 95% CI 2.43– 10.90) and operative vaginal delivery (OR 2.20; 95% CI 1.02–4.87), were observed to be implicated with sepsis. In addition other characteristics, already defined as

significant predictors of sepsis, were confirmed such as: multiparty (OR 12.04), anaemia (OR 18.49), labour induction (OR 3.92), caesarean section (13.35), and preterm birth (OR 2.46) [80].

A population-based case-control study conducted by UKOSS between 2011 and 2012 [61] allowed to collect data prospectively and to identify risk factors associated with maternal sepsis, using more reliable data. Features such as minor black or other minority ethnic origin, Primiparity, pre-existing medical problem, fever or taking antibiotics in the 2 weeks prior to presentation were significantly associated with an increased risk to develop sepsis. Furthermore, having an operative vaginal delivery (aOR = 2.49; 95% CI 1.32–4.70), a pre-labour caesarean section (aOR = 3.83; 95% CI 2.24–6.56) or a cesarean section after the onset of labour (aOR = 8.06; 95% CI 4.65–13.97), or having a complication of delivery (aOR= 1.69; 95% CI 1.09–2.63), resulted to be other risks factor for this complication.

Data collected by ItOSS between 2013 and 2016, reported that 31% of women who died were obese and that the caesarean section was an independent factor associated with infection [22], which are consistent with the UKOSS study [61]. An emergency caesarean section appears to be a critical event, because it carries a 5-20 fold increased risk of infection compared to vaginal birth [81]. Third- and fourth-degree tears can increase the chance of perineal wound infection during the post-natal period [82] and might compromise women's quality of life.

2.6.1.6 Etiology

The UKOSS study reported that the largest proportion of sepsis was due to genital tract infection(31%) and urinary tract infections (19.7%), followed by respiratory infections [61]. The most common organism causing infection was Escherichia coli (21.1%).

The infection source and the causative organism differ between women who develop sepsis during the antenatal and the post-natal period. The urinary tract infections represent one third of all cases during pregnancy, while during the post-natal period one third of the infections were due to the genital tract [61]. Table 4 shows the most common source of infection and the consequences that a women could develop during pregnancy, childbirth and the post-natal period [83].

Source of Infection	**Consequences**
Genital tract	Chorioamnionitis, endometritis, septic miscarriage, perineal wound infection, episiotomy or caesarean wound infection
Urinary tract	Low genital tract infection, pyelonephritis.
Respiratory	Viral or bacterial pneumonia, tubercolosis.

Wound	Ruptured appendix, acute appendix, Acute cholecystitis, intestinal ischemia.
Other	Mastitis, breast abscess, septic thrombophlebitis, necrotic fasciitis, malaria, tuberculosis.

Table 5. Source of infections and consequences

Between 2013 and 2017 ItOSS identified 5 maternal deaths due to H1N1 influenza, 4 in pregnancy and 1 post-natally, none of the women who died received the vaccination during pregnancy [78].
The Italian maternal mortality surveillance system described the genital tract sepsis as responsible for 18.3% (n = 11) of the direct deaths, with 3 cases occurring post miscarriage during the first trimester, 3 during the second trimester as a consequence of internal miscarriage leading to chorionamnionitis. The remaining 5 cases occurred during the third trimester of pregnancy, 1 after a vaginal birth and 4 after a caesarean section. The delay in diagnosis and treatment and the lack of adequate communication between professionals have been reported as the most frequent criticism [78].

2.6.1.7 Management

Timely management of women with sepsis or at risk of developing it, is critical. In 2001 and 2012 two studies [84,85] demonstrated the reduction of the mortality rate when patients were cared using the Early Gold Direct Therapy. This approach involves adjustments of cardiac preload, afterload, and contractility to balance oxygen delivery with oxygen demand, with an early used of antibiotic and permanence in ICU. This approach has recently been recommended [86] and adopted into the Surviving Sepsis Campaign guideline [62]. Although the Early Goal Direct Therapy has not been validated within the obstetric population yet, this should be adopted also with pregnant women, due to the absence of a specific guideline dedicated to them.
This approach has been integrated into the Sepsis Six bundle [86], which is a resuscitation package with three diagnostic and three therapeutic steps designed to offer basic intervention within the first hour to patients with suspected or confirmed sepsis (Figure 3).

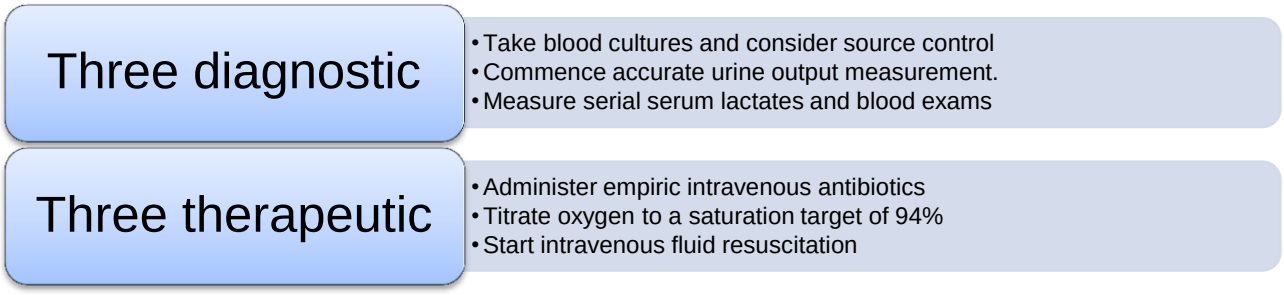


Figure 4. Sepsis Six bundle

Maternal sepsis is a critical situation for the foetal wellbeing too. The effects of maternal sepsis on foetal wellbeing include the direct effect of infection in the foetus, the effect of maternal illness/shock and the effect of maternal treatment [87]. The risk of neonatal encephalopathy and cerebral palsy is increased in the presence of intrauterine infection [88], this is the only reason to accelerate the birth. Otherwise, the mother should be stabilized first and then the birth should be considered. If the women is unstable, the risk of maternal and foetal mortality rates increases, unless the source of infection is intrauterine [87].

2.6.2 Eclampsia

Hypertension disorders complicate around 10% of pregnancies worldwide and are one of the leading cause of maternal and neonatal morbidity and mortality [71]. Has been estimated that maternal mortality associated to pre-eclampsia counts 50'000-60'000 deaths per year worldwide [89]. Among the hypertensive disorders, preeclampsia and eclampsia have the greatest impact on maternal and newborn morbidity and mortality [90]. The majority of deaths related to pre-eclampsia and eclampsia could be avoided if women received timely and effective care, delivered according to evidence-based standards [90], however a substandard of care still exists [91].

2.6.2.1 Definition

Eclampsia is a severe condition that women could develop during the antepartum (38-53%), intrapartum (18-36%), or postpartum (11-44%) period [92]. According to the experts panel of the Delphi study, eclampsia is characterized by [54]:

- Seizures in a woman during pregnancy or up to 14 days postpartum, without any other attributable cause, with at least one of the following signs:
- Hypertension (≥140 mmHg systolic and/or ≥90 mmHg diastolic)
- Proteinuria [spot urine protein/creatinine >30 mg/mmol (0.3 mg/mg) OR >300 mg/day OR at least 1 g/l ['2 +'] on dipstick testing]
- Thrombocytopenia (platelet count of $<100 \times 10^9$/l)
- Raised plasma ALT or AST (twice the upper limit of normal)

The definition introduced by the Delphi study, overturn the concept that eclampsia is a result given by the binomial of hypertension associated with proteinuria. The proteinuria as a diagnostic requirement, is no longer needed as some women had advanced disease before proteinuria detection.

2.6.2.2 Diagnosis

In case of seizures during pregnancy, childbirth or postnatally, an eclamptic episode should always be suspected, even in the absence of hypertension, proteinuria or pre-eclampsia [92]. A differential

diagnosis should be made with epilepsy or cerebrovascular diseases (haemorrhage, ischemia, thrombosis).

2.6.2.3 Epidemiology

In 2000-2 eclampsia accounted for 6% of direct maternal deaths in the UK [93]. A national prospective, descriptive study conducted in UK in 1992 [94] reported an incidence of 4.9/10,000 maternities with a case fatality rate of 1.8% and a perinatal mortality of 54/1000 births. A total of 35% of women had additional major maternal morbidity and 41% further fits. Since this study took place there have been major advances in the management of eclampsia, in fact magnesium sulphate has demonstrated to be effective in preventing recurrent eclampsia by helving the risk of eclampsia in women with severe pre-eclampsia [93,95,96]. A UKOSS study conducted in 2005 described the epidemiology of eclampsia in UK and had the opportunity to evaluate the impact of the introduction of magnesium sulphate therapy [94]. The estimated incidence rate of eclampsia was 2.7 cases per 10 000 births (95% CI 2.4–3.1/10 000), among them 45% were pregnant, 19% were labouring and 36% post-natal women. Women who experienced further seizures after the initial episode were 26%. No maternal deaths were reported, while the perinatal mortality was 2.2% (N= 5/223 neonates). This study showed that very few women with severe pre-eclampsia experienced an eclamptic episode, this demonstrated that these women are managed with magnesium sulphate, in accordance with the evidence, preventing them from having an ecliptic fit [97].

Data collected from February 2013 to January 2015 in 8 Italian regions using ItOSS, representing the 73% of live births in Italy, found an MMR of 10 out of 100’000 live births. Maternal mortality varied from 5 deaths in Tuscany to 13 in Campania. The MMR due to Hypertensive disorders was 0.8 out of 100’000 live births, this means that every 13 women deceased 1 had hypertensive disorders in pregnancy

The first retrospective Italian study regarding the near miss, conducted between 2004 and 2005 in 6 Italian regions (Piemonte, Emilia-Romagna, Toscana, Campania, Lazio e Sicilia) [21], collected 1259 cases, representing a maternal morbidity of 2.0 out of 1000 births. Hospital Discharge Database was used to find near miss cases, haemorrhage and eclampsia were the most frequent near misses, 39% and 29% respectively.

Data collected using the prospective maternal mortality system between 2013 and 2017 described that hypertensive disorders of pregnancy were responsible for 15.5% (n = 9) of the direct deaths, 4 of whom by preeclampsia, 3 eclampsia, and 2 HELLP syndrome cases. The most frequent criticism reported by the confidential enquiries was the delay in the treatment mainly related to the inappropriate use of Magnesium Sulphate and antihypertensive drugs.

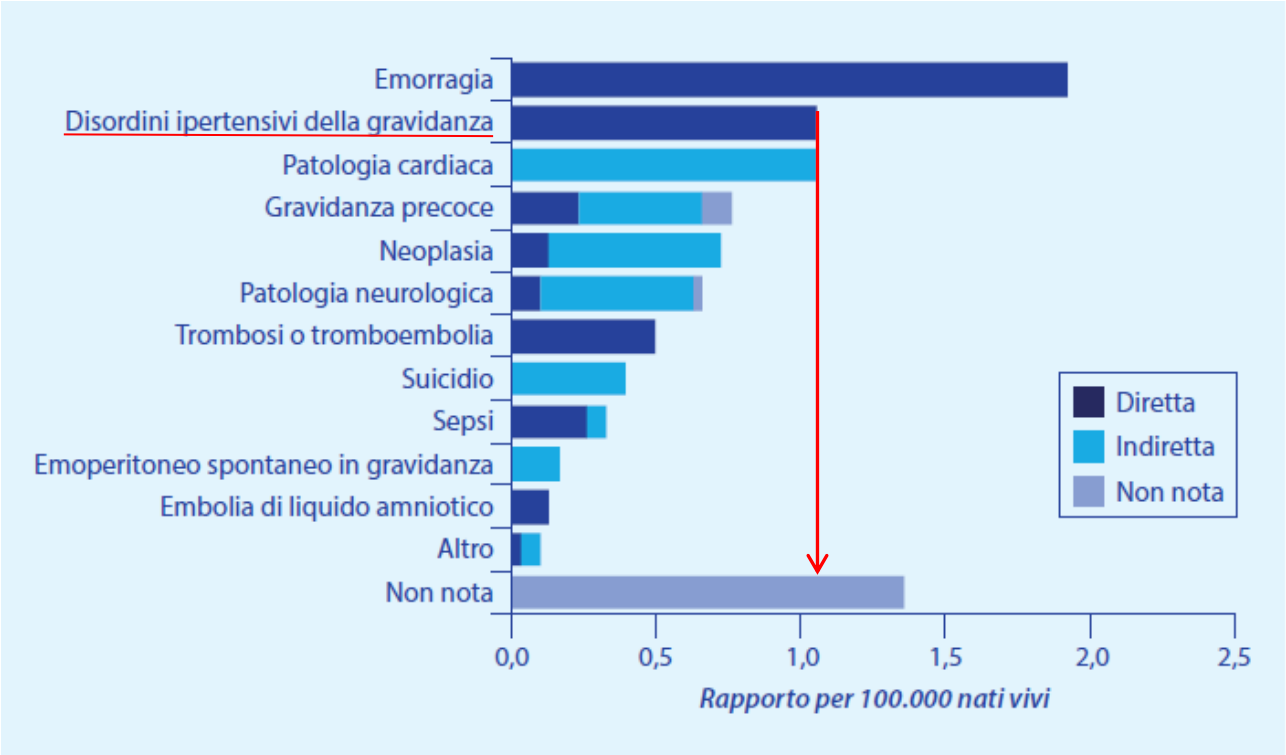


Figure 5. ItOSS Report - MMR with causes of maternal deaths ≤ 42 days (years 2006-2012) [22]

Other countries conducted studies regarding eclampsia. The Netherland retrieved data from a nationwide cohort study of Severe Maternal Morbidity in the Netherlands (LEMMoN Study) between 1 August 2004 and 1 August 2006, all Dutch obstetrics units participated [19]. Comparative analysis between Netherland and UK, using the LEMMoN study and the one conducted by UKOSS in the same period [97], showed that the incidence of eclampsia in the Netherlands was twice as high as in the UK: 6.2/10'000 births versus 2.7/ 10'000 births, respectively [98].

Between 2013 and 2016 the Netherlands collected prospective data using the Obstetric Surveillance System (NethOSS) and found a total of 88 cases of eclampsia, resulting in an incidence of 1.8 (95% CI 1.4-2.2) per 10'000 births [99]; 1 maternal death (1.1%) was reported and there were no cases of neonatal mortality (95% CI 0.22-0.36). This demonstrated the efforts made in the Netherland to improve obstetric and midwifery care.

The Australasian Maternity Outcomes Surveillance System (AMOSS), carried out a two-years (2010-2011) population based study, collecting data from 263 maternity units in Australia and all 24 in New Zealand. The incidence of eclampsia was 2.2 per 10,000 women giving birth (83% in Australia and 17% in New Zealand). There were no maternal deaths. The perinatal mortality rate was 43.5 per 1000 births, four were stillbirths and one was a neonatal death (N=116).

A secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health (WHOMCS) database found that the risk of death is nearly four times higher for women with pre-eclampsia when compared with non pre-eclamptic women, and the risk increased exponentially (adjusted OR = 42.38; 95% CI, 25.14–71.44) for those with eclampsia. Moreover, the risk of a maternal near miss is eight and sixty times higher in women with pre-eclampsia and eclampsia, respectively.

In the study by Chantry et al. [79], already cited in the Sepsis paragraph, the Hospital Discharge Databases were used to assess the feasibility of monitoring life-threatening complications using common definitions across Europe. Eight European countries participated: Finland, France, Italy, Portugal, Switzerland, and three nations of the United Kingdom (England, Scotland, Wales). Together with sepsis, eclampsia was one of the indicator that the authors decided to investigate. Number of births were 2,826,868, rate of eclampsia are reported in table 9.

Finland	France	Italy	Portugal	Switzerland	United Kingdom	Scotland	Wales
0.3/1000	0.7/1000	0.6/1000	0.3/1000	0.5/1000	0.6/1000	0.9/1000	1.0/1000

Table 6. Rate of Eclampsia across Europe [79]

Authors commented that the use of indicator of eclampsia from Hospital Discharge Databases should be limited due to its low quality.

2.6.2.4 Risk factors

The Italian near miss study found that the risk to experience a near miss was higher in women of 35 years old or older (RR=1.6; IC 95% 1.4-1.8), was 5 times higher in women who had a caesarean section and if women were from the South or the Central part of Italy [77,100].

The comparison study between the Netherland and the UK data found that Dutch women were significantly older, significantly fewer women had a body mass index >30 kg/m2, fewer women were smoker and there were more women with a multiple pregnancy. Furthermore women in the Netherlands had a higher highest diastolic blood pressure before eclampsia compared with the UK, a lower platelet count nadir, a higher highest aspartate aminotransferase and a higher highest alanine aminotransferase ALT [98].

2.6.2.5 Etiology

The pathogenesis of eclamptic convulsions remains unknown. Cerebral imaging suggests that cerebral abnormalities in eclampsia (mostly vasogenic edema) are similar to those found in

hypertensive encephalopathy [92]. However, cerebral imaging is not necessary for the diagnosis or management of most women with eclampsia.

Other than early detection of preeclampsia, there are no reliable tests or symptoms for predicting the development of eclampsia.
A systematic review by Hastie et al. [101] concerning to estimate the predictive value of signs and symptoms that occur before onset of eclampsia among, found that even most commonly reported symptoms, such as visual disturbances, epigastric pain, and headache, were unable to accurately predict eclampsia.
In developed countries, the majority of cases reported in recent series are considered unpreventable [92].

2.6.2.6 Management

Magnesium sulphate is the drug of choice for reducing the rate of eclampsia developing intrapartum and immediately postpartum. Therefore Prophylactic magnesium sulphate is recommended only for women who are hospitalized with established diagnoses of preeclampsia. Its use is recommended only during labour and for 12-24 hours postpartum [102].
The UkOSS study [97], found that magnesium sulphate has been shown to be effective in preventing recurrent eclampsia and reduces the risk of eclampsia in women with severe pre-eclampsia. This study shows the practical benefits of the incorporation of research evidence into practice.

Also the NethOSS study [99] showed a strong reduction of eclampsia and associated perinatal mortality in the Netherlands compared with findings from the previous trial [98], this is partly due to a more active management of all women with hypertension, throughout an increase of antihypertensive treatment.

2.6.3 Amniotic fluid embolism (AFE)

2.6.3.1 Definition

AFE is an acute cardio-respiratory collapse within 6 hours after labour, delivery or ruptured membranes, with no other identifiable cause, followed by acute coagulopathy in those women who survive the initial event [54]. AFE is a devastating obstetric complication, its diagnosis is hard to make, an in-depth study would facilitate the improvement of it. AFE is an extremely rare, but life-threatening complication that affects pregnant women shortly before, during, or immediately following labour and childbirth [103]. It involves a complex sequence of events triggered in certain

women by the entrance into the maternal circulation of material from the foetal compartment, resulting in an abnormal activation of pro-inflammatory mediator systems similar to the systemic inflammatory response syndrome. Amniotic fluid embolism is characterized by a triad of sudden hypoxia and hypotension, followed in many cases by coagulopathy [104].

In 2016 a working group of the Society for Maternal-Fetal Medicine (SMFM) and the Amniotic Fluid Embolism Foundation proposed 4 uniform diagnostic criteria to identify cases of AFE for research purposes [105]:

1. Sudden onset of cardiorespiratory arrest, or both hypotension (systolic blood pressure <90 mm Hg) and respiratory compromise (dyspnoea, cyanosis, or peripheral capillary oxygen saturation [SpO2] <90%).
2. Documentation of overt DIC following appearance of these initial signs or symptoms, using scoring system of Scientific and Standardization Committee on DIC of the ISTH, modified for pregnancy. Coagulopathy must be detected prior to loss of sufficient blood to itself account for dilutional or shock-related consumptive coagulopathy.
3. Clinical onset during labour or within 30 minutes of delivery of placenta.
4. No fever (≥ 38.0 ˚C) during labour.

2.6.3.2 Diagnosis

The diagnosis of amniotic fluid embolism is clinical, based on the presence of the elements described above, in addition comprises the exclusion of other likely causes [103]. Amniotic fluid embolism should be considered in the differential diagnosis in any pregnant or postnatal women who suffers sudden cardiovascular collapse or cardiac arrest, seizures, severe respiratory difficulty, or hypoxia, particularly if such events are followed by a coagulopathy that cannot be otherwise explained [105]. The clinical manifestations of AFE are not uniform, and variation exists within the general triad of hypotension, hypoxia and coagulopathy [106].

2.6.3.4 Epidemiology

The rarity of AFE together with the fact that diagnosis is based upon identification of characteristic clinical symptoms only and often is one of exclusion, makes it difficult to obtain reliable data regarding the incidence, risk factors, management and outcomes [107]. A review on AFE [108] demonstrates differences in the reported incidence of this complication in high-resource countries; the reported incidences vary according to the study methodology and the definition of AFE used within the study. For this reason a recommendation to collect cases using population-based database studies or population-based system generated to collect data on rare diseases, has been made [108].

According to this review the incidence of AFE varies from 1.9 cases per 100'000 maternities (UK) to 6.1 per 100'000 maternities (Australia); the fatality rate ranged from 0.4 per 100'000 live births in the Netherland between 1993 and 2005 [59] to 1.3 per 100'000 live births in the United States between 1997 and 2001 [109] and 1.1 in Australia in 1994-2005 [110]. Data collected adopting retrospective database, reported an incidence more than double compared with the one estimated by population-based prospective studies with validated definition [108]. Due to the rarity of this obstetric complication, multinational studies are needed to obtain sufficient cases, giving an appropriate statistical power, a stable incidence and reliable risk factors.

A population-based cohort study conducted in Canada with data from 1991 to 2009 [111] found an AFE incidence of 2.5 per 100'000 birth. Among these, 42 were fatal cases, with a fatal outcome of 0.8 per 100'000 births, meaning a fatality rate of 27%. Significant risk factors were induction of labour, caesarean section, instrumental vaginal birth, and uterine or cervical trauma. The authors had the opportunity to link the maternal hospital number with those of their newborns. This allowed to investigate the impact of AFE on the foetal wellbeing. AFE was significantly associated with stillbirth, asphyxia, mechanical ventilation, bacterial sepsis, seizures and prolonged length of neonatal hospital stay, association that became even more strong when the complication occurred after 37 weeks of gestation.

A national study conducted in France using data collected from the French Confidential Enquiry into Maternal Deaths between 2007 and 2011 [112], reviewed the AFE cases in accordance with the definition proposed by the Society for Maternal-Fetal Medicine (SMFM) and the Amniotic Fluid Embolism Foundation [105]. The estimated maternal mortality ratio due to AFE was 0.95/100,000 live births. There were 36 women who died due to AFE and the French experts panel confirmed that only 21 (58%) were in accordance with the definition proposed by the SMFM. It means that this definition would exclude more than one-third of AFE-related maternal deaths identified by the national experts committee. One of the criteria proposed is the early laboratory documentation of the coagulopathy, which could be hard to obtain when cardiac arrest occurs. For this reason the French authors suggested to change the criteria of early documented DIC proposed by the SMFM to early clinical coagulopathy with bleeding.
Interesting, the experts panel found a substandard care in more than half of the cases.

A population-based cohort and nested case-control study was conducted using the INOSS Network, collecting data from some of the studies described above, conducted in Australia, France, the Netherlands, Slovakia, and the UK [107]. Data on AFE were pooled along with secondary data on a sample of control women (*n* = 4,938) collected in Australia and the UK. This research reported an estimated incidence of AFE ranged from 0.8 to 1.8 per 100'000 maternities, and the

proportion of women who died or had permanent neurological injury ranged from 30% to 41%, depending on the case definition.

The present study has been planned to investigate the incidence of AFE, using the Italian Obstetric Surveillance System as part of a collaborative project for the International Network of Obstetric Surveillance Systems (INOSS). This multicountry project will help to have a stable incidence of AFE, giving more information about this complication.

2.6.3.5 Risk factors

The population-based cohort and nested case–control study using the UK Obstetric Surveillance System conducted between 2005 and 2014 [103] (data that have been used into the INOSS study) described risk factors associated with AFE, such as older maternal age, multiple pregnancy, placenta praevia and induction of labour. In addition, instrumental vaginal birth and caesarean section were associated with the occurrence of AFE after birth. Women who died or had permanent neurological injury more often presented a cardiac arrest, were from ethnic minority groups, had an hysterectomy, a shorter time interval between AFE and the surgical intervention of hysterectomy and less likely to receive cryoprecipitate

In the INOSS study different case definitions adopted into the research considered, changed the estimated incidence of AFE and the estimated proportion of women with poor outcomes, however did not alter findings regarding risk factors associated with AFE and with poor outcome following the complication.

The INOSS study [107] found that women who died were more likely to have a cardiac arrest than those who survived (89% vs 40%), were less likely to receive concentrated fibrinogen (40% vs 56%) and platelets (24% vs 49%). They presented a lower dose of tranexamic acid and were less likely to have an obstetrician and/or anaesthetist present at the time of the AFE event (61% vs 75%). This study confirmed the findings of the UKOSS study [103], where older maternal age, multiple pregnancy, polyhydramnios, placenta praevia, and induction of labour were significantly associated with the occurrence of AFE.

2.6.3.6 Etiology

The cause of AFE is not completely understood yet, there are two main theories regarding the pathogenesis of this rare complication . The first hypothesis was that complicated labour, abnormal placentation, surgical trauma or any other issue causing the entrance of the amniotic fluid into the systemic circulation and the physical obstruction of the pulmonary circulation, could be a trigger for the disease [113–115].

The second one, and more recent theory, increasingly recognise that the entrance of the amniotic

fluid into the maternal circulation activates inflammatory mediators, causing a humoral or immunologic response [116]. Mast cell degranulation and complement activation may play a role in this anaphylactoid or systemic inflammatory response syndrome [106].

2.6.3.7 Management

Although the diagnosis of AFE is not an easy one to make, an early recognition is crucial. Other key factors in the management of this complication are prompt resuscitation, and birth of the foetus [117].

The Society for Maternal-Fetal Medicine recommended the immediate high-quality cardiopulmonary resuscitation with a multidisciplinary team involved. Following the supportive and resuscitative management, the immediate delivery of the foetus if > 23 weeks of gestation is recommended [104], timely hysterectomy and adequate blood transfusion.

2.6.4 Spontaneous Haemoperitoneum in Pregnancy (SHiP)

2.6.4.1 Definition

SHiP represents a spontaneous (nontraumatic) intraperitoneal haemorrhage during pregnancy and up to 42 days postpartum, requiring surgical intervention or embolisation. Excluding ectopic pregnancy, uterine rupture and caesarean section associated bleeding [54]. It is potentially lethal for both the mother and the foetus. Currently is challenging to estimate his incidence rate.

2.6.4.2 Diagnosis

The diagnosis of this obstetric complication is difficult. Women could present with (sub)acute abdominal or side pain in combination with signs of hypovolemic shock and/or a decreased level of haemoglobin. Signs of foetal distress could be observed [118].

Numerous cases are diagnosed postoperatively, when free peritoneal fluid is visualized. This could be confirmed by ultrasound sonography [118].

Differential diagnosis should be made with placental abruption or uterine rupture [119].

2.6.4.3 Epidemiology

So far, no national studies have been conducted that inform about a potential incidence of SHiP.

ItOSS participate to the multinational study promoted by INOSS. The study will be coordinated by Denmark which is part of the Nordic Obstetric Surveillance Study, where also the analysis of data will take place.

Up to now, UKOSS reported that six maternal deaths occurred between 2009 and 2012 in the UK that were attributed to rupture of non-aortic aneurysms, however little is known about morbidity during that time (https://www.npeu.ox.ac.uk/ukoss/current-surveillance/ship).

In addition, the Belgian Obstetric Surveillance System (B.OSS) in their 2nd Biennial report between 2014 and 2015, reported four cases of SHiP (https://organesdeconcertation.sante.belgique.be/sites/default/files/documents/b.oss_report_2014-2015-2016.docx.pdf).

A systematic review on SHiP was conducted by Lier at al., to gain a better insight in this potentially life-threatening complication of pregnancy [118]. Articles appraised by authors were either case reports or case-series, a total of 59 cases of SHiP were collected. Although incidence and risk factors need further research to be investigated and known, findings of the review gave the opportunity to understand some features about SHiP. The majority of cases occurred in the third trimester of pregnancy (50.8%), 94.9% of women presented with (sub)acute abdominal pain, 47.5% with hypovolemic shock and 62.7% with decreased level of haemoglobin. Signs of foetal distress were observed in 40.7% of cases. Imaging confirmed free peritoneal fluid in the 62.7% of women. Nearly all women had active bleeding at the time of surgery, originating from endometriotic implants (21.6%), ruptured utero-ovarian vessels (56.8%), hemorrhagic nodules of decidualized cells (2.0%)) or a combination (19.6%). Median amount of hemoperitoneum was 1600 mL. Among women with surgical intervention, 15.6% remained pregnant and 8.5% had a recurrent SHiP.
The perinatal mortality rate was 26.9% (18/67 fetus), and the maternal mortality rate was 1.7 (1/59 cases) [118].

2.6.4.4 Risk factors

There are growing evidence suggesting that endometriosis represent the main risk factor to develop SHiP, however is still not possible to identify women who are at increased risk to develop the complication [118]. Also controlled ovarian hyperstimulation for artificial reproductive techniques (ART) seems to be another factor contributing to the occurrence of SHiP [119,120], which is a significant element as these techniques are used more frequently in women with endometriosis [121].

2.6.4.5 Etiology

Endometriosis seems to play a critical role in the development of SHiP [118,120]. SHiP has been associated also with rupture of uterine artery or varicose veins and aneurysms of the splenic artery. A literature review investigated maternal and foetal complications in women with endometriosis and adenomyosis [122] found that the overall prevalence of endometriosis-related

spontaneous hemoperitoneum in pregnancy is estimated to be around 0.4%. Although the risk of endometriosis in pregnancy nowadays is well known, no evidence exists whether treatment of endometriosis or surgery prior to pregnancy could represent a preventive measure to lower the risk of SHiP bleedings. It should be considered that extensive surgery may have negative consequences on the uterus contributing to further adhesions formation [118].

2.6.4.6 Management

Management of SHiP depends on the women's wellbeing that is often the result of the extent of the intra-abdominal haemorrhage and the gestational age. In the majority of cases, a laparotomy is the first-choice treatment to stop the bleeding and could be an opportunity to diagnose an endometriosis that in approximately 33% of the SHiP cases was not known [118]. When there are no signs of hypovolemic shock or fetal distress, or during the post-natal period, an expectant management combined with fluid resuscitation, could be considered paying attention to monitor closely the clinical situation as recurrence of SHiP has been observed [118]. It is important to take a biopsy during the laparotomy intervention from the bleeding lesions. A histological will confirm the presence of endometriosis as the decidual changes may impede the diagnosis [120,123].

2.7 Summary of Literature Review

Maternal deaths in high income countries became a rare event, therefore near miss episodes have been designated as better indicators to monitor the quality of maternity care. The WHO in "Beyond the Numbers" recommended to review near miss cases to improve maternal health.

Near miss are severe and rare life-threatening obstetric complications, that usually represent no more than one case per 2000 births, but are important cause of maternal or perinatal morbidity and mortality and could be a burden for the women's family and the Healthcare Systems.

Monitoring near miss episodes, might be the way to identify risk factors involved in maternal deaths and could facilitate to determine preventive strategies to improve obstetric and midwifery care.

The study of near miss cases can be addressed using the methodology generated by the Obstetric Surveillance Systems (prospective descriptive, cohort or case-control studies), which gave the opportunity to make multinational comparison, collecting stable incidence of rare diseases and reliable risk factors associated with them.

CHAPTER THREE: METHODS

3.1 Introduction

This chapter describes the research activities performed by each Operation Unit involved into the study. It explains the research design, including methodology and data collection approach. The tools to collect women's information will be presented, based on case definitions developed by INOSS, and ethical considerations will be considered.

3.2 Time period of research

The project has been approved and funded by the Italian Ministry of Health and is part of the 2016 research activities of the National Centre for Disease Prevention and Control.
The Lombardy region with the Fatebenefratelli – Sacco Hospital National Health System Trust, is the Unit that proposed and coordinated the project.

This study is part of the surveillance activities between the Italian National Institute of Health, representing ItOSS, and the Italian regions. The Italian National Institute of Health coordinated the research activities.

The research started on the 24th of March 2017 and was planned to last 24 months, ending on the 23rd of March 2019. However, the Italian Ministry of Health approved to extend the deadline of the research by one more year, in order to collect further cases, until the 23rd of March 2020.
Cases of sepsis were collected from the 1st of November 2017 until the 31st of October 2019 (22 months of data collection) and the remaining complications were reported until the 31st of March 2020 (27 months of data collection).

3.3 Units involved into the study

Ten Units have been involved into the study, each one of them had one or more contact persons who performed different activities as shown in table 6.

Units involved into the project	Activities
Research Projects Coordination Unit	
Lombardy Region and Fatebenefratelli – Sacco Hospital National Health System Trust	- To be responsible for administrative tasks - To supervise the project - To develop and implement a training programme - To train the contact persons of each maternity Unit involved into the study - Interpretation of research results - To organize the closing conference - To disseminate research findings

Operational Unit 1	
National Centre for Epidemiology, Surveillance, and Health Promotion Italian National Institute of Health	- To coordinate the research activities - To collaborate in the supervision of the project - To develop and implement a training programme - To train the contact persons of each maternity Unit involved into the study - To assess research tools - To clean collected data - Interpretation of research results - To organize the closing conference - To disseminate research findings - To conduct the study in Lazio Region
Operational Unit 2	
University of Milano - Bicocca	- To collaborate in the project coordination - To assess research tools - To contribute to the research activities included data analysis and interpretation of findings - To disseminate research findings
Operational Unit 3	
Piedmont Region	- To assess research tools - To disseminate research findings - Operational support activities
Operational Unit 4	
Friuli Venezia Giulia Region	- To assess research tools - To disseminate research findings - Operational support activities
Operational Unit 5	
Emilia-Romagna Region	- To assess research tools - To disseminate research findings - Operational support activities
Operational Unit 6	
Tuscany Region	- To assess research tools - To disseminate research findings - Operational support activities
Operational Unit 7	
Campania Region	- To assess research tools - To disseminate the research findings - Operational support activities
Operational Unit 8	
Puglia Region	- To assess research tools - To disseminate research findings - Operational support activities
Operational Unit 9	
Sicily Region	- To assess research tools - To disseminate research findings - Operational support activities

Table 7. Research activities performed by the Operational Units

3.4 Research activities

The contact persons of each Operational Unit participated into an introduction skype meetings to have an overview of the research and to share future tasks and activities. In addition, one live meeting has been held in Rome at the Italian National Institute of Health, where participants

discussed about the methodology of the research and about the method of data collection, they assessed data collection forms and shared the case definitions that would have been adopted for the study.

The Operational Units conducted a census of all Public and Private Maternity Units in their own Region and nominated an Obstetrician, Midwife or Risk Manager to be the contact person responsible to report cases in each participating hospital.

The University of Milano – Bicocca conducted a Literature Review regarding the obstetric complications under surveillance and about the data collection forms, which have been used previously by UKOSS to investigate the same diseases.
Data collection forms have been translated from English to Italian and have been adapted to the Italian birth context, adding some more evidence-based information about the disease.

Data collection forms were developed individually for each condition, than were reviewed by the National Centre for Epidemiology, Surveillance, and Health Promotion of the Italian National Institute of Health and by the Research Projects Coordination Unit. Following the approval of the contact person of each Operational Unit, data collection forms have been subjected to an experts panel review. The panel, which involved Obstetricians, Midwives and Anaesthetists, made suggestions and allowed to develop the last version of the data collection forms adopted to collect women's information during the study.

A company was than employed to generate the website and web-based data-collection was gradually introduced and completed by the 31st of October 2017, enhancing data collection on the following day. The website facilitating monthly reporting and completion of data collection forms online. Restricted access to the website was provided to the appointed contact person via a personal login. They have access to the reporting forms and data collection forms of their Maternity Unit.

A training programme was developed, than study days and workshops were conducted in each Region between September and October 2017. This allowed to train healthcare professionals nominated as contact person in each Maternity Unit involved into the study. The study days provided information on the study design, aim and objectives, method of data collection, how to identify cases and how to complete a data collection form.

The National Centre for Epidemiology, Surveillance, and Health Promotion of the Italian National Institute of Health calculated the expected incidence rate of the obstetric complications under

surveillance, using the National Hospital Discharge Database for the period between 2008 and 2014. This offered the opportunity to communicate during the training, how many cases were expected in each Italian Region.

The nominated person at the University of Milano – Bicocca had a personal login to enter into the website platform as administrator with the responsibilities to ensure that the reporting of near miss was complete and check the appropriateness of data collection forms. In addition, a monthly remind was sent to all the nominated person of each unit to report cases or alternatively to state that there was “nothing to report”. All the contact clinicians could get in contact with the nominated person of the University to discuss potential cases to report, to ask questions and doubts concerning the way to complete the data collection form or in case they have any issue regarding the project.

The National Centre for Epidemiology, Surveillance, and Health Promotion of the Italian National Institute of Health and the University of Milano – Bicocca developed an accredited distance learning course for Midwives and Doctor in the field of maternal sepsis, involving clinical case sessions.

The contact person of each Operational Units were required to submit quarterly progress reports for their activities to the Ministry of Health.

The National Centre for Epidemiology, Surveillance, and Health Promotion of the Italian National Institute of Health and the Coordination Unit offered a Webinar with the aim to divulgate data regarding the study (this was needed following the Covid-19 pandemic).

3.4.1 Research activities of the University of Milano – Bicocca

I was the contact person at the University of Milano-Bicocca. Since march 2017, when the project was approved by the Italian Ministry of Health I participated to different skype or face-to-face meetings in order to plan the research activities together with the National Institute of Health and the Lombardy Region.

From march 2017 I conducted a literature review with the aim to collect the more recent evidence regarding the complications under surveillance, which enable to develop all data collection forms.

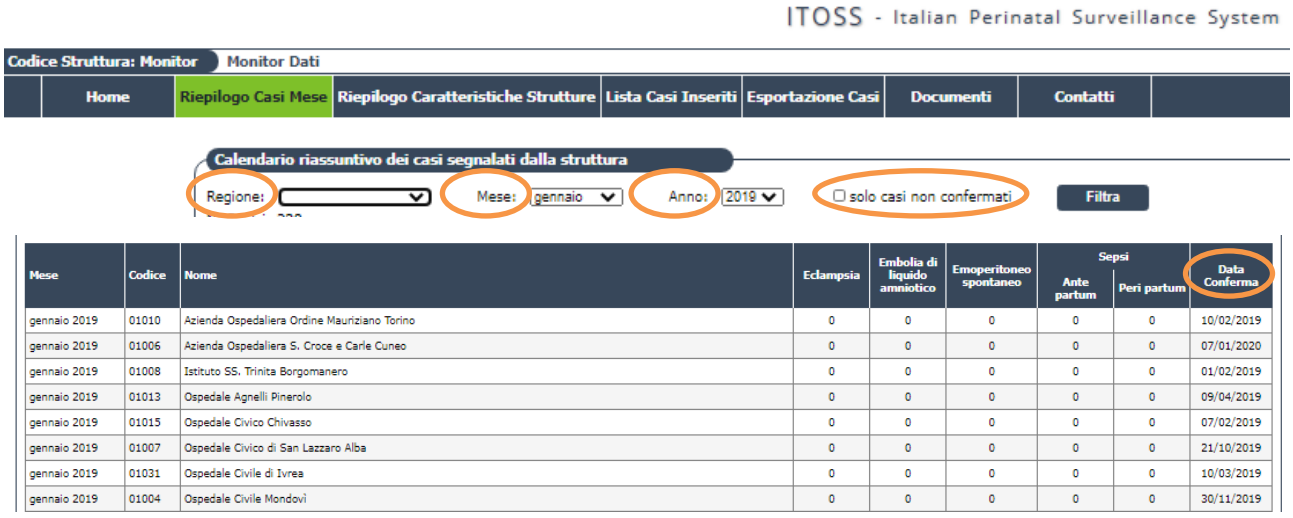
Data collection forms were completed following the literature revision step and after the translation of the UKOSS collection forms, which have already been adopted in similar UK studies.

This phase took several months and consisted of continuous contacts with the National Institute of Health and the company that generated the on-line data collection forms.

Furthermore, using a personal ID and Password as administrator, I had the responsibility to monitor the monthly number of cases response (Figure 6), whereas the characteristics of the Maternity Units were communicated (Figure 7) and the appropriateness and the completeness of the data collection forms (Figure 8a). This login enabled to monitor data, choosing different options (Figure 8b) and selecting a particular month and year of data collection:

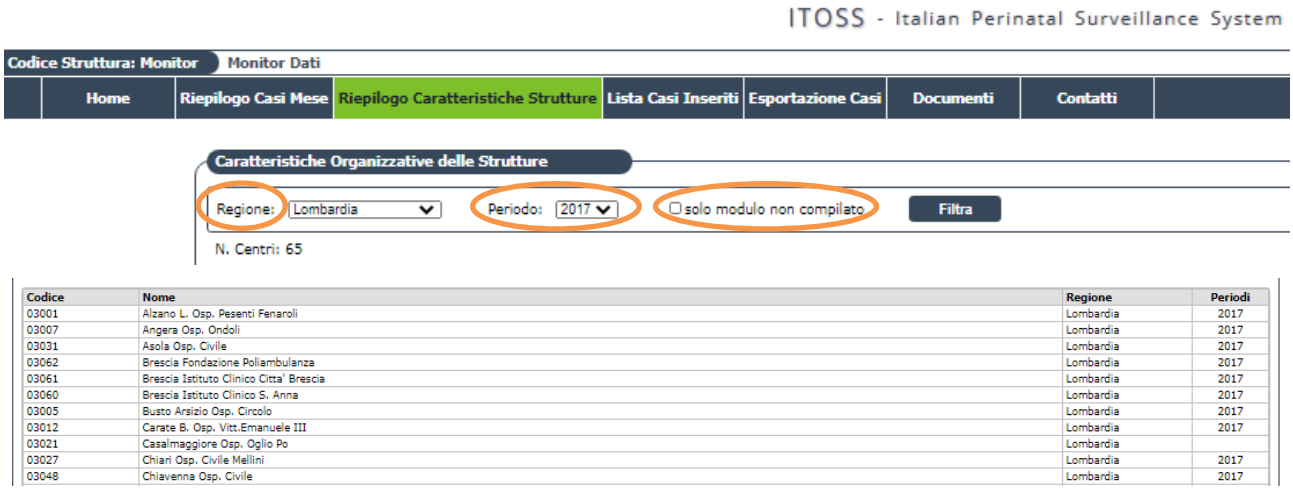
1. One Region in order to check all the near miss cases reported within that territory
2. A single Maternity Units, to check cases happened in a single participating hospital
3. One of the four obstetric complications under surveillance, called pathways, to check all cases related to one of the near misses under study.

I will show the platform pages with the options developed to monitor the data of the 9 participating Regions.



Mese	Codice	Nome	Eclampsia	Embolia di liquido amniotico	Emoperitoneo spontaneo	Sepsi		Data Conferma
						Ante partum	Peri partum	
gennaio 2019	01010	Azienda Ospedaliera Ordine Mauriziano Torino	0	0	0	0	0	10/02/2019
gennaio 2019	01006	Azienda Ospedaliera S. Croce e Carle Cuneo	0	0	0	0	0	07/01/2020
gennaio 2019	01008	Istituto SS. Trinita Borgomanero	0	0	0	0	0	01/02/2019
gennaio 2019	01013	Ospedale Agnelli Pinerolo	0	0	0	0	0	09/04/2019
gennaio 2019	01015	Ospedale Civico Chivasso	0	0	0	0	0	07/02/2019
gennaio 2019	01007	Ospedale Civico di San Lazzaro Alba	0	0	0	0	0	21/10/2019
gennaio 2019	01031	Ospedale Civile di Ivrea	0	0	0	0	0	10/03/2019
gennaio 2019	01004	Ospedale Civile Mondovì	0	0	0	0	0	30/11/2019

Figure 6. Data monitor of monthly number of cases response



Codice	Nome	Regione	Periodi
03001	Alzano L. Osp. Pesenti Fenaroli	Lombardia	2017
03007	Angera Osp. Ondoli	Lombardia	2017
03031	Asola Osp. Civile	Lombardia	2017
03062	Brescia Fondazione Poliambulanza	Lombardia	2017
03061	Brescia Istituto Clinico Citta' Brescia	Lombardia	2017
03060	Brescia Istituto Clinico S. Anna	Lombardia	2017
03005	Busto Arsizio Osp. Circolo	Lombardia	2017
03012	Carate B. Osp. Vitt.Emanuele III	Lombardia	2017
03021	Casalmaggiore Osp. Oglio Po	Lombardia	
03027	Chiari Osp. Civile Mellini	Lombardia	2017
03048	Chiavenna Osp. Civile	Lombardia	2017

Figure 7. Data monitor of the characteristics of the Maternity Units

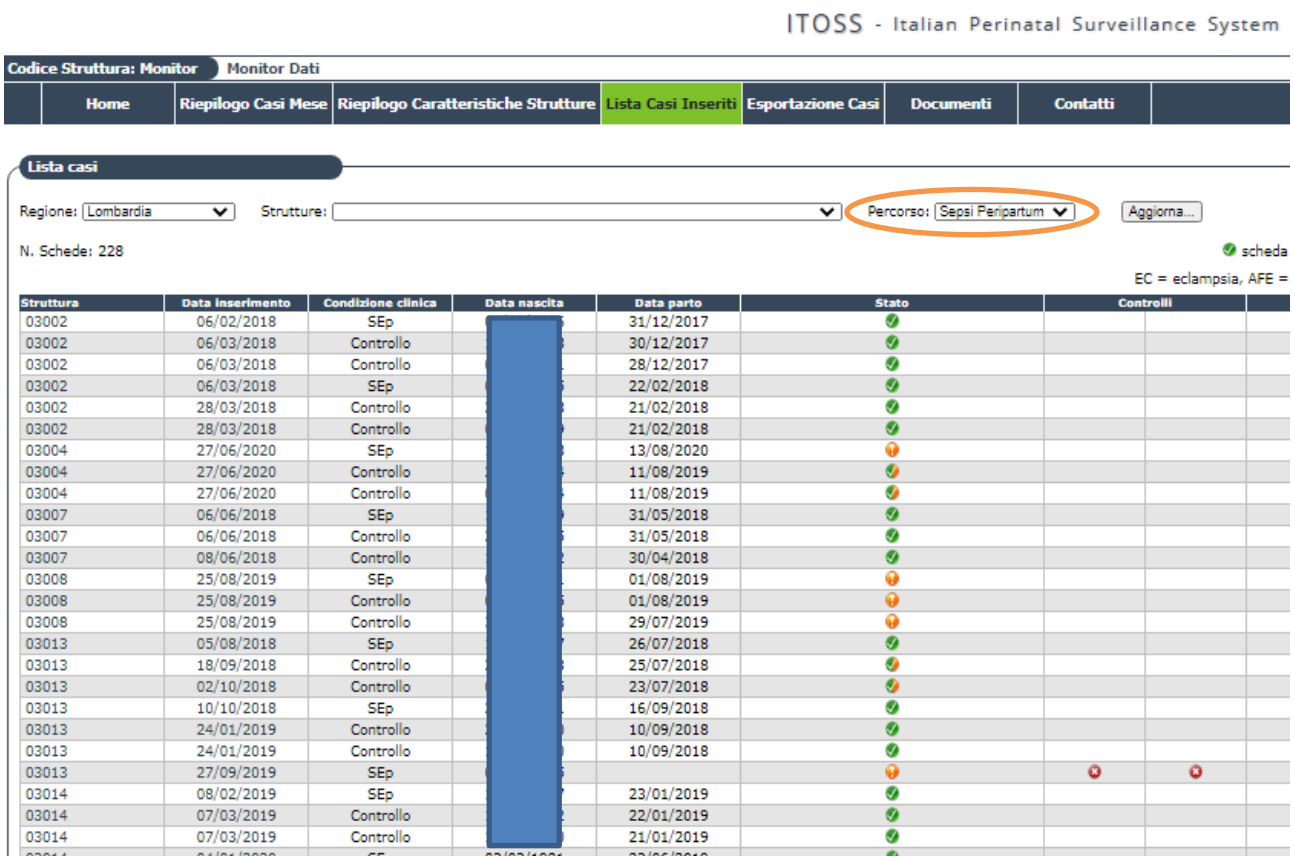


Figure 8a. Data monitor of near miss cases reported by clinicians

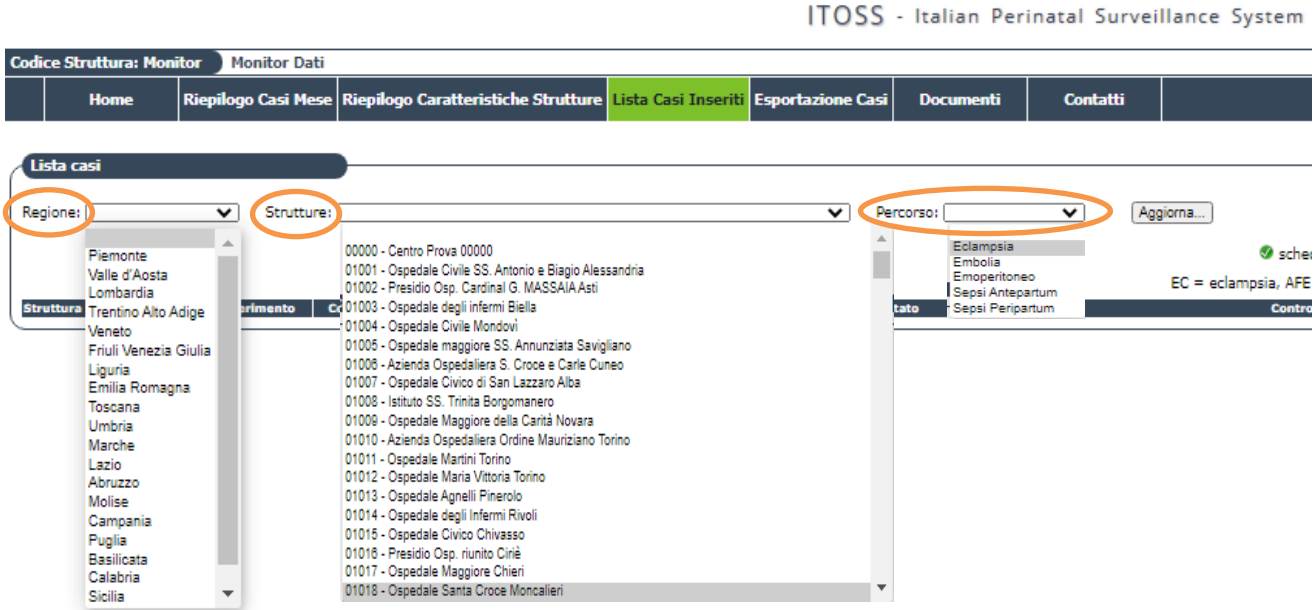


Figure 8b. Data monitor of near miss cases reported by clinicians according to Region, Maternity Unit or obstetric pathway

3.5 Primary aim and objectives of the study

The aim of the project is to collect and analyse the incident cases of near misses due to sepsis, eclampsia, AFE and SHiP at the Maternity Units involved into the study.

Six Objectives have been planned:

- to measure the expected incidence rate of the obstetric complications under surveillance, using the National Hospital Discharge Database for the period between 2008 and 2014;
- to describe and to share the research protocol with the contact persons of the Units involved into the study, including the definition of cases, data collection forms and the organisation of the on-line website that will be adopted for collection of cases;
- to monitor the near miss cases due to the complications under surveillance, that will be reported by the contact person of each Maternity Units involved into the study. This will gave the opportunity to measure the Maternal Near Miss ratio (MNMR) per 1000 live births for each complication;
- to identify the risk factors associated with the obstetric complications, making comparisons with findings generated by other INOSS members. To evaluate whereas there are system or clinical practice related-failures, and to plan interventions of education and training to support healthcare professional;
- to provide an accredited e-learning for Midwife and Doctors;
- to offer a conference once the study has been concluded, in order to divulgate and to discuss findings.

3.6 Research study design

1. Descriptive population-based multicentre study to collect near miss cases due to eclampsia, AFE and SHiP in women during pregnancy or within 42 days following a miscarriage, a TOP, a molar pregnancy or an ectopic pregnancy, and near miss cases due to sepsis in pregnancy or in women who gave birth vaginally or by CS up to 19+6 weeks of gestation (*Antepartum sepsis*).
2. 1:2 matched case-control population-based multicentre study to collect near miss cases due to sepsis in women who gave birth vaginally or by CS (post-partum sepsis) from 22+0 weeks of gestation and up to 42 days following the end of pregnancy (*Peripartum sepsis*).

3.7 Case definitions

The Literature offers various definitions for the obstetric complications under surveillance. This study adopted the definitions developed, applying the Delphi method, by INOSS for Eclampsia,

AFE and SHiP [54]. As already described, the definition of maternal sepsis will be hopefully developed when the findings of the GLOSS study will be available. In the meantime the definition of sepsis adopted into the Surviving Sepsis Campaign guideline, is the one that was used also for this study. ItOSS proposed a set of criteria to identify an infection and an organ failure (Chapter two, paragraph 2.6.1). In addition, as pathogenesis of sepsis is known to differ between pregnant and postpartum women, this complication was investigated making difference between sepsis developed during the antenatal period and one developed during the peripartum period.
In order to perform a case–control study regarding the peripartum sepsis, anonymised information on control women was also collected. For these complications only, clinicians who reported a case of peripartum sepsis were also asked to identify two appropriate control women and complete a similar data collection form from their case notes. The process of selecting control women consisted to identify two women who delivered in the same hospital immediately before the case gave birth and who gave birth throughout the same way as the case did (vaginally or by CS).
This design offered the opportunity to perform more reliable analysis, which allowed to identify risk factors associated with the peripartum sepsis.

Definitions of near miss cases that have been adopted during the research are shown in table 7. Figure 3 shows the timing of recruitment for each obstetric complications under study.

Sepsis	• Life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or postpartum period.
	  ○ Sepsis in pregnancy: sepsis developed during pregnancy, in case of miscarriage, ectopic pregnancy, termination of pregnancy (TOP) or molar pregnancy, up to 19^{+6} weeks of gestation.
	  ○ Peripartum sepsis: sepsis developed after giving birth vaginally or by Caesarean section (CS) from 22+0 weeks of gestation, within 42 day following the end of pregnancy.
	  ▪ Two Controls: women who delivered immediately before the case gave birth and throughout the same way as the case did (vaginally or by CS).

Eclampsia	• Seizures in a woman during pregnancy or up to 14 days postpartum, without any other attributable cause, with at least one of the following signs:
	  ○ Hypertension (≥140 mmHg systolic and/or ≥90 mmHg diastolic)
	  ○ Proteinuria [spot urine protein/creatinine >30 mg/mmol (0.3 mg/mg) OR >300 mg/day OR at least 1 g/l [‘2 +’] on dipstick testing]

	○ Thrombocytopenia (platelet count of <100 × 10^9/l) ○ Raised plasma ALT or AST (twice the upper limit of normal)
AFE	• Acute cardio-respiratory collapse within 6 hours after labour, delivery or ruptured membranes, with no other identifiable cause, followed by acute coagulopathy in those women who survive the initial event.
SHiP	• Spontaneous (nontraumatic) intraperitoneal haemorrhage during pregnancy and up to 42 days postpartum, requiring surgical intervention or embolisation. Excluding ectopic pregnancy, uterine rupture and caesarean section associated bleeding.

Table 8. Definitions of near miss cases adopted during the study

Figure 9 shows the time of recruitment of the diseases of interest, considering the definition adopted during the research.

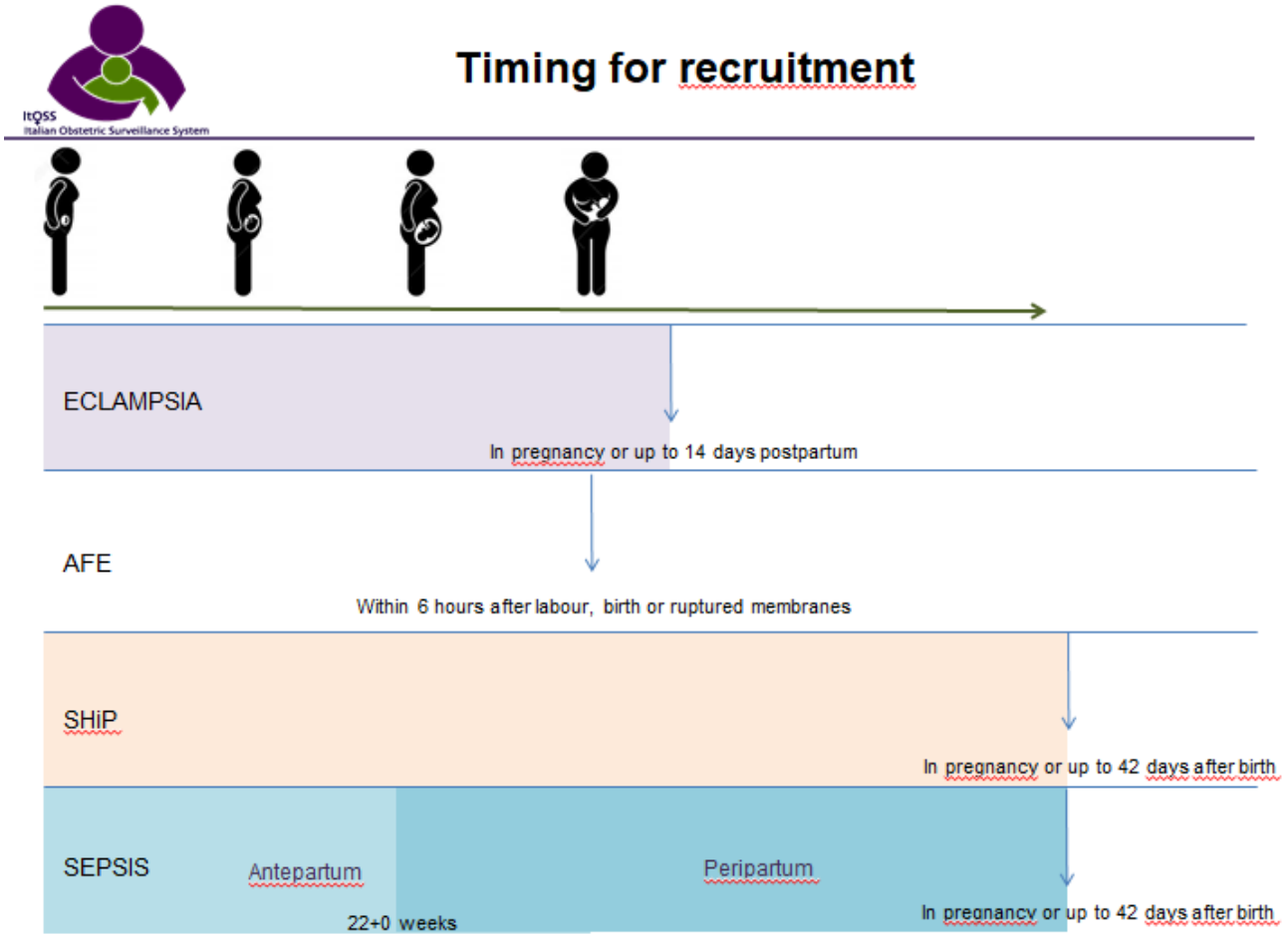


Figure 9. Timing of recruitment

3.8 Sampling and setting

All women who were admitted or gave birth at participating Maternity Units constituted the study population. Reported cases had to meet the definitions established for the project.

This study involved the participation of 9 Italian regions: Lombardia, Piemonte, Friuli-Venezia-Giulia, Emilia-Romagna, Toscana, Lazio, Campania, Puglia and Sicilia. All public and private Maternity Units accepted to participate into the study. A total of 323 Maternity Units have been included. Each Maternity Unit had a nominated clinician who was responsible to report cases.

3.9 Method of data collection

ItOSS has adopted the methodology for case reporting developed by UKOSS. A nominated clinician (Obstetrician, Midwife or Risk Manager) in each Maternity Unit was invited by monthly mailing to report one of the rare obstetric complications under surveillance that occurred in the preceding month or alternatively to state that there was “nothing to report”, as it was mostly the case. Reported cases had to meet the case definition identified by the project.

A website platform was specifically developed for this study, (https://www.salutedonnabambino.it/ITOSS/login.aspx).

Restricted access to the website platform was provided to the appointed contact person via a personal ID and Password (Figure 10).

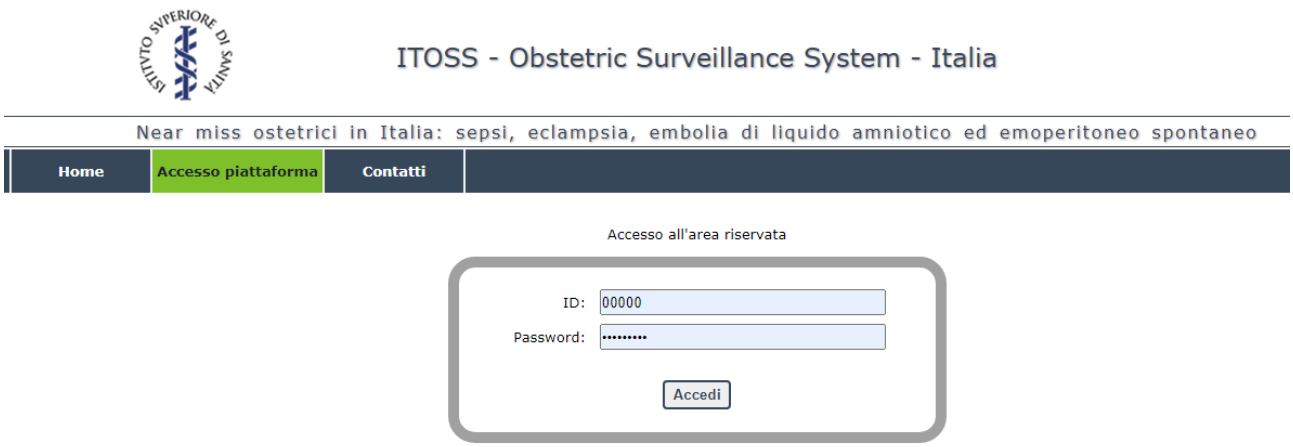


Figure 10. Clinician access to the on-line platform

The platform addressed the clinician to a page dedicated to his maternity unit, where the following information were included:

- a session to communicate the monthly number of cases or “nothing to report” response (Figure 11);
- the definitions of the obstetric complications currently studied (Figure 12);
- the data collection forms that the contact professional might have already completed and, in case of a post-partum sepsis, whereas controls required to be included yet (Figure 13);
- a session to communicate the characteristics of the Maternity Unit during every year of data collection (number of vaginal births, number of assisted vaginal delivery and of CS per year, number of labour rooms present into the Ward, availability of 24h Midwife, Obstetrician, Anaesthetist and Paediatrician, availability of 24h services within the Hospital, such as Transfusion Unit, Radiology, Laboratory and Intensive Care Unit). These data were important to analyse structural and organizational characteristics in order to underlined potential different outcomes between I and II Level Maternity Unit (Figure 14);
- a session including a guide explaining how to complete and send the data collection form, papers about and the ICD-9CM code related to the obstetric complications under surveillance (Figure 15);
- the email address of the contact person of each Operational Unit (Figure 16);
- the data collection forms to complete if a case needed to be reported. I will show the data collection form of eclampsia (Figure 17).

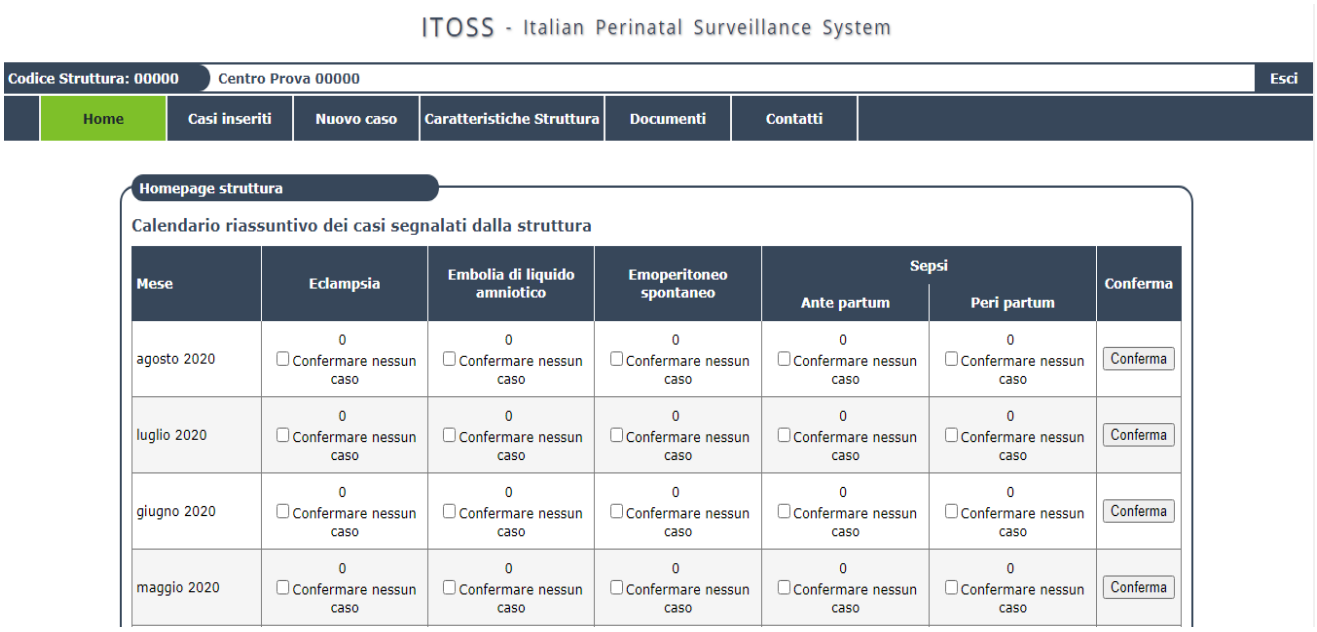


Figure 11. Session to communicate the monthly number of cases or “nothing to report” response

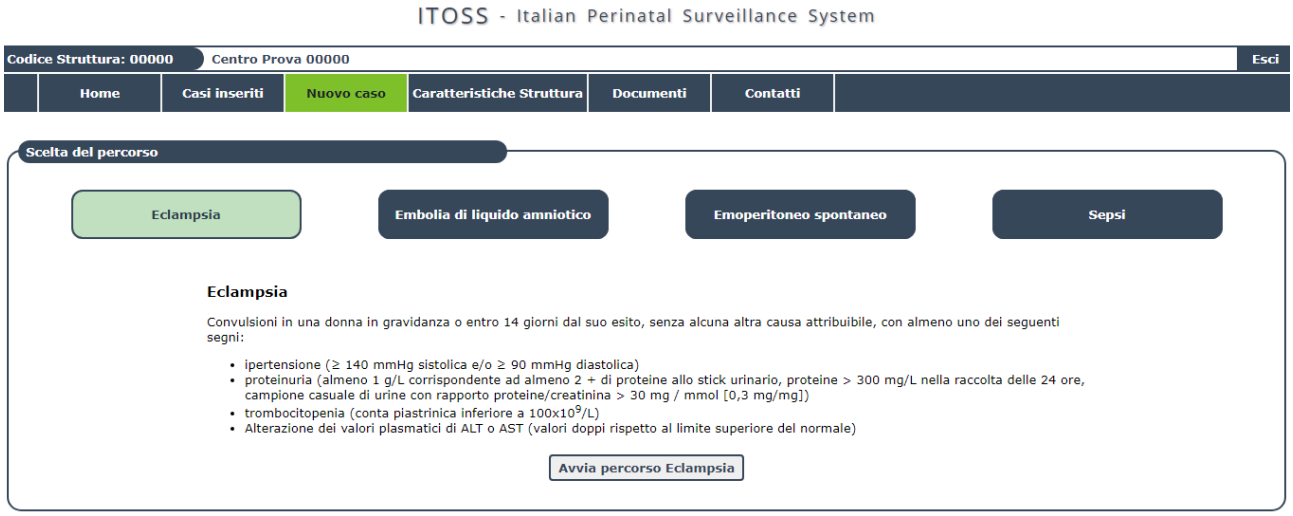


Figure 12. Session with the definitions of near miss cases

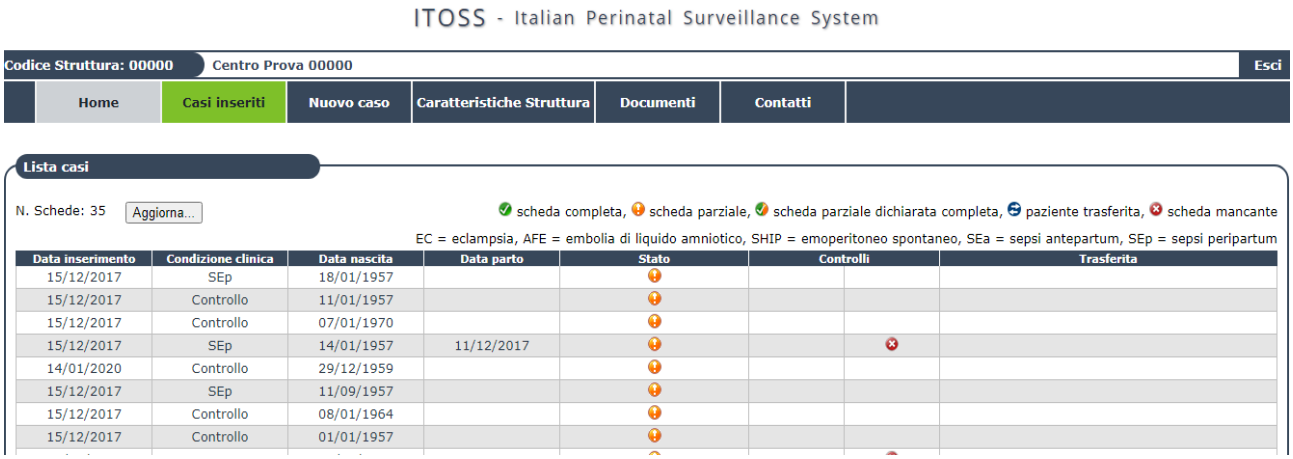


Figure 13. Session with the data collection forms already completed and sent. In case of post-partum sepsis, whereas controls needed to be completed.

Figure 14. Session to communicate the characteristics of the Maternity Unit

Figure 15. Session with further information about the project

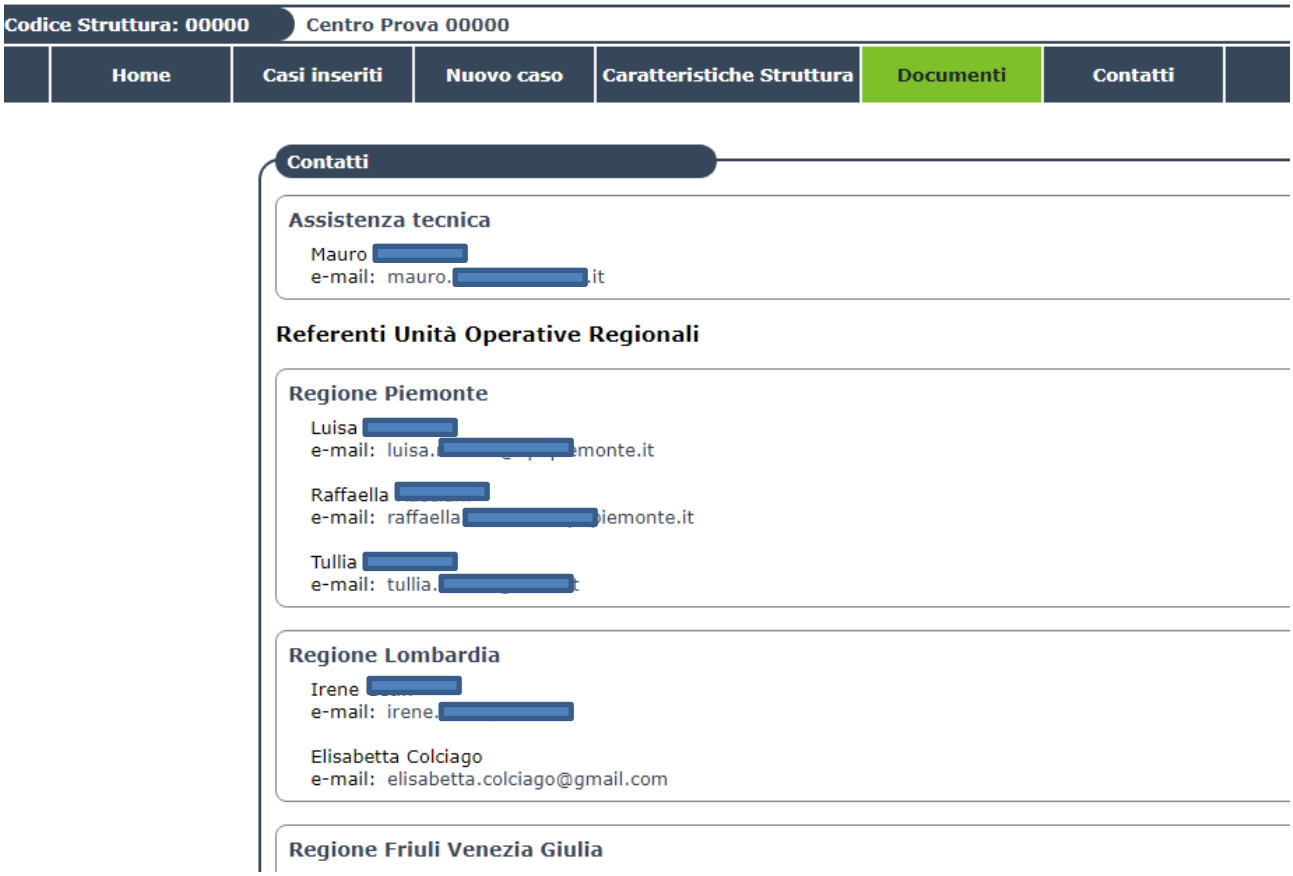


Figure 16. Session with details of the contact person of each Operational Unit

3.10 Data collection forms

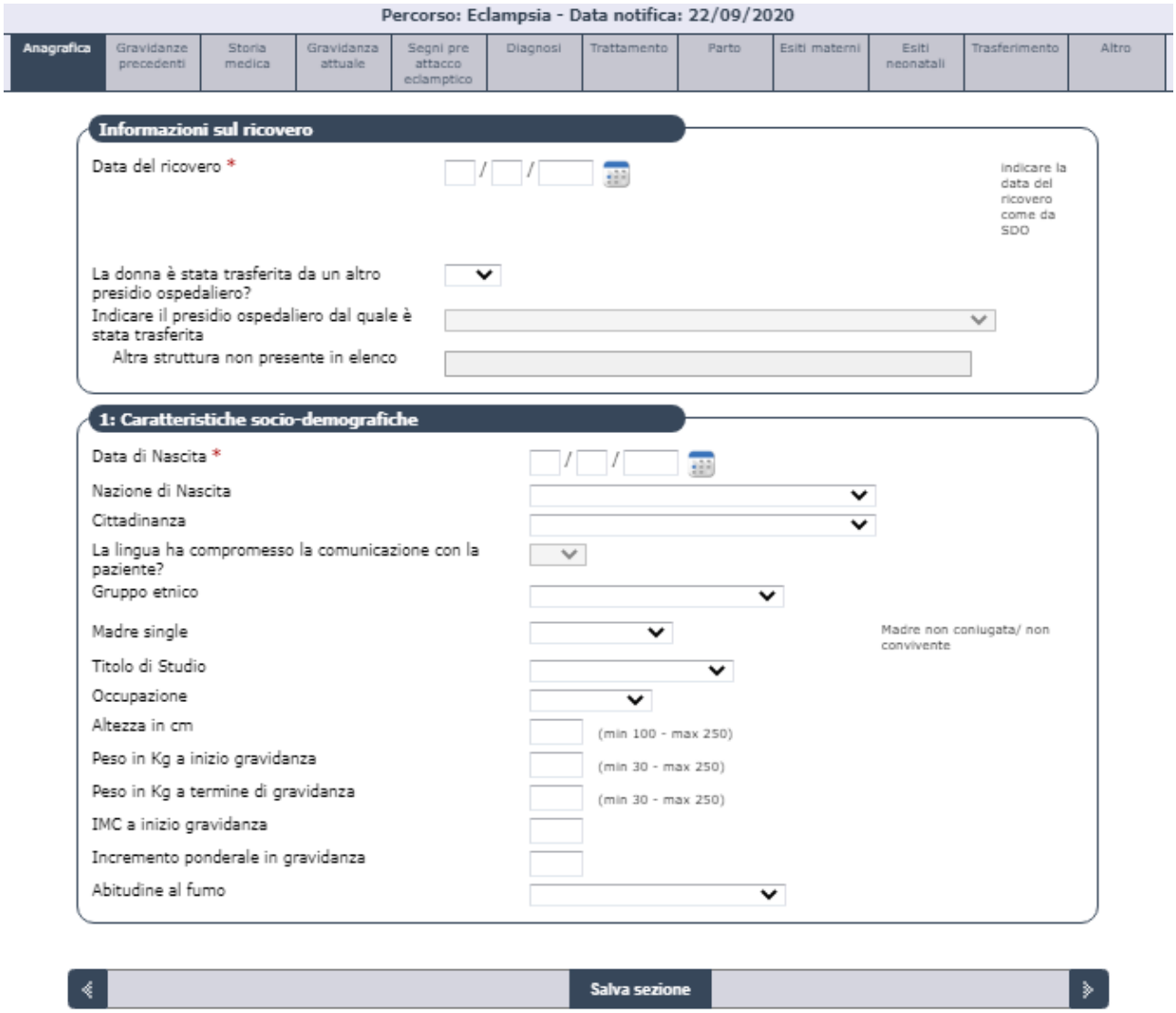
Data collection forms were developed individually for each condition and were designed to be short and easily completed from a woman's case notes, without requiring reference to any other sources of information. They were developed following a phase of literature review and the translation from the English version. The Italian data collection forms were based on the English one, however in view of the evidence, further questions were added and the Italian birth context was considered. They sought confirmation of the appropriate case definition and additional information on risk factors, management and outcomes according to the protocol relating to each condition. ItOSS did not collect any personally identifiable information, such as names, addresses or hospital numbers.

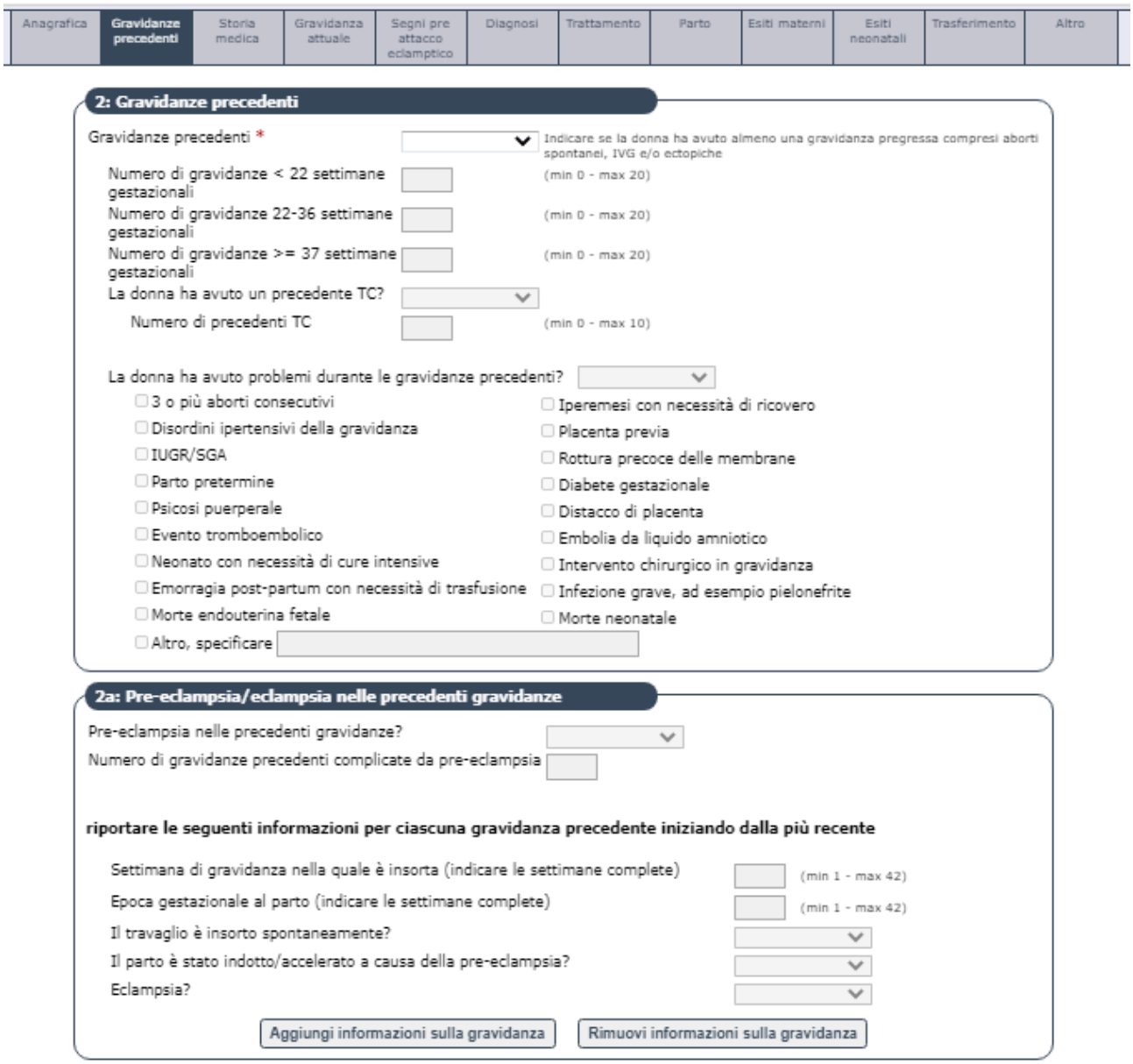
For each condition, data collection forms comprised the following 11 sections, with common headings and labels, but different questions (the data collection form dedicated to the Controls do not include Section 5 and 6):

- Section 1: Woman's details
- Section 2: Previous Pregnancy
- Section 3: Previous Medical History
- Section 4: Current Pregnancy
- Section 5: Diagnosis of case

- Section 6: Therapy
- Section 7: Birth
- Section 8: Maternal Outcomes
- Section 9: Neonatal Outcomes
- Section 10: Transfer
- Section 11: Other Information

I will show the data collection form dedicated to Eclampsia (Figure 17), to explain the pathway to report a case.




Anagrafica
Gravidanze precedenti
Storia medica
Gravidanza attuale
Segni pre attacco eclamptico
Diagnosi
Trattamento
Parto
Esiti materni
Esiti neonatali
Trasferimento
Altro
2: Gravidanze precedenti
Gravidanze precedenti *
Indicare se la donna ha avuto almeno una gravidanza pregressa compresi aborti spontanei, IVG e/o ectopiche
Numero di gravidanze < 22 settimane gestazionali
(min 0 - max 20)
Numero di gravidanze 22-36 settimane gestazionali
(min 0 - max 20)
Numero di gravidanze >= 37 settimane gestazionali
(min 0 - max 20)
La donna ha avuto un precedente TC?
Numero di precedenti TC
(min 0 - max 10)
La donna ha avuto problemi durante le gravidanze precedenti?
3 o più aborti consecutivi
Disordini ipertensivi della gravidanza
IUGR/SGA
Parto pretermine
Psicosi puerperale
Evento tromboembolico
Neonato con necessità di cure intensive
Emorragia post-partum con necessità di trasfusione
Morte endouterina fetale
Altro, specificare
Iperemesi con necessità di ricovero
Placenta previa
Rottura precoce delle membrane
Diabete gestazionale
Distacco di placenta
Embolia da liquido amniotico
Intervento chirurgico in gravidanza
Infezione grave, ad esempio pielonefrite
Morte neonatale
2a: Pre-eclampsia/eclampsia nelle precedenti gravidanze
Pre-eclampsia nelle precedenti gravidanze?
Numero di gravidanze precedenti complicate da pre-eclampsia
riportare le seguenti informazioni per ciascuna gravidanza precedente iniziando dalla più recente
Settimana di gravidanza nella quale è insorta (indicare le settimane complete)
(min 1 - max 42)
Epoca gestazionale al parto (indicare le settimane complete)
(min 1 - max 42)
Il travaglio è insorto spontaneamente?
Il parto è stato indotto/accelerato a causa della pre-eclampsia?
Eclampsia?
Aggiungi informazioni sulla gravidanza
Rimuovi informazioni sulla gravidanza

Percorso: Eclampsia - Data notifica: 22/09/2020

Anagrafica | Gravidanze precedenti | **Storia medica** | Gravidanza attuale | Segni pre attacco eclamptico | Diagnosi | Trattamento | Parto | Esiti materni | Esiti neonatali | Trasferimento | Altro

3: Precedente storia medica

Patologie mediche precedenti?

è possibile selezionare più voci

- Malattia cardiaca (congenita o acquisita)
- Diabete
- Storia di epilessia
- Disordini endocrini (ad esempio ipotiroidismo o ipertiroidismo)
- Ipertensione pre-gravidica (insorta prima della 20ª settimana di gravidanza)
- Disordini ematologici (ad esempio talassemia o trombofilia)
- Disordini infiammatori (ed esempio Chron, retto-colite ulcerosa)
- Disturbi psichiatrici
- Malattie renali
- Patologie autoimmuni (ad esempio LES, sindrome da anticorpi antifosfolipidi)
- Altro
  - specificare

Episodio di epilessia durante l'ultimo anno?

Ipertensione pre-gravidica (insorta prima della 20ª settimana di gravidanza) nella gravidanza attuale o nelle precedenti?

se Sì, specificare i farmaci utilizzati

è possibile selezionare più voci

- Metildopa
- Labetalolo
- Nifedipina
- Solfato di Magnesio
- Altro
  - specificare

Salva sezione

Percorso: Eclampsia - Data notifica: 22/09/2020

Anagrafica | Gravidanze precedenti | Storia medica | **Gravidanza attuale** | Segni pre attacco eclamptico | Diagnosi | Trattamento | Parto | Esiti materni | Esiti neonatali | Trasferimento | Altro

4: Gravidanza attuale

Data presunta del parto (ecografica se disponibile, oppure in base a U.M) / /

Gravidanza insorta a seguito di PMA? (non segnalare se la donna si è sottoposta a trattamento di inseminazione semplice)

PMA eterologa?

Età gestazionale (in settmane complete) al momento della prima visita ostetrica (min 4 - max 41)

La gravidanza attuale è plurima? *

Numero feti (min 2 - max 9)

Problemi durante la gravidanza attuale? *

- Iperemesi con necessità di ricovero
- Diabete gestazionale
- Infezione grave, ad esempio pielonefrite
- Intervento chirurgico in gravidanza
- Placenta previa
- Distacco di placenta
- Rottura precoce delle membrane
- IUGR/SGA
- Idrope fetale
- Minaccia di parto pretermine
- Psicosi puerperale
- Evento tromboembolico
- Embolia di liquido amniotico
- Emorragia
- Emorragia post-partum con necessità di trasfusione
- Patologie fetali
- Morte endouterina fetale
- Morte neonatale
- Altro
  - specificare

È stata diagnosticata una pre-eclampsia prima dell'eclampsia? *

data in cui è stata diagnosticata

È stata eseguita una profilassi in gravidanza per la prevenzione della pre-eclampsia?

Acido acetilsalicilico a basso dosaggio

Eparina a basso peso molecolare

Altro trattamento

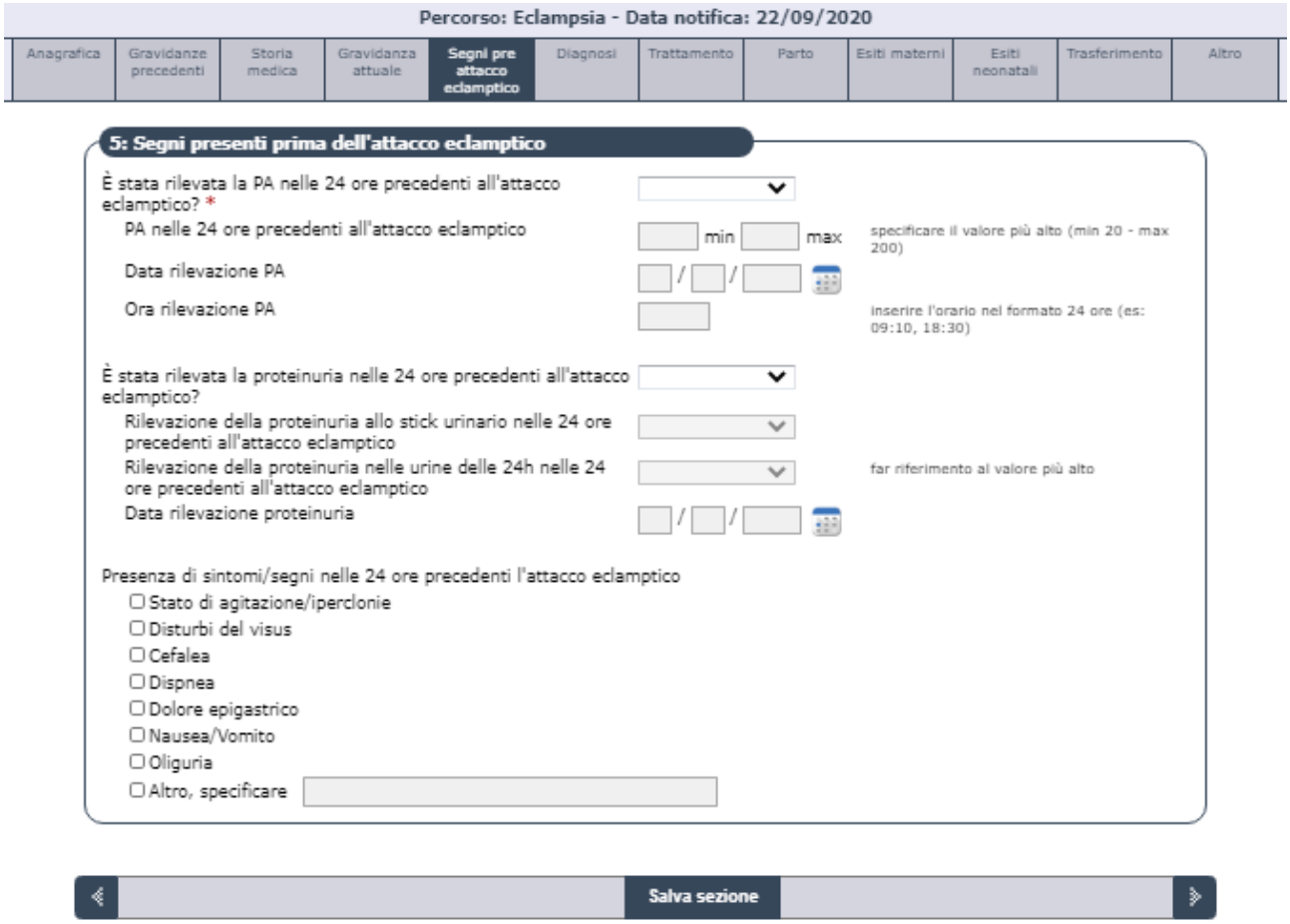
specificare

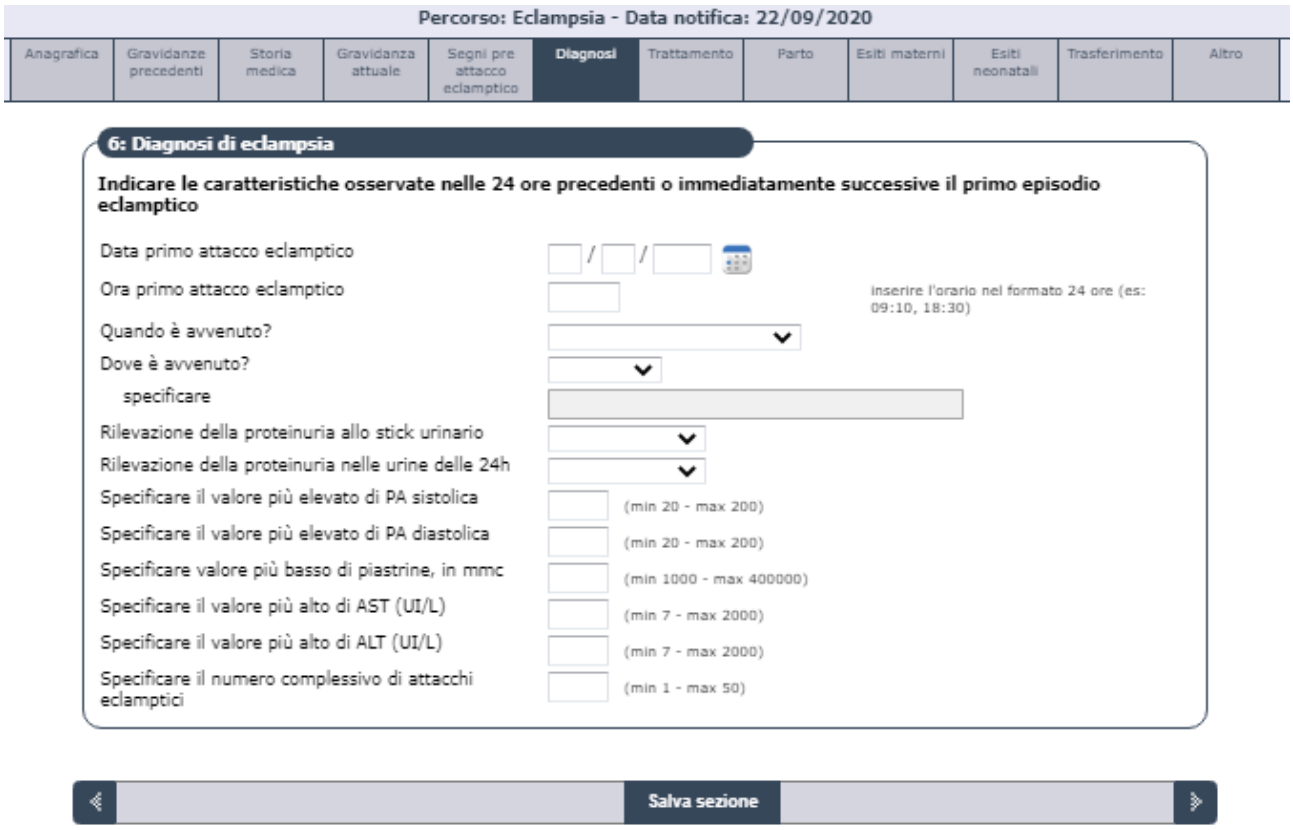
La terapia per l'ipertensione è iniziata/modificata durante la gravidanza attuale?

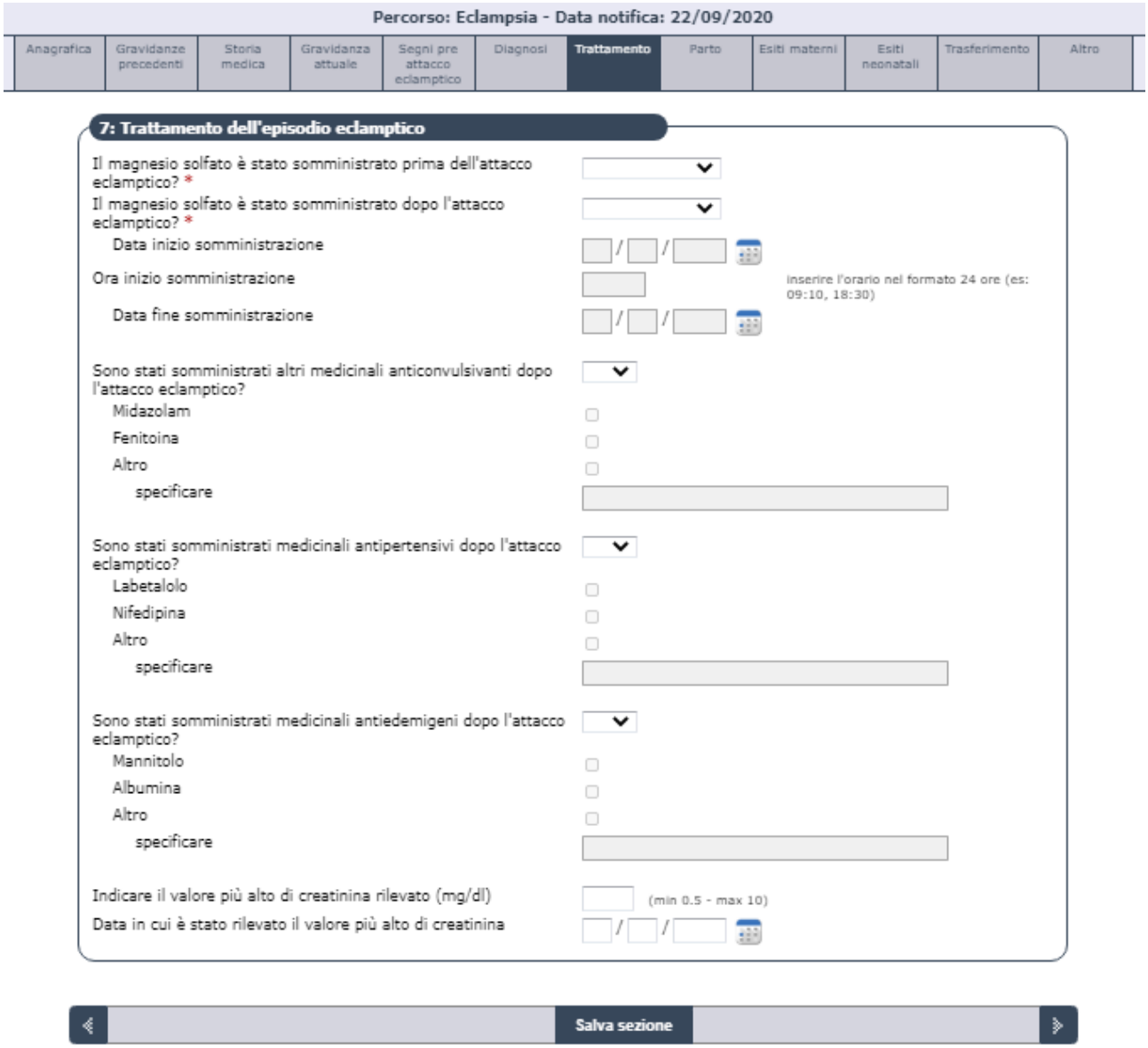
Trattamento	Principio attivo	Data inizio trattamento
anti-ipertensivo		
Magnesio solfato		
Altri anti-convulsivanti (es. diazepam, fenitoina)		
Altri farmaci		
Altri farmaci		

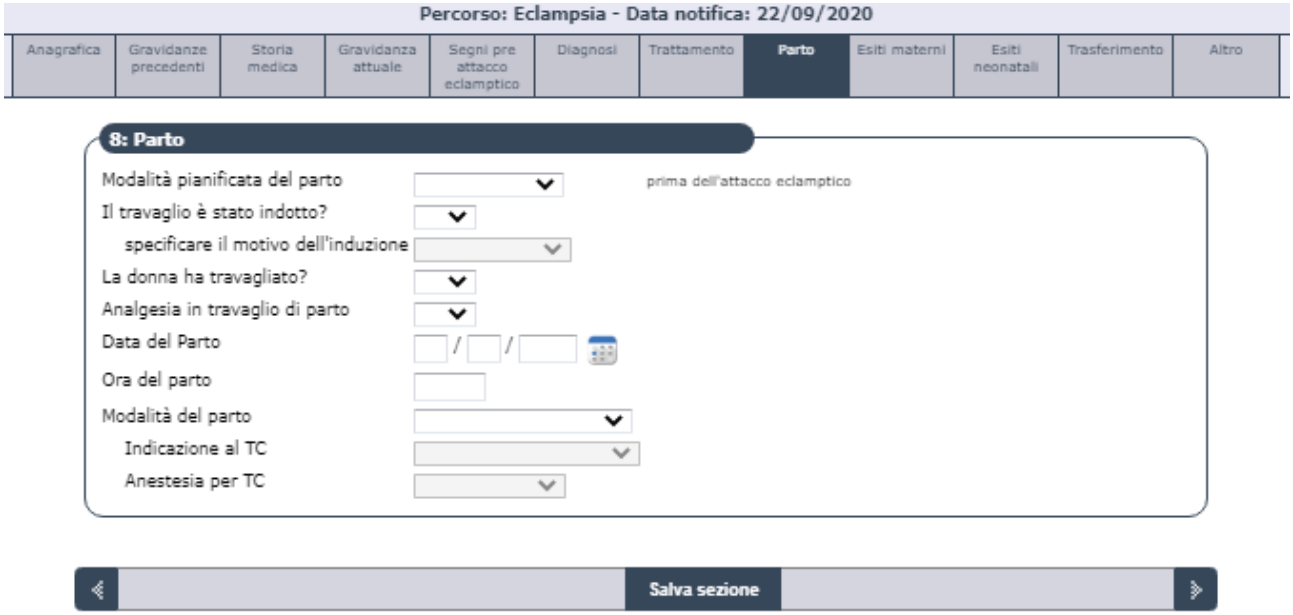
Ricoveri ospedalieri durante la gravidanza (con modalità come adesso)

Salva sezione


Percorso: Eclampsia - Data notifica: 22/09/2020
Anagrafica
Gravidanze precedenti
Storia medica
Gravidanza attuale
Segni pre attacco eclamptico
Diagnosi
Trattamento
Parto
Esiti materni
Esiti neonatali
Trasferimento
Altro
5: Segni presenti prima dell'attacco eclamptico
È stata rilevata la PA nelle 24 ore precedenti all'attacco eclamptico? *
PA nelle 24 ore precedenti all'attacco eclamptico
min
max
specificare il valore più alto (min 20 - max 200)
Data rilevazione PA
Ora rilevazione PA
inserire l'orario nel formato 24 ore (es: 09:10, 18:30)
È stata rilevata la proteinuria nelle 24 ore precedenti all'attacco eclamptico?
Rilevazione della proteinuria allo stick urinario nelle 24 ore precedenti all'attacco eclamptico
Rilevazione della proteinuria nelle urine delle 24h nelle 24 ore precedenti all'attacco eclamptico
far riferimento al valore più alto
Data rilevazione proteinuria
Presenza di sintomi/segni nelle 24 ore precedenti l'attacco eclamptico
Stato di agitazione/iperclonie
Disturbi del visus
Cefalea
Dispnea
Dolore epigastrico
Nausea/Vomito
Oliguria
Altro, specificare
Salva sezione


Percorso: Eclampsia - Data notifica: 22/09/2020
Anagrafica
Gravidanze precedenti
Storia medica
Gravidanza attuale
Segni pre attacco eclamptico
Diagnosi
Trattamento
Parto
Esiti materni
Esiti neonatali
Trasferimento
Altro
6: Diagnosi di eclampsia
Indicare le caratteristiche osservate nelle 24 ore precedenti o immediatamente successive il primo episodio eclamptico
Data primo attacco eclamptico
Ora primo attacco eclamptico
inserire l'orario nel formato 24 ore (es: 09:10, 18:30)
Quando è avvenuto?
Dove è avvenuto?
specificare
Rilevazione della proteinuria allo stick urinario
Rilevazione della proteinuria nelle urine delle 24h
Specificare il valore più elevato di PA sistolica
(min 20 - max 200)
Specificare il valore più elevato di PA diastolica
(min 20 - max 200)
Specificare valore più basso di piastrine, in mmc
(min 1000 - max 400000)
Specificare il valore più alto di AST (UI/L)
(min 7 - max 2000)
Specificare il valore più alto di ALT (UI/L)
(min 7 - max 2000)
Specificare il numero complessivo di attacchi eclamptici
(min 1 - max 50)
Salva sezione


Percorso: Eclampsia - Data notifica: 22/09/2020
Anagrafica
Gravidanze precedenti
Storia medica
Gravidanza attuale
Segni pre attacco eclamptico
Diagnosi
Trattamento
Parto
Esiti materni
Esiti neonatali
Trasferimento
Altro
7: Trattamento dell'episodio eclamptico
Il magnesio solfato è stato somministrato prima dell'attacco eclamptico? *
Il magnesio solfato è stato somministrato dopo l'attacco eclamptico? *
Data inizio somministrazione
Ora inizio somministrazione
inserire l'orario nel formato 24 ore (es: 09:10, 18:30)
Data fine somministrazione
Sono stati somministrati altri medicinali anticonvulsivanti dopo l'attacco eclamptico?
Midazolam
Fenitoina
Altro
specificare
Sono stati somministrati medicinali antipertensivi dopo l'attacco eclamptico?
Labetalolo
Nifedipina
Altro
specificare
Sono stati somministrati medicinali antiedemigeni dopo l'attacco eclamptico?
Mannitolo
Albumina
Altro
specificare
Indicare il valore più alto di creatinina rilevato (mg/dl)
(min 0.5 - max 10)
Data in cui è stato rilevato il valore più alto di creatinina
Salva sezione


Percorso: Eclampsia - Data notifica: 22/09/2020
Anagrafica
Gravidanze precedenti
Storia medica
Gravidanza attuale
Segni pre attacco eclamptico
Diagnosi
Trattamento
Parto
Esiti materni
Esiti neonatali
Trasferimento
Altro
8: Parto
Modalità pianificata del parto
prima dell'attacco eclamptico
Il travaglio è stato indotto?
specificare il motivo dell'induzione
La donna ha travagliato?
Analgesia in travaglio di parto
Data del Parto
Ora del parto
Modalità del parto
Indicazione al TC
Anestesia per TC
Salva sezione

Percorso: Eclampsia - Data notifica: 22/09/2020

Anagrafica | Gravidanze precedenti | Storia medica | Gravidanza attuale | Segni pre attacco eclamptico | Diagnosi | Trattamento | Parto | **Esiti materni** | Esiti neonatali | Trasferimento | Altro

9: Esiti materni

È stata eseguita TAC/RM encefalo?

E' stata diagnosticata una Sindrome da encefalopatia posteriore reversibile (PRES)?

La donna è stata trasferita in Terapia Intensiva? *

- Data trasferimento in Terapia Intensiva
- Ora trasferimento
- La donna è ancora in Terapia Intensiva?
- Data dimissione dalla Terapia Intensiva

Si è verificata un'altra complicanza materna grave?

- Edema polmonare
- Emorragia cerebrale
- CID
- HELLP
- Sindrome da distress respiratorio
- Necessità di ventilazione
- Sepsi
- Evento trombotico
- Sindrome da encefalopatia posteriore reversibile
- Insufficienza renale
- Coma
- Arresto cardiaco
- Altro
  - specificare

Richiesta esame istologico/batteriologico della placenta?

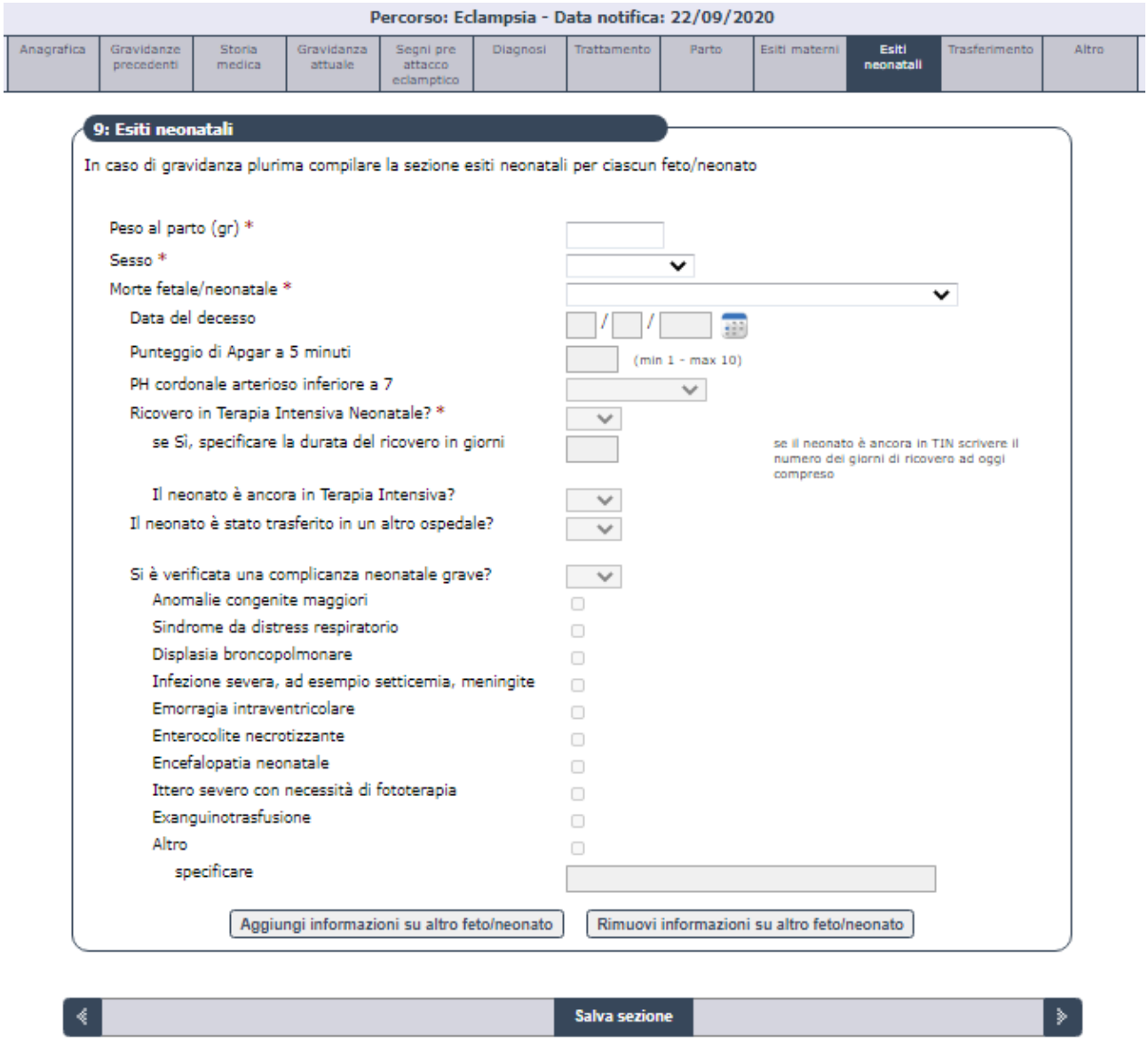
Data di dimissione — indicare la data di dimissione come da SDO

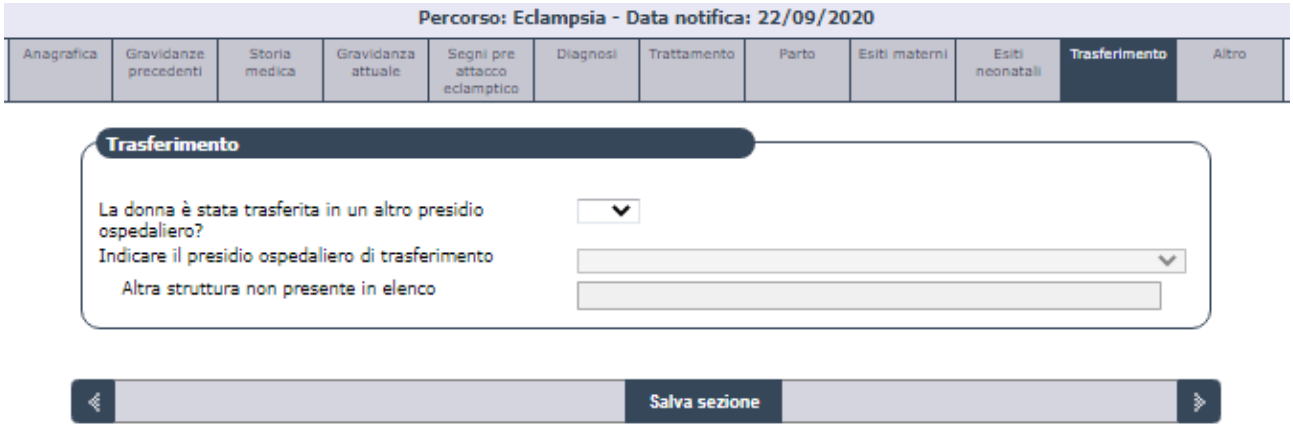
La donna è deceduta?

- Data del decesso
- Ora del decesso
- Causa principale del decesso — specificare se sconosciuta

Richiesta riscontro diagnostico

Salva sezione


Percorso: Eclampsia - Data notifica: 22/09/2020
Anagrafica
Gravidanze precedenti
Storia medica
Gravidanza attuale
Segni pre attacco eclamptico
Diagnosi
Trattamento
Parto
Esiti materni
Esiti neonatali
Trasferimento
Altro
9: Esiti neonatali
In caso di gravidanza plurima compilare la sezione esiti neonatali per ciascun feto/neonato
Peso al parto (gr) *
Sesso *
Morte fetale/neonatale *
Data del decesso
Punteggio di Apgar a 5 minuti
(min 1 - max 10)
PH cordonale arterioso inferiore a 7
Ricovero in Terapia Intensiva Neonatale? *
se Si, specificare la durata del ricovero in giorni
se il neonato è ancora in TIN scrivere il numero dei giorni di ricovero ad oggi compreso
Il neonato è ancora in Terapia Intensiva?
Il neonato è stato trasferito in un altro ospedale?
Si è verificata una complicanza neonatale grave?
Anomalie congenite maggiori
Sindrome da distress respiratorio
Displasia broncopolmonare
Infezione severa, ad esempio setticemia, meningite
Emorragia intraventricolare
Enterocolite necrotizzante
Encefalopatia neonatale
Ittero severo con necessità di fototerapia
Exanguinotrasfusione
Altro
specificare
Aggiungi informazioni su altro feto/neonato
Rimuovi informazioni su altro feto/neonato
Salva sezione


Percorso: Eclampsia - Data notifica: 22/09/2020
Anagrafica
Gravidanze precedenti
Storia medica
Gravidanza attuale
Segni pre attacco eclamptico
Diagnosi
Trattamento
Parto
Esiti materni
Esiti neonatali
Trasferimento
Altro
Trasferimento
La donna è stata trasferita in un altro presidio ospedaliero?
Indicare il presidio ospedaliero di trasferimento
Altra struttura non presente in elenco
Salva sezione

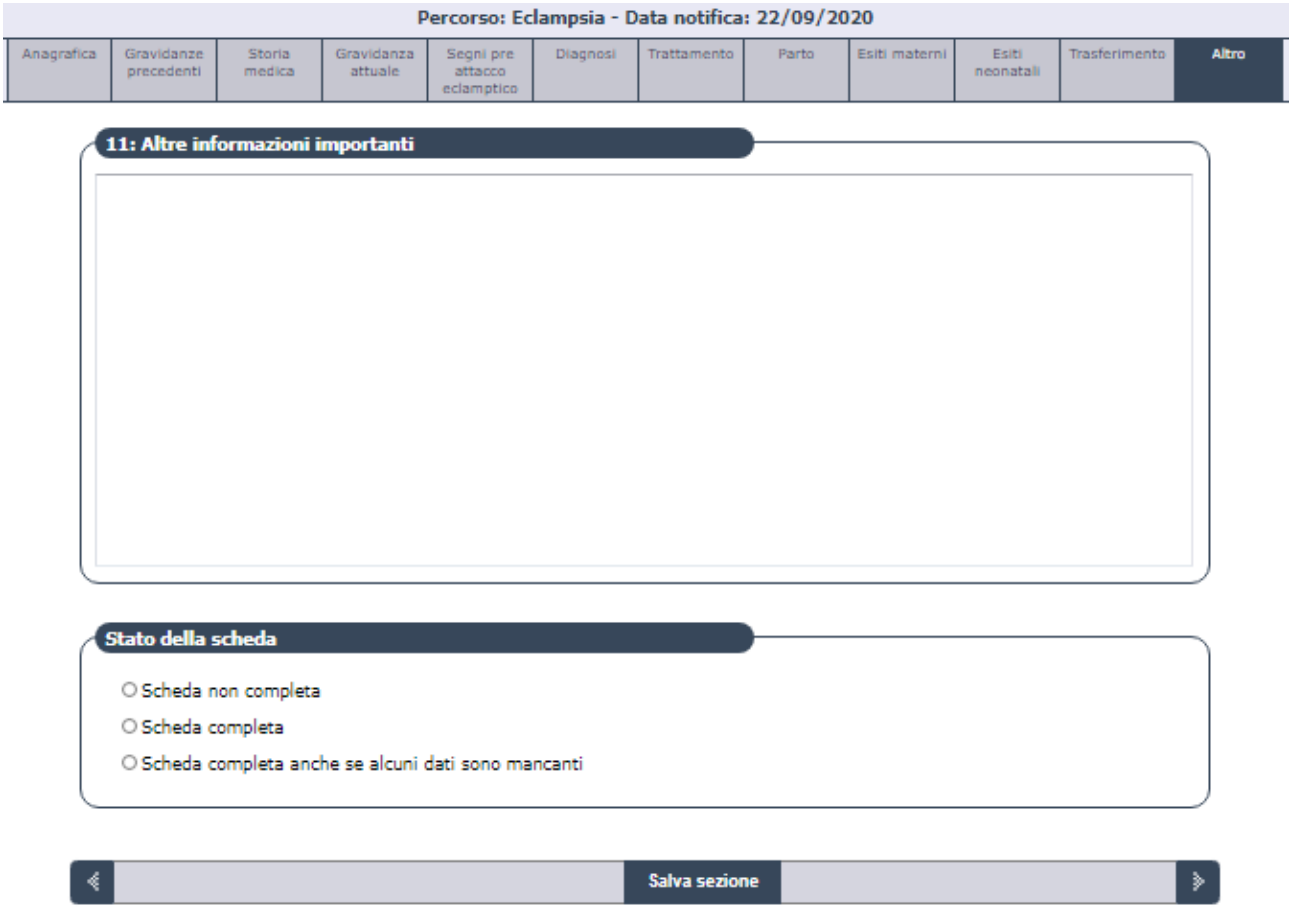


Figure 17. Eclampsia data collection form

Each session needed to be saved.

At the end of the data collection form there were different save options:

1. Data collection non completed, when the clinician needed to collect more information;
2. Data collection completed, if all information were included;
3. Data collection completed with some missing values, in case the clinician was unable to collect some of the information required.

3.11 Analysis of data

Descriptive analysis of socio-demographics, medical and obstetric variables, eclampsia treatment and management, pregnancy and birth outcomes was performed. The eclampsia episode was also classified in antepartum, intrapartum or postpartum, according to when the first seizure occurred. The incidence of eclampsia was reported.

Risk factors to develop eclampsia were calculated with 95% confidence intervals, using as the denominator 2017 birth data and an estimation of births occurred in 2018 and 2019, this was performed considering the number of maternities in 2017 and applying a reduction in birth rates

equal to 3% (N= 716,222). Data regarding the number of births were extrapolating from the National Hospital Database Register and from the National Birth Register.

The study regarding sepsis included a descriptive analysis of the incidence, women's characteristics, causative organisms, sources of infection, and outcomes of peripartum sepsis. In order to assess risk factors for developing post-partum sepsis, all cases were compared with non-septic controls. A 1:2 matched case-control study was conducted considering as controls non-septic women who gave birth into the same hospital of the case, immediately before and throughout the same mode of birth.

A conditional logistic regression model was applied, accounting for matching factors. Conditional logistic regression (CLR) is a specialized type of logistic regression usually employed when case subjects with a particular condition or attribute are each matched with *n* control subjects without the condition. The odd ratio (OR) with 95% Confidence Intervals for maternal post-partum sepsis was calculated for each variable.

All analyses were carried out using STATA and SAS softwares.

3.12 Ethical Considerations

The present study has been approved by the Ethical Committee of the Italian National Institute of Health on the 18th of July 2017 (n. PRE 544/17).

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter is concerned with presenting the analysis of the data regarding two of the obstetric complications under surveillance: Eclampsia and Sepsis. As already mentioned, the data on AFE and SHiP won't be described into the thesis, but they will be used to participate in a multinational study promoted by INOSS; this will give the opportunity to obtain sufficient cases, an appropriate statistical power, a stable incidence and reliable risk factors related to these extremely rare complications.

Results related to eclampsia will be described first, followed by findings regarding sepsis.

4.2 Participating Maternity Units

During the study period a national reorganisation of the maternity services was in progress, some of the Maternity Units included into the census phase were closed during the data collection stage.

Some other Units never accessed the on-line platform neither reported near miss cases or confirmed the "nothing to report" response, these Units were excluded from the study.

We had a response rate of 94.2% (Table 9).

Region	N° of Maternity Units at the census phase	N° of Maternity Units closed during the study	N° of Maternity Units excluded as not reporting	% Participating Maternity Units
Piemonte	31	0	2	93.5%
Lombardia	65	5	0	100.0%
Friuli Venezia Giulia (FVG)	10	0	0	100.0%
Emilia Romagna	23	0	0	100.0%
Toscana	24	1	0	100.0%
Lazio	38	1	3	91.9%
Campania	55	2	0	100.0%
Puglia	29	2	8	70.4%
Sicilia	48	2	5	89.1%
Total	323	13	18	**94.2%**

Table 9. Participating Maternity Units response rate

4.3 Results regarding eclampsia

The following paragraphs will report findings regarding eclampsia.

Data will be described reporting the expected number of cases of eclampsia within the participating Regions, the incidence rate of eclampsia found during the data collection period, the characteristics of women with eclampsia, their medical and obstetric history, risk factors associated with eclampsia considering data from the National Hospital Discharge Database and the national birth register as comparison population, diagnosis and management of eclampsia and maternal and neonatal outcomes.

The project adopted the definition of Eclampsia developed by the Delphi study [54].

Cases of Eclampsia should met the following definition:

- Seizures in a woman during pregnancy or up to 14 days postpartum, without any other attributable cause, with at least one of the following signs:
    - Hypertension (≥140 mmHg systolic and/or ≥90 mmHg diastolic)
    - Proteinuria [spot urine protein/creatinine >30 mg/mmol (0.3 mg/mg) OR >300 mg/day OR at least 1 g/l ['2 +'] on dipstick testing]
    - Thrombocytopenia (platelet count of $<100 \times 10^9$/l)
    - Raised plasma ALT or AST (twice the upper limit of normal)

4.3.1 Expected incidence rate

The assessment of the expected incidence rate of this obstetric complication was performed using the ICD-9CM diagnosis and procedure codes, that identify eclampsia under the code 642.6 named "Eclampsia causing complications in pregnancy, during birth or during the post-partum period". Hospital Discharge Databases have been extensively used for both surveillance and research purposes.

The National Hospital Discharge Database has been used considering the years 2014-2015 (Table 10) to assess the code related to eclampsia and the expected incidence rate of this complication.

Year considered	Birth in Italy	Birth at participating Region	Total
2014	493'025	478'936	971'961
2015	478'936	359'491	729'185

Table 10. Number of births during the years 2014 and 2015

Region	N	‰ 2014-2015
Piemonte	36	0.56
Lombardia	50	0.30
Friuli Venezia Giulia (FVG)	5	0.29
Emilia Romagna	31	0.43
Toscana	20	0.35
Lazio	21	0.22
Campania	49	0.47
Puglia	152	2.37
Sicilia	44	0.50
Participating Regions	**408**	**0.56**
Italian Regions	531	0.55

Table 11. Expected incidence rate of eclampsia

From data, it could be observed that the incidence rate found across the 9 participating Regions provides a reasonable approximation of the national one.

The incidence rate of eclampsia assessed throughout the last 16 years, showed a slow but progressive reduction of this complication (Figure 18).

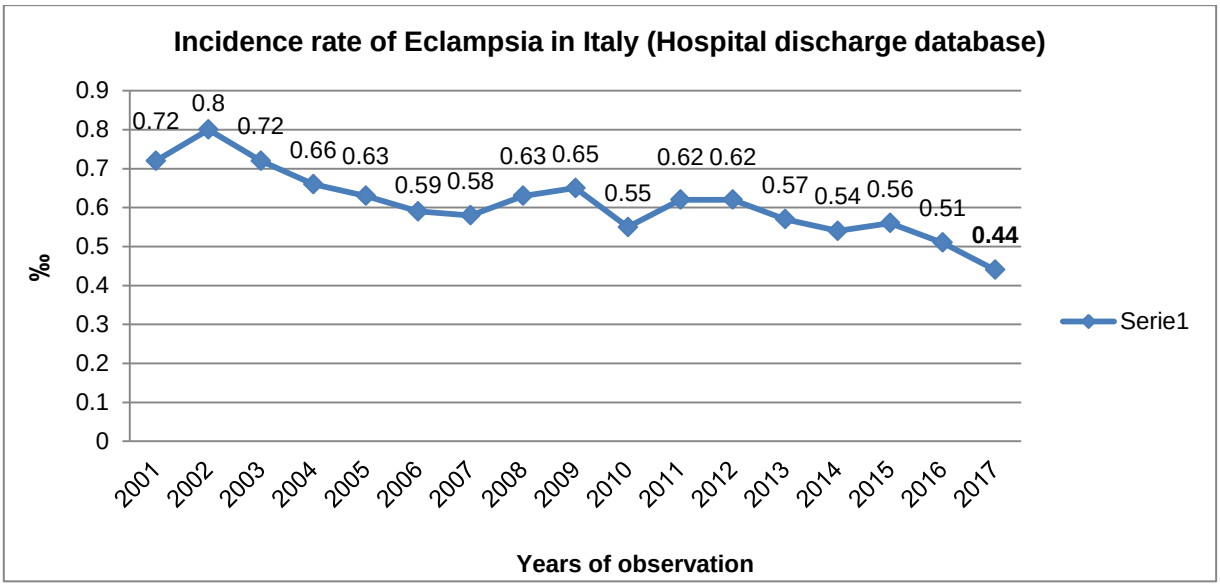


Figure 18. Incidence rate of Eclampsia in Italy between 2001 and 2017

4.3.2 Observed incidence rate

During the data collection period, from the 1st November 2017 until the 30th March 2020, 124 cases of eclampsia were reported. Figure 19 shows the case reporting and completeness of data collection. Among all cases notified, 8 did not meet the definition of the project and were classified as women having pre-eclampsia without any ecliptic fit.

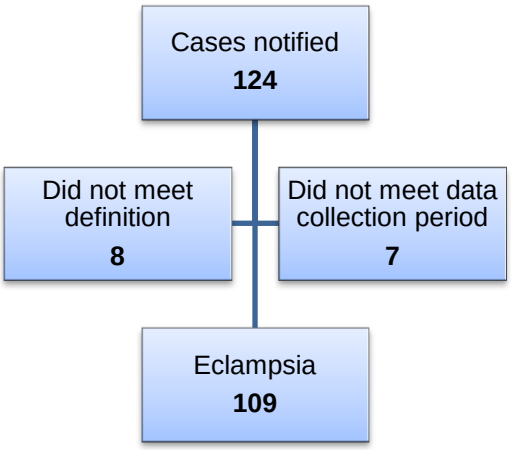


Figure 19. Case reporting and completeness of data collection

After checking to confirm that each reported case met the case definition, 109 near misses of eclampsia were identified, representing an estimated incidence rate of 0.15 cases per 1,000 births. Figure 20 shows the signs included into the definition of eclampsia. The majory of women (n= 98) had hypertension, followed by proteineuria (n=46), thromocytopenia (n=38), raised AST (n=29) and raised ALT (n=26).

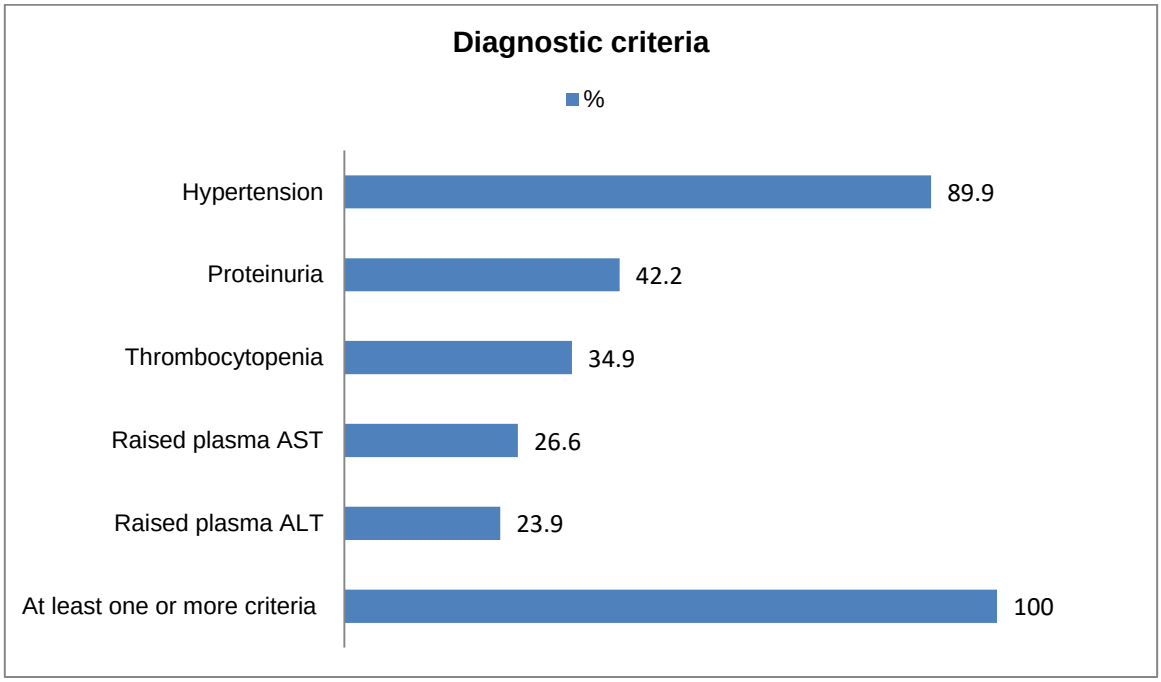


Figure 20. Diagnostic criteria collected among reported cases (N=108, 1 of the signs missing).

Figure 21 compares the incidence rate found with the data of the near miss study with the one calculated using the ICD-9CM code 642.6 of the Hospital Discharge Database.

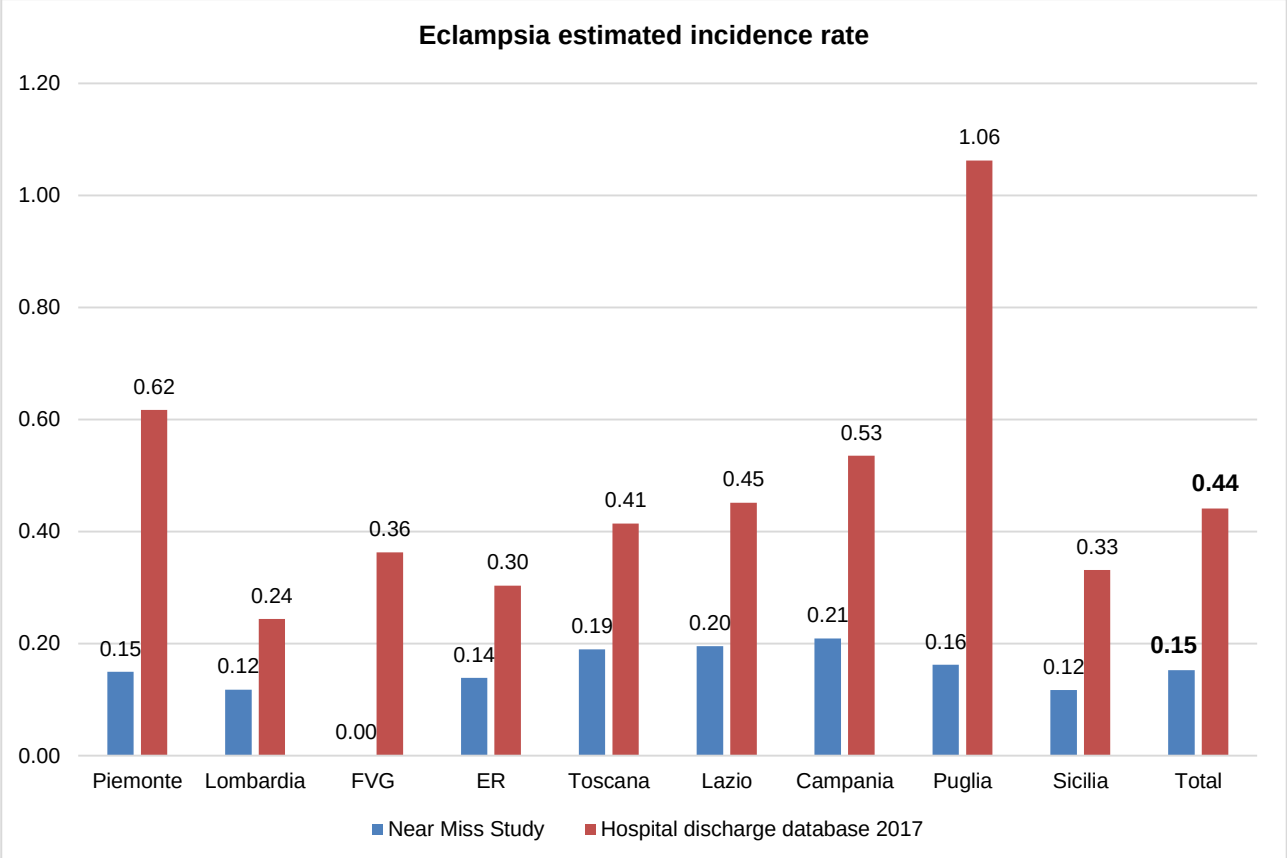


Figure 21. Eclampsia estimated incidence rate, comparison between Near Miss reported cases and events found using the Hospital Discharge Database.

The Hospital Discharge Database incidence rate overestimates the one that we observed during the study. Eclampsia cases identified using the National Hospital Discharge Database, were double checked with the nominated clinician of each Maternity Unit where the event was registered. Most of the time a pre-eclampsia occurred, the eclamptic seizure was not confirmed and then it was not included into the sample. Data collected throughout the near miss project estimate the true incidence rate of eclampsia as the ICD-9CM code was frequently used inappropriately.

There were no significant disparities in severe maternal outcomes between women of the North, the Centre and the South of Italy.
Severe maternal morbidities resulted 35.9% in the North, 23.1% in Central Italy and 39.0% in the South of the Country. Tuscany Region was the one with the lower rate of poor maternal outcomes, 10%.

4.3.3 Socio-demographic characteristics

Table 10 describes the socio-demographic characteristics of the women who suffered of eclampsia. Variables related to smoking behaviour and to the Body Mass Index (BMI) present too many missing values, a recurrent problem that leads to inefficient analysis that does not allow comparison between data of the other INOSS studies.

Socio-demographic characteristics		**n**	**%**
Age (years)	<20	6	5.6
	20-34	69	63.9
	>=35	33	30.6
	<40	94	87.0
	>=40	14	13.0
		mean	**sd**
		31.9	6.7
		n	**%**
Nationality	Italian	71	65.7
	Foreing	37	34.3
Citizenship	Italian	72	69.2
	Foreign	32	30.8
Ethnic Group	Caucasian	76	75.2
	Negroid	18	17.8
	Asian	7	6.9
	Other	8	7.9

Education	Lower secondary school	42	38.5
	Upper secondary school	32	29.4
	Degree or more	17	15.6
	Not known	18	16.5
Employment status	Employed	39	35.8
	Unemployed	17	15.6
	Housewife	42	38.5
	Other	1	0.9
	Not known	10	9.2
Single	No	89	81.7
	Yes	10	9.2
	Not known	10	9.2
Smoking status	Never	67	61.5
	Stopped in pregnancy or before	10	9.2
	Smoking	4	3.7
	Not known	28	25.7
BMI	≤ 18.4	3	2.8
	18,5-24,9	48	44.0
	25-29,9	25	22.9
	≥ 30	12	11.0
	Not known	21	19.3

Table 12. Women's socio-demographic characteristics

BMI: body mass index

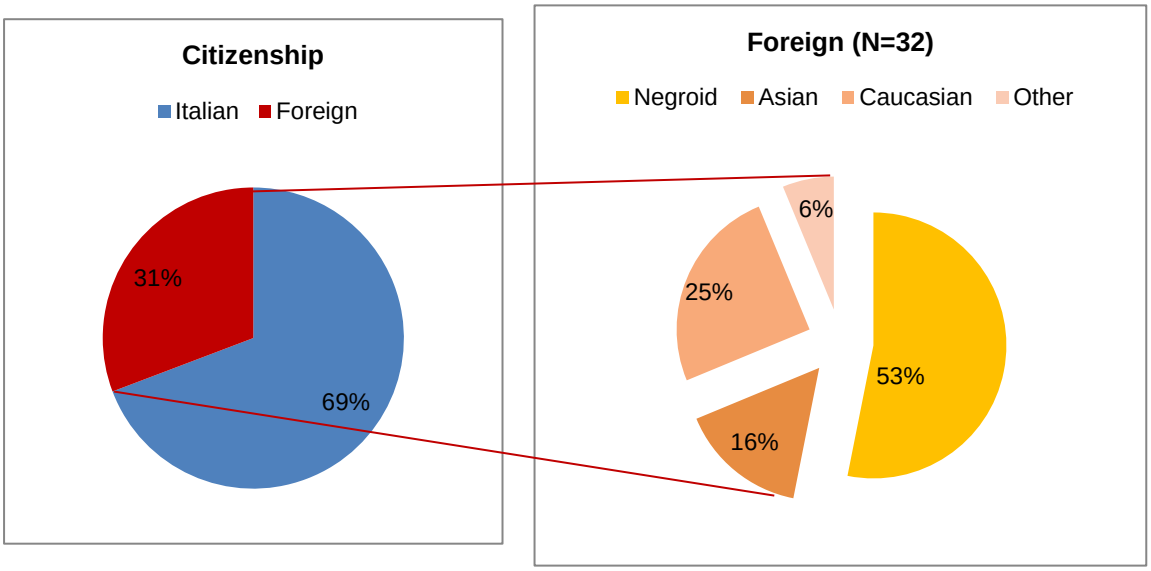


Figure 22. Women's citizenship and foreign women divided into ethnic groups

Figure 22 shows the citizenship and the ethnic groups of the foreign women who experienced an eclamptic episode. When the eclamptic fit occurred in a non-Italian woman, an issue of language barrier was reported in 45.9% of cases.

4.3.4 Obstetric and medical history

Women's medical and obstetric history are shown in table 11 and 12, respectively. Women with pre-existing medical conditions were 18, consisting of 2 women with diabetes, 6 with endocrine disorders, 2 with chronic hypertension (there were 4 women with blood pressure issues, however only 2 were reported also in this part of the data collection form), 6 had hematologic diseases, 1 with mental health disorders and 1 with renal diseases.

Medical History		**n**	**%**
Epilepsy last year	No	97	89.0
	Yes	1	0.9
	Not known	11	10.1
Pre-existing medical complications **(13 missing – 11.9%)**	No	71	74
	Yes	18	18.8
	Not known	7	7.3
Chronic hypertension	No	92	84.4
	Yes	4	3.7
	Not known	13	11.9

Table 13. Women's medical history

Multiparous women were 43 and 30.2% of them had a complication during the childbearing continuum, consisting of 6 with recurrent miscarriages, 1 had a pre-term birth, 1 with a post-partum haemorrhage needing blood transfusion, 3 with placenta praevia, 1 with hypertension in pregnancy and 1 woman who was admitted to Intensive Care Unit due to coma after pre-eclampsia.

Previous pregnancy history **(n=43 multiparous)**		**n**	**%**
Complications in pregnancy	No	26	60.5
	Yes	13	30.2
	Not known	4	9.3
Previous pre-eclampsia	Yes	2	4.7
Previous CS	No	24	55.8
	Yes	19	44.2
Number of Previous CS	1	15	78.9
	2+	4	21.1

Table 14. History of previous pregnancies

CS: caesarean section

4.3.5 Current pregnancy

The sample included 66 nulliparous women (60.6%), 8 multiple pregnancies (7.3%) and 9 (8.3%) pregnancies achieved throughout in vitro fertilization technique, of those 5 were gamete donations, 4 oocyte donations and 1 oocyte together with sperm donation (table 13).

A pre-eclampsia before the ecliptic episode was diagnosed in 21 women, of those 11 were multiparous.

History of current pregnancy (N= 109)		n	%
Parity	Nulliparous	66	60.6
	Multiparous	43	39.4
Multiple pregnancy	No	101	92.7
	Yes	8	7.3
ART	No	94	86.2
	Yes	9	8.3
	Not known	6	5.5
Complications in pregnancy	No	46	42.2
	Yes	49	45.0
	Not known	14	12.8
Hospital admission	No	68	62.4
	Yes, 1	6	5.5
	Yes, 2+	1	0.9
	Not known	34	31.2
Diagnosis of pre-eclampsia before eclampsia (1 missing)	No	83	76.9
	Yes	21	19.4
	Not known	4	3.7

Table 15. History of current pregnancy.

ART: assisted reproductive technology; G.E.: gestational age

During the current pregnancy 29 women (26.6%) started or changed their treatment for the hypertensive disorders.

Magnesium sulphate prophylaxis was given to 19 women (17.4%). Among the women who had any hypertensive issues during the previous or the current pregnancy, 12 (30.77%) were given magnesium sulphate as a prophylactic treatment, of those 5 were multiparous. Among multiparous with pre-eclampsia during the previous pregnancy, none were given magnesium sulphate in this pregnancy.

Among the 83 women who were admitted in hospital prior the eclamptic episode, a total of 18 (21.7%) received the prophylaxis, of those 6 were part of the pre-eclamptic group (n= 21), none of the remaining women with pre-eclampsia received the prophylaxis with magnesium sulphate.

Treatment in pregnancy		n	%
Magnesium sulphate prophylaxis	Yes	19	17.4
Low-dose aspirin	No	1	7.1
	Before 16 weeks	4	28.6
	After 16 weeks	2	14.3
	G.E. not known	3	21.4
Low molecular-weight heparin		10	71.4
One antihypertensive medication	Only Methyldopa	12	11.0
	Only Nifedipine	14	12.8
	Only Labetalol	11	10.1
Two antihypertensive medications		7	6.4
Three antihypertensive medications		1	0.9
Anticonvulsants		4	3.7
Other		2	14.3

Table 16. Medications received in current pregnancy

4.3.6 History of the eclamptic episode

Among the 71 women who had their Blood Pressure (BP) checked within 24 hours before the eclamptic fit, 56.3% had at least a pathological diastolic value and 32.4% had at least a pathological systolic value. Means of the diastolic and systolic BP were 123 mmHg and 124 mmHg, respectively. Only 22 women had a proteinuria assessment 24 hours before eclampsia (table 16). Among them 11.9% had proteinuria with at least 1+ at the urine dipstick, and/or a pathological 24 hours urine collection, that was reported in 27.3% of cases.

Pre-eclampsia was diagnosed in 21 women before the eclamptic episode and all of them had the BP checked within 24 hours before their fit.

Blood pressure and urinary signs in women with eclampsia (N= 109)		n	%
Assessment of BP 24h before fit	No	31	28.4
	Yes	71	65.1
	Not known	7	6.4
BP 24h before fit (mmHg)	Diastolic >110	40	56.3
	Systolic >140	23	32.4
BP at the time of clinical diagnosis	Diastolic >110	33	30.3
	Systolic >140	89	81.7
	No	80	73.4

Assessment of proteinuria 24h before fit	Yes	22	20.2
	Not known	7	6.4
Proteinuria with urine dipstick 24h before fit	Negative	2	9.1
	1+	5	22.7
	2+	3	13.6
	3+	4	18.2
	4+	1	4.5
	Not assessed	2	9.1
	Not known	5	22.7
Proteinuria in 24h urine collection 24h before fit	0,3g - 2g	3	13.6
	≥ 2g	3	13.6
	Not assessed	10	45.5
	Not known	6	27.3

Table 17. Maternal assessment within 24h before the eclamptic episode

BP: Blood Pressure

In figure 23 is shown the comparison between the diastolic and the systolic blood pressure assessed within 24 hours before the eclamptic fit and at the time of diagnosis, in a sample of 83 women, who were admitted prior to their eclamptic episode. The majority of women reported a higher increased diastolic blood pressure in both occasions.

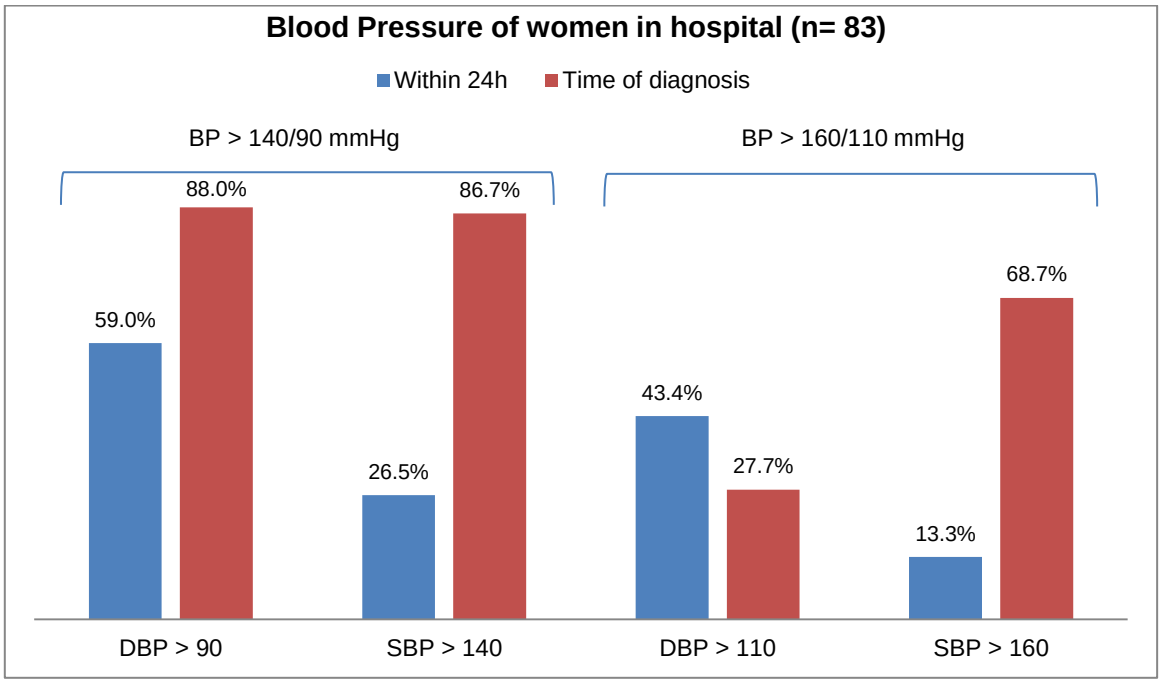


Figure 23. Assessment of blood pressure in women admitted to hospital 24 h prior the eclamptic episode and at the time of diagnosis

BP: blood pressure; DBP: diastolic blood pressure; SBP: systolic blood pressure

Clinicians were also asked to report premonitory symptoms and sign of eclampsia within the 24 hours before the eclamptic episode. Data indicated that 41.3% of the sample did not show any

warning signs. A total of 83 women had their first fit in hospital and no symptoms were reported in 38.6% of them (Table 17).

Premonitory symptoms and signs preceding the eclamptic episode within 24h

Symptom or sign	Women with eclamptic fit (n=109)		Women with eclamptic fit in hospital (n=83)	
	n	%	n	%
Headaches	47	43.1	35	42.2
Vomiting e/o epigrastric pain	25	22.9	20	24.1
Nausea and vomiting	15	13.8	11	13.3
Visual disturbance	14	12.8	10	12.0
Epigastric pain	17	15.6	14	16.9
State of agitation e/o hyper-reflexia	8	7.3	6	7.2
Oliguria	4	3.7	4	4.8
Dyspnea	2	1.8	2	2.4
No symptoms	45	41.3	32	38.6

Table 18. Signs and symptoms reported prior the ecliptic episodes

The median gestational age at the time of the eclamptic episode was 37 weeks (range 21 – 41 weeks), in those with pre-eclampsia was 36^{+5} (n= 21). A total of 45.9% (n=50) of women gave birth pre-term (mean= 33 weeks, range 21 – 36 weeks), among them 76% had their fit in pregnancy, 2% in labour and 22% post-nataly. The gestational age distribution at the time of the eclamptic fit (antepartum and intrapartum fits) or birth (post-nataly fits) is shown in Figure 24.

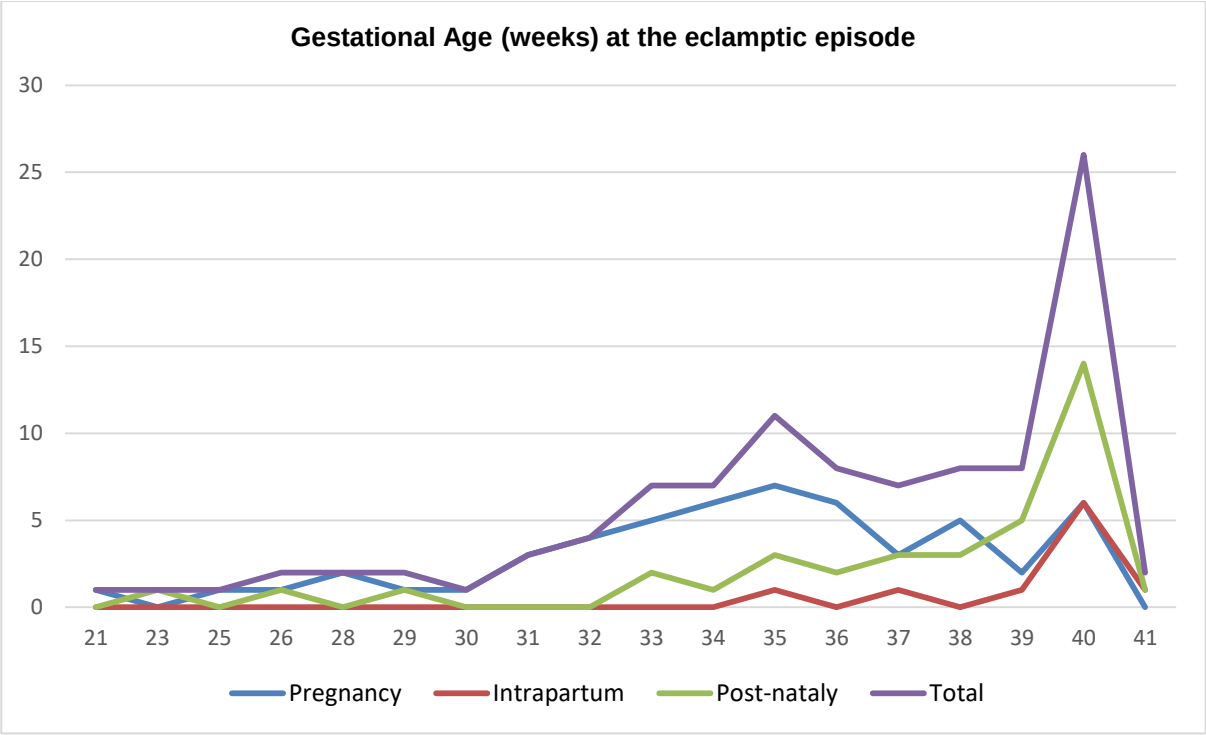


Figure 24. Gestational age distribution at the time of the eclamptic fit (antepartum and intrapartum fits) or birth.

A total of 50.5% (n=55) of women had their first fit antepartum, 10.1% (n= 10) intrapartum and 35.8% (n=39) post-nataly (5 missing), with a quite considerable number of seizure more than 48 hours after birth (Figure 25).

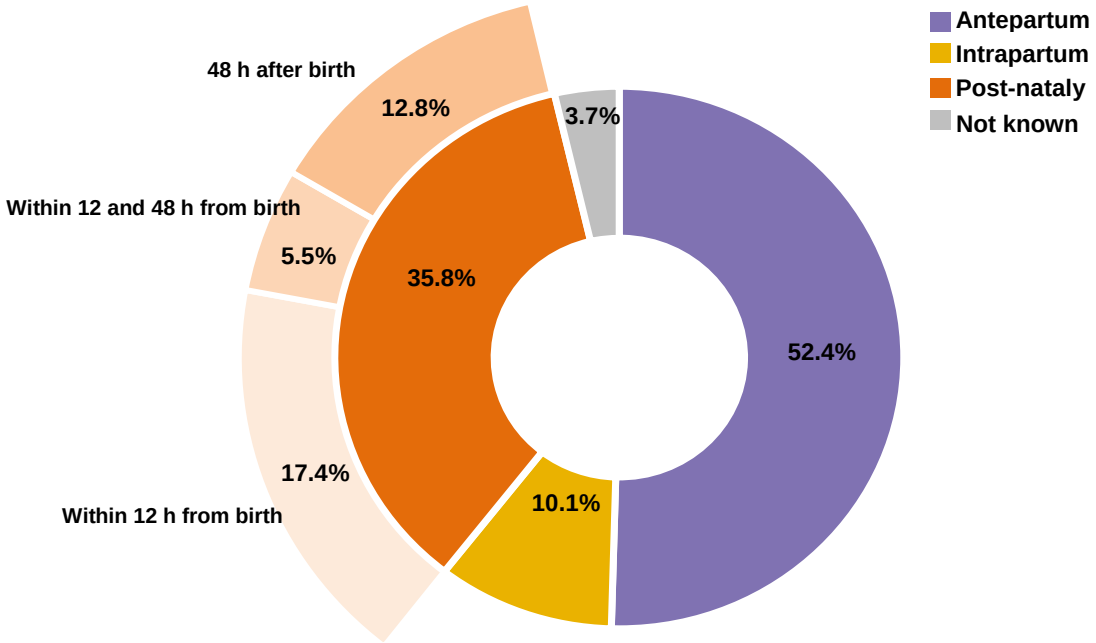
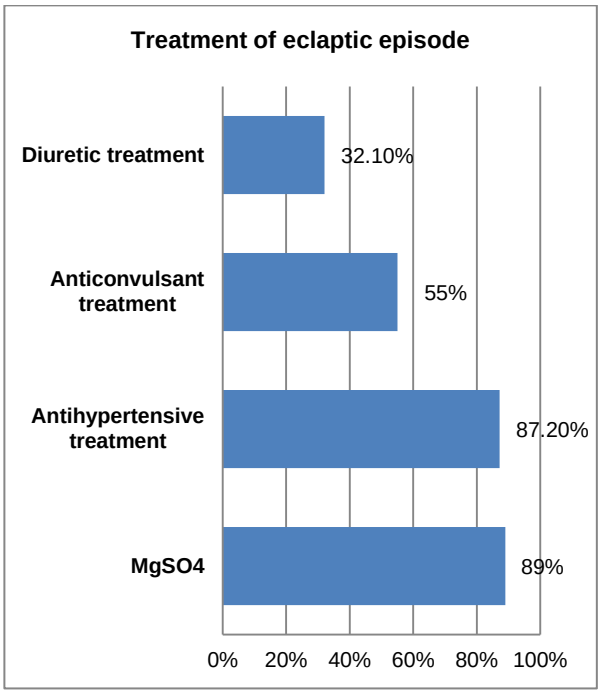


Figure 25. Timing of eclamptic episode.

There were 58.7% of women who experienced a single episode of seizure and 32.1% of women had recurrent fits (21.1%: two episodes; 7.3%: three episodes; 3.7% four or more episodes), for 9.2% of women we have no information about the number of eclamptic seizure.
No symptoms or signs were reported in 34.5% of women who experienced a single fit and in 47.8% who had a second or more episodes.
The majority of women (76.1%) had their fit in hospital, 17.4% had their first eclamptic episode at home, 3.7% was in a place such as the ambulance or the car park of the hospital and in 2.8% of women we have no information.

There were 16.5% of women who were given magnesium sulphate both before and after the eclamptic episode. A total of 97 (89%) women received magnesium sulphate after the fit, 11 (10.1%) did not receive magnesium sulphate at any stage.
A quite significant number of women (55%) had anticonvulsant medications, while there was a limited amount of diuretic drugs (32.10%) (Figure 26).



Mannitol	19.3%
Albumin	8.3%
Other	5.5%

Benzodiazepine (Midazolam)	48.6%
Phenytoina/Anticonvulsant drugs	8.3%
Opioids	5.5%
Barbiturates	2.8%

Beta-blockers (Labetalol)	55%
Calcium channel blockers (Nifedipine)	45%
Alpha-2 agonists (Methyldopa)	22.9%
Angiotensin-converting enzyme (ACE) inhibitors	4.6%
Other	11.9%

Figure 26. Treatment after the first eclamptic episode

4.3.7 Risk Factors

Risk factors for developing eclampsia were assessed, and all women who gave birth during the years of surveillance were considered as control population. The Hospital Discharge Database was used to calculate the total of women who gave birth in 2017 at the 9 participating Regions. The Hospital Discharge Database with the women giving birth in 2018, 2019 and 2020 were not

available at the time of analysis yet. For this reason an estimation of the number of births per year was performed, considering the number of maternities in 2017 and applying a reduction in birth rates equal to 3% for the following years (n= 716, 222).

Table 18 shows that non-Italian women (p= 0.0079, C.I. 95%) have a significant risk to develop eclampsia, for women using artificial reproductive techniques (ART) (p=0.000, C.I. 95%) and having multiple pregnancy (p=0.000, C.I. 95%) the risk was nearly five-fold higher.

	Eclampsia		Background population		Rate (‰)	Relative Risk (95%CI)			p-value
Cases	**N=109**		**N=716,222**		**0.15**				
	n	**%**	**n**	**%**					
Maternal age (1 missing)									
<40 years	94	87.0	655,343	91.5	0.14	*reference*			
≥40 years	14	13.0	60,879	8.5	0.23	1.60	(0.91	2.81)	0.096
Citizenship (5 missing)									
Italian	72	69.2	572,262	79.9	0.13	*reference*			
Not Italian	32	30.8	143,961	20.1	0.22	1.77	(1.16	2.68)	0.007
Educational level * (18 missing)									
High	17	18.7	164,731	23.0	0.10	*reference*			
Low	74	81.3	551,491	77.0	0.13	1.30	(0.77	2.20)	0.328
Parity									
Multiparous	40	36.7	323,016	45.1	0.12	*reference*			
Nulliparous	69	63.3	393,206	54.9	0.18	1.42	(0.96	2.09)	0.078
ART (6 missing)									
No	94	91.3	702,399	98.1	0.13	*reference*			
Yes	9	8.7	13,823	1.9	0.65	4.86	(2.45	9.63)	0.000
Multiple pregnancy									
No	101	92.7	704,942	98.4	0.14	*reference*			
Yes	8	7.3	11,280	1.6	0.71	4.95	(2.41	10.76)	0.000

Table 19. Characteristics of women with eclampsia compared with all woman who gave birth at the participating regions

4.3.8 Birth Outcomes

Most women (n = 88; 80.7%) gave birth by caesarean section, in 75% of cases the indication for surgery was not reported. General anaesthesia was common, particularly among women who experienced antenatal eclampsia (n = 39; 70.9%). Labour and birth outcomes are shown in table 19.

Mean interval between first antepartum eclamptic fit and birth was 122 minutes, while was 19 minutes when the first eclamptic episode occurred intrapartum.

Birth Outcomes			Overall (n=109)		Antepartum (n=55)		Intrapartum (10)		Post-partum (39)	
G.E. (mean)			36 weeks		34 weeks		39 weeks		37 weeks	
			n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Pre-term birth			50	45.9	38	76	1	2	11	22
IOL **(9 missing – 8.3%)**			20	20.0	4	7.3	6	60	10	25.6
Any Labour **(18 missing - 16.5%)**			29	31.9	N.A.		10	100	19	48.7
Analgesia/anaesthesia **(2 missing – 2.3%)**	**Epidural/Spinal**		39	36.4	15	27.3	3	30	21	87.5
	General		47	43.9	39	70.9	6	60	2	5.1
Mode of birth **(5 missing – 4.6%)**	**CS**	**Overall**	88	84.6	55	100	8	80	24	61.5
		Planned	5	4.8	0	0	0	0	5	12.8
		Emergency	83	79.8	55	100	9	90	19	48.7
	Vaginal birth	**Spontaneous**	15	14.4	N.A.		1	10	14	35.9
		Instrumental	1	0.9	N.A.		0	0	1	2.6

Table 20. Birth outcomes

A total of 39 (35.78%) women who experienced an eclamptic episode, had a pre-existing hypertensive disorders or blood pressure issues during the previous or the current pregnancy, of those 16 (41.03%) were multiparous.

4.3.9 Maternal outcomes

Other severe morbidities after the eclamptic episode were reported in 33% of the sample. Women admitted to Intensive Care Unit were 68 (62.4%) and 77 (70.6%) had a computed tomography (CT) or a magnetic resonance imaging (MRI). An HELLP Syndrome was reported in 13 (13.8%) women, 12 (11.0%) required ventilation. Other morbidities observed in individual women included respiratory distress (n= 4; 3.7%), pulmonary oedema, cerebrovascular accident (n= 3; 2.8%), disseminated intravascular coagulopathy (n= 3; 2.8%), sepsis (n= 3; 2.8), persistent vegetative state (n= 2; 1.8%), pulmonary embolism (n= 2; 1.8%), acute thrombotic event (n= 1; 0.9%) and renal failure (n= 1; 0.9%).

There was 1 maternal death, representing a lethality rate of 0.9%. The woman who died was obese, with a severe hypertensive disorder during pregnancy, who performed an in vitro fertilization, had the eclamptic episode at 34 weeks of gestation and did not receive an appropriate treatment.

4.3.10 Neonatal outcomes

The 109 women gave birth to 113 neonates. A number of neonates were born in poor condition with 13 (14.4%) neonates having a five-minute Apgar score less than seven. Neonates requiring admission to a Neonatal Intensive Care Unit (NICU) were 46 (41.4%) and 15 (14.3%) had other severe complications (Table 20). Of those with complications, 8 neonates had a neonatal respiratory distress syndrome, 1 had sepsis, 1 had a severe neonatal jaundice, 1 experienced episodes of seizures, 4 were Intrauterine Growth Restrictions (IUGR) of those 1 had also tachypnoea**.**

Neonatal Outcomes		**n**	**%**
Gender	**Female**	46	40.7
	Male	66	58.4
pH < 7mmol **(37 missing – 32.7%)**	**Yes**	7	9.2
5-min Apgar <7 **(23 missing – 20.4%)**	**Yes**	13	14.4
	Mean	8.3	
	Mean Antepartum	7.6	
	Mean Intrapartum	8.7	
	Mean Post-nataly	9.1	
Admitted to NICU **(2 missing – 1.8%)**	**Yes**	46	41.44
	Length mean (day)	15.3 days (s.d.= 9.2)	
		Min= 1 day	
		Max= 49 days	
Severe complications **(8 missing – 7.1%)**	**Yes**	15	14.3
Perinatal death	**Foetal death**	2	1.77
	Neonatal death	1	0.9
Birthweight (g)	**Mean**	2421.0 g	
		Min= 390 g	
		Max= 4170 g	
	Mean Antepartum	2122.0 g	
	Mean Intrapartum	2672.9 g	
	Mean Post-nataly	2763.2 g	

Table 21. Neonatal outcomes

The perinatal mortality rate was 2.7%, consisting of 2 stillbirths and 1 neonatal death. Neonates born to women who experienced antenatal eclampsia were more likely to be born preterm.

4.4 Results regarding sepsis

The following paragraphs will report findings regarding near miss cases due to maternal sepsis.
Data will be described reporting the expected number of cases of sepsis within the participating Regions and the incidence rate of sepsis found during the data collection period.
The analysis will proceed considering peripartum cases only. These consisted of near misses due to sepsis, including cases that occurred after 22 weeks of gestation, both antepartum and post-partum. The characteristics of women with peripartum sepsis, their medical and obstetric history, management of sepsis, including microorganisms implicated and sources of infection will be outlined, together with maternal and neonatal outcomes.
The case-control design will be conducted only on cases occurred after birth (post-partum sepsis) and the identified risk factors associated with the complications will be presented.

As already mentioned, the lack of a standardised definition for maternal sepsis, lead ItOSS to develop a definition of sepsis, based on previous literature, to be adopted during the study, in order to report cases. This is the first research that considered the principles written during *The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)*, which consist of considering the organ failure criteria to define a condition of sepsis, surpassing the SIRS criteria which have been considered unhelpful. Especially in the obstetric population, the clinical parameters of SIRS are often altered.
Cases of peripartum sepsis should met the following definition:

- Life-threatening condition defined as *organ dysfunction* resulting from *infection* from 22 weeks of gestation up to 42 days after birth (peripartum cases). Women with signs and symptoms of sepsis prior to birth, were classified as an antepartum cases, while mothers with signs and symptoms of sepsis after birth were reported as post-partum episodes.
  Diagnosis of *infection* should be based at least on one of the following signs/symptoms:
    - Fever
    - Headache and/or nuchal rigidity
    - Respiratory symptoms (frequency ≥ 20/min; SpO2<95%)
    - Urinary symptoms
    - Abdominal pain/pelvic pain
    - Diarrhoea or vomiting
    - Rush
    - Offensive vaginal discharge
    - Foetal or neonatal signs of infection

  Diagnosis of *organ failure* should be based on one or more of the following vital signs or laboratory exams:
    - Cardiovascular: SBP<90mmHg or MAP<65mmHg

- Respiratory: oxygen to maintain SpO2>95%
- Renal: creatinine>1.2 mg/dl
- Hepatic: bilirubin>1.2 mg/dl
- Central Nervous System: altered state of consciousness
- Haematological: platelets<100.000mm3 or ↓ 50% of normal levels

The case-control design, planned for post-partum near miss episodes, involved the recruitment of 1 case matched with two non-septic controls.

Controls should be represented by:

- two women who delivered immediately before the case gave birth and throughout the same way as the case did (vaginally or by CS);
- in case of maternal transfer or readmission after discharge, controls were chosen from the hospital where the women who developed sepsis, gave birth.

4.4.1 Expected incidence rate

The assessment of the expected incidence rate of maternal sepsis was performed using the ICD-9CM diagnosis and procedure codes, that identify this obstetric complication under the code 670.0 named “Major puerperal infections” or 659.3 as alternative code, denominated “Systemic infections during labour or childbirth”. Hospital Discharge Databases have been extensively used for both surveillance and research purposes.

The national Hospital Discharge Database has been used considering the years 2014-2015 to assess the code related to sepsis and the expected incidence rate of this complication.

Region	N	‰ 2014-2015
Piemonte	18	0.28
Lombardia	105	0.62
Friuli Venezia Giulia (FVG)	18	1.04
Emilia Romagna	81	1.14
Toscana	16	0.28
Lazio	49	0.52
Campania	10	0.10
Puglia	10	0.16
Sicilia	10	0.11
Participating Regions	**317**	**0.43**
Italian Regions	408	0.42

Table 22. Expected incidence rate of sepsis

From data (Table 21), it could be observed that the incidence rate found across the 9 participating Regions provides a reasonable approximation of the national one. However, expected incidence rates appear quite low, meaning that the ICD codes used to report maternal sepsis, should not be considered appropriate.

4.4.2 Observed incidence rate

During the data collection period, from the 1st November 2017 until the 31th October 2019, 394 cases of maternal sepsis were reported. Figure 22 shows the case reporting and completeness of data collection. Among all cases notified, 12 did not report the gestational age in which the sepsis was diagnosed, therefore they were excluded from the sample. Near miss were divided based on gestational age, cases that occurred at or before 19^{+6} weeks and cases happened from 22 completed weeks of gestation.

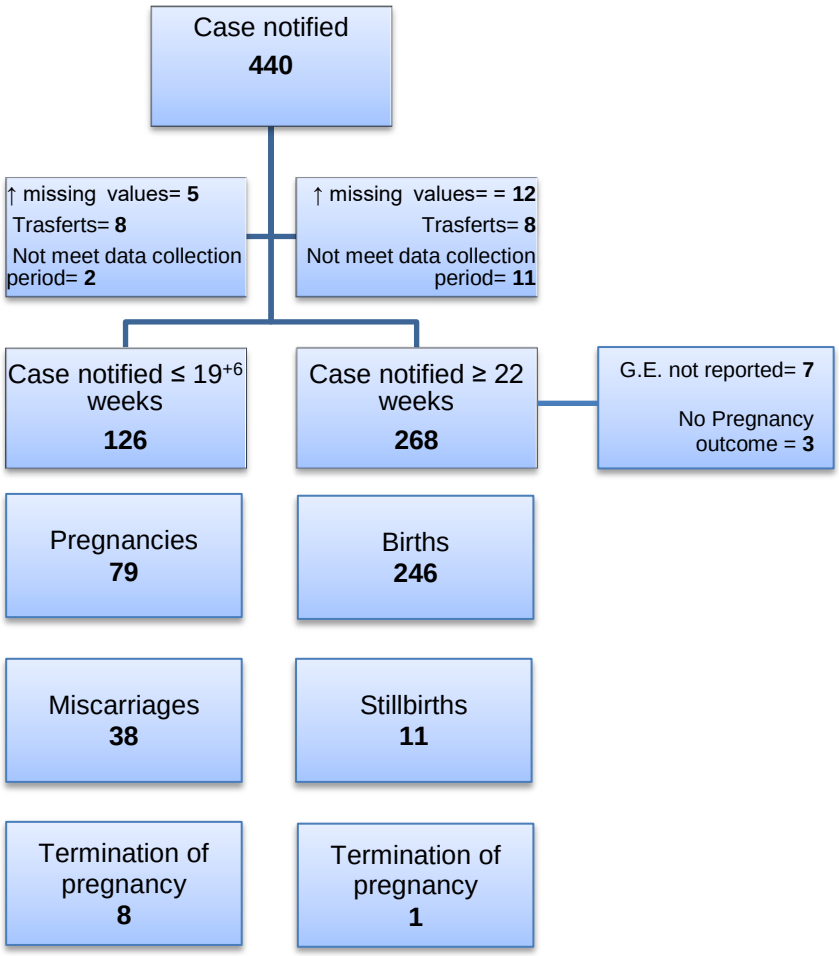


Figure 22. Case reporting and completeness of data collection

After checking to confirm that each reported case met the case definition, 394 near misses of sepsis were identified, representing an estimated incidence rate of 0.62 cases per 1,000 births (Figure 23).

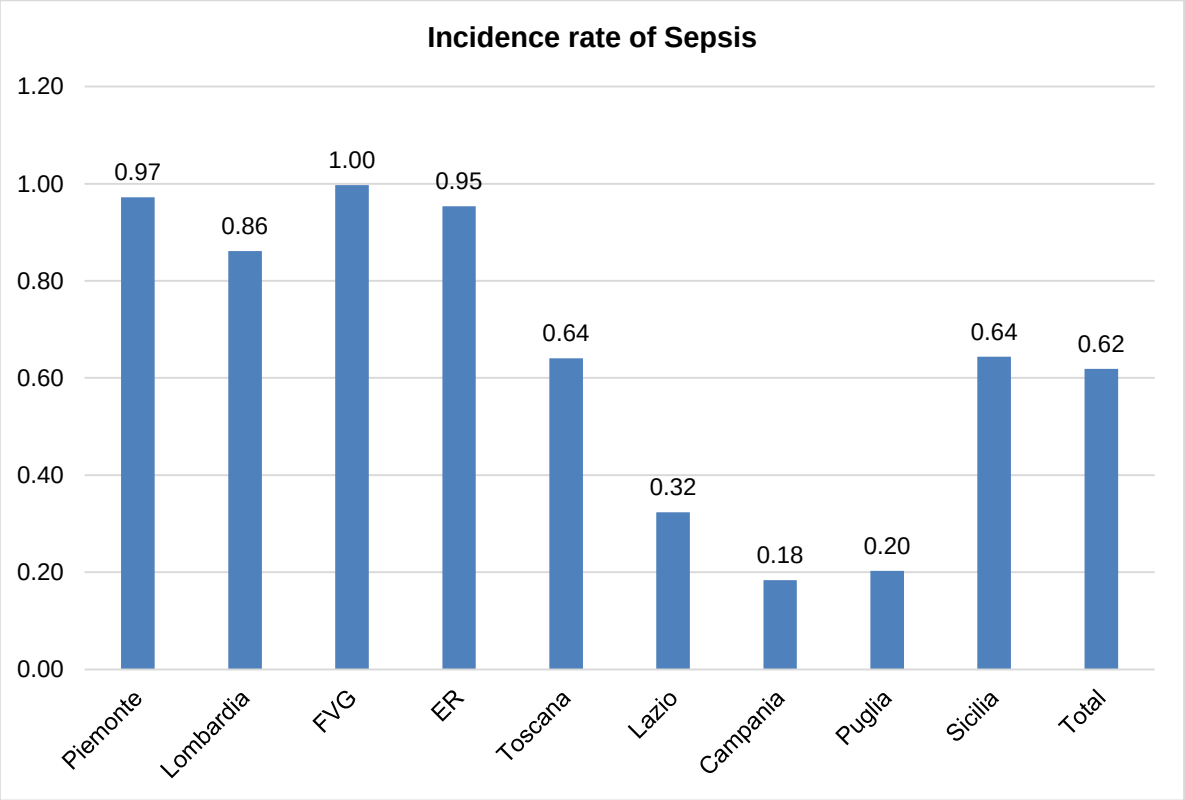


Figure 23. Incident rate of sepsis across the 9 participating Regions

The estimated incidence rate observed in 4 Regions involved into the surveillance, Lazio, Campania, Puglia and Sicilia, was evaluated as unreliable, because very few cases were reported. For this reason the incidence rate was re-calculated excluding the 4 Regions from the total rate of sepsis, giving an estimated incidence rate of 0.87 cases per 1,000 births (Figure 24). All cases reported by those 4 Regione were included in the analysis.

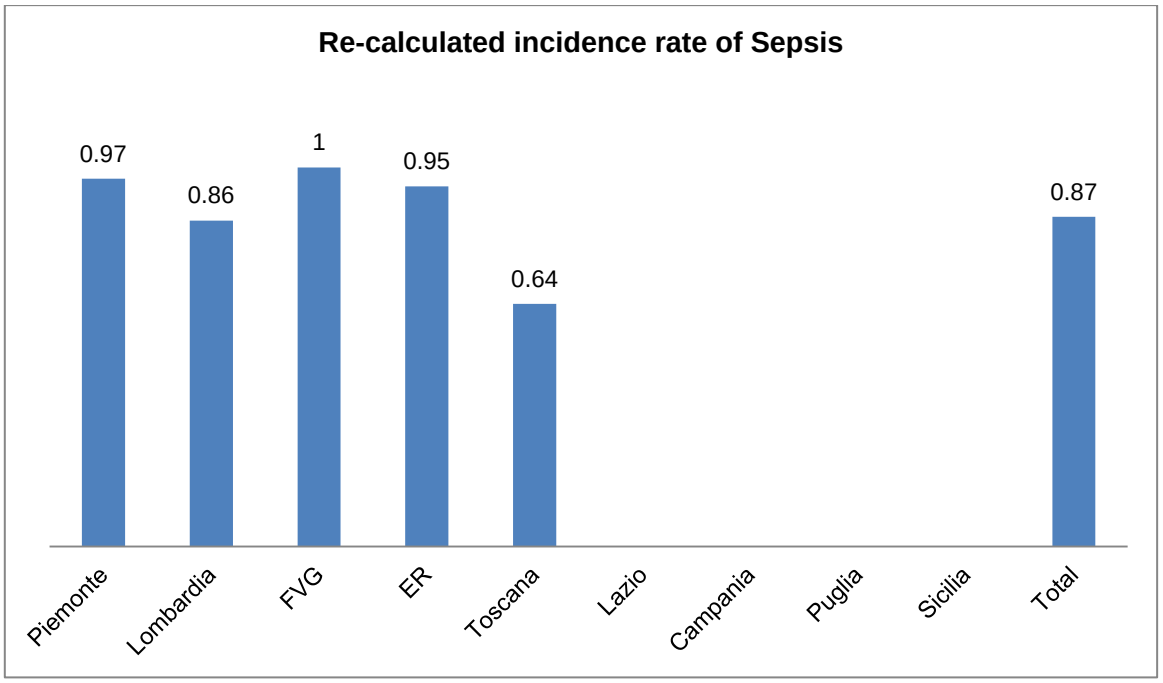


Figure 24. Re-calculated incidence rate of sepsis, excluding 4 Regions – Lazio, Campania, Puglia, Sicilia.

4.4.3 Results regarding peripartum sepsis

The following analysis will include cases of women who experienced a near miss due to peripartum sepsis, from 22 weeks of gestation. Reported events comprised both antepartum and post-partum cases up to 42 days after birth, as shown in figure 25.

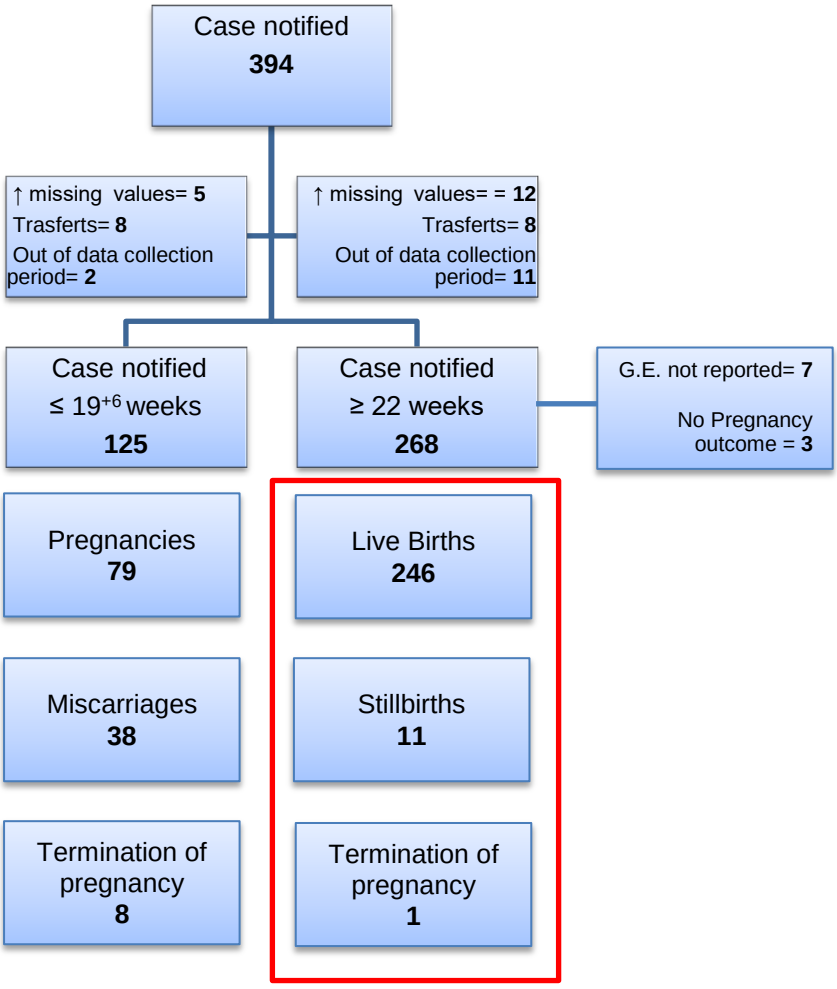


Figure 25. Cases of peripartum sepsis considered into the analysis

A total of 258 peripartum sepsis were reported, of those 64 were antepartum (24.8%) and 194 were post-partum episodes (75.2%). Among the 64 maternal sepsis occurred during the antepartum period, 52 (81.25%) had a live birth outcome, with a total of 246 births.

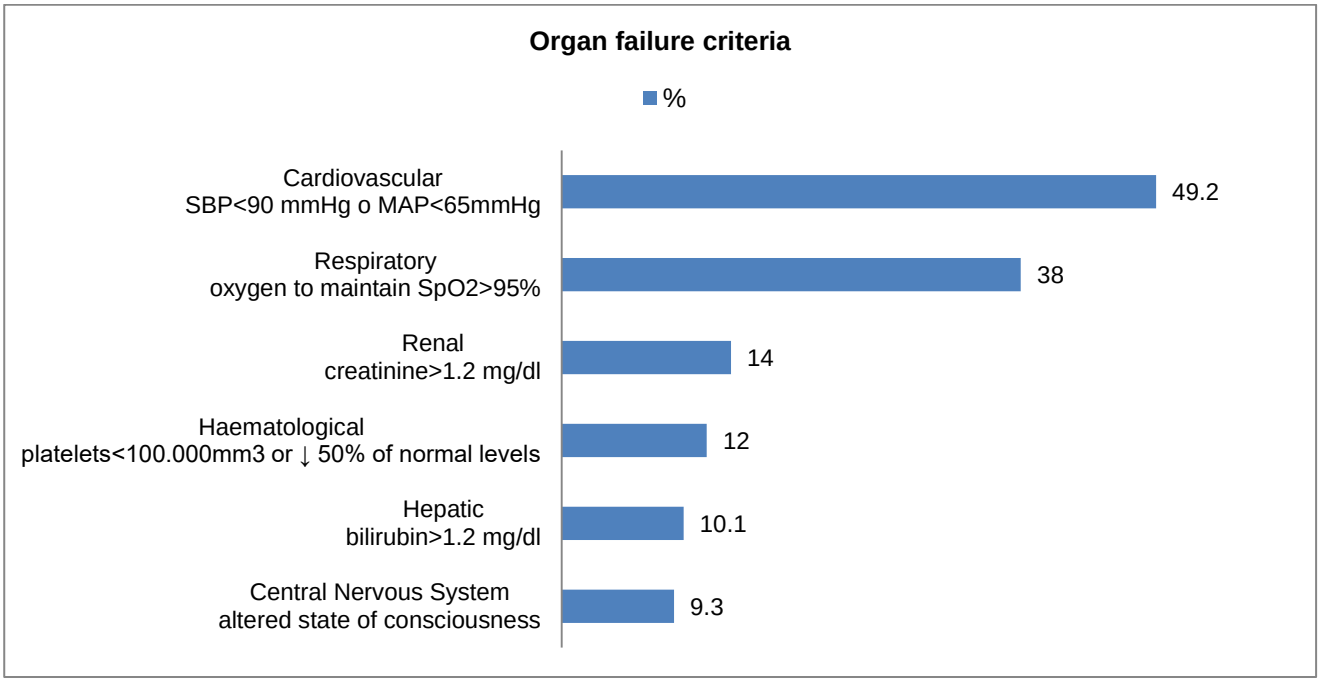


Figure 26. Organ failure diagnostic criteria collected among reported cases (N= 258)

Sepsis was diagnosed when both organ failure and suspected or confirmed infection occurred.

Figure 26 shows the organ failure criteria included into the definition of sepsis, a single woman could also have multi-organ failure. The majory of women had an organ failure related to the cardiovascular system (n= 127), followed by the failure of the respiratory system (n= 98), the remaining organ failure criteria were less represented.

The most frequent syptoms reported by women were abdominal pain (n= 89) and flu-like symptoms (n= 82) or signs such as productive cough or sore throat (n= 61) (Figure 27).

Vital parameters were also reported and the majority of women (70.2%) had temperature higher than 38°C and/or tachycardia (44.2%), followed by a high white blood cell count (WBC) (WBC> 17x109/L) (28.7%) and tachypnea (17.4%).

A total of 222 women (94.1% - 22 missing values) had a C-Reactive Protein (PCR) > 5 mg/dl.

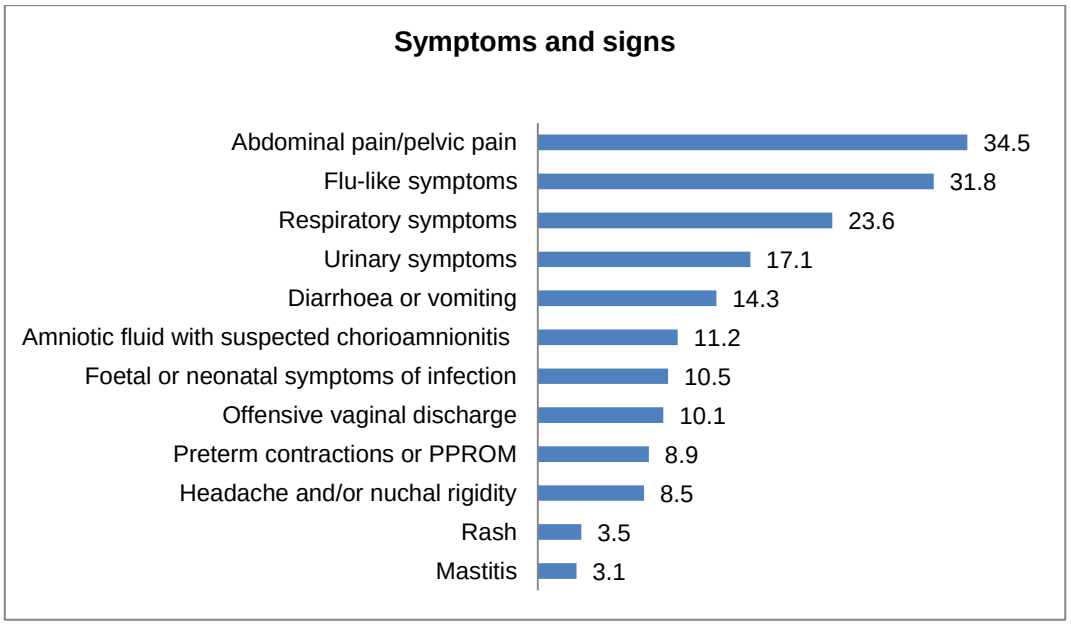


Figure 27. Infection criteria among reported cases

PPROM: pre-term premature rupture of membranes

4.4.3.1 Socio-demographic characteristics

Table 22 describes the socio-demographic characteristics of women with sepsis. The mean maternal age was 32 years old.

Socio-demographic characteristics (N= 258)		**n**	**%**
Age (years)	<20	9	3.5
	20-34	169	65.5
	>=35	80	31.0
	<40	231	89.5
	>=40	27	10.5
Nationality	Italian	170	65.9
	Foreign	87	33.7
	Not known	1	0.4
Citizenship	Italian	173	67.1
	Foreign	78	30.2
	Not known	7	2.7
Ethnic Group	Caucasian	203	78.7
	Negroid or Asian	47	18.2
	Missing	8	3.1
Education	Lower secondary school	81	31.4
	Upper secondary school	97	37.6
	Degree or more	56	21.7
	Not known	24	9.3
Employment	Employed	120	46.5

	Unemployed	29	11.2
	Housewife	94	36.4
	Other	4	1.6
	Not known	11	4.3
Single	No	231	89.5
	Yes	12	4.7
	Not known	15	5.8
Smoking status	Never	186	72.1
	Stopped in pregnancy	19	7.4
	Stopped before pregnancy	11	4.3
	Smoking	23	8.9
	Not known	19	7.4
BMI	<18.5	13	5.5
	18,5-24,9	144	60.5
	25-29,9	49	20.6
	≥30	32	13.4
	Missing	20	7.8

Table 23. Women's socio-demographic characteristics

BMI: body mass index

Figure 28 shows the nationality of the foreign women (n=87) who experienced a peripartum sepsis. When sepsis occurred in a non-Italian woman, an issue of language barrier was reported in 29.5% of cases.

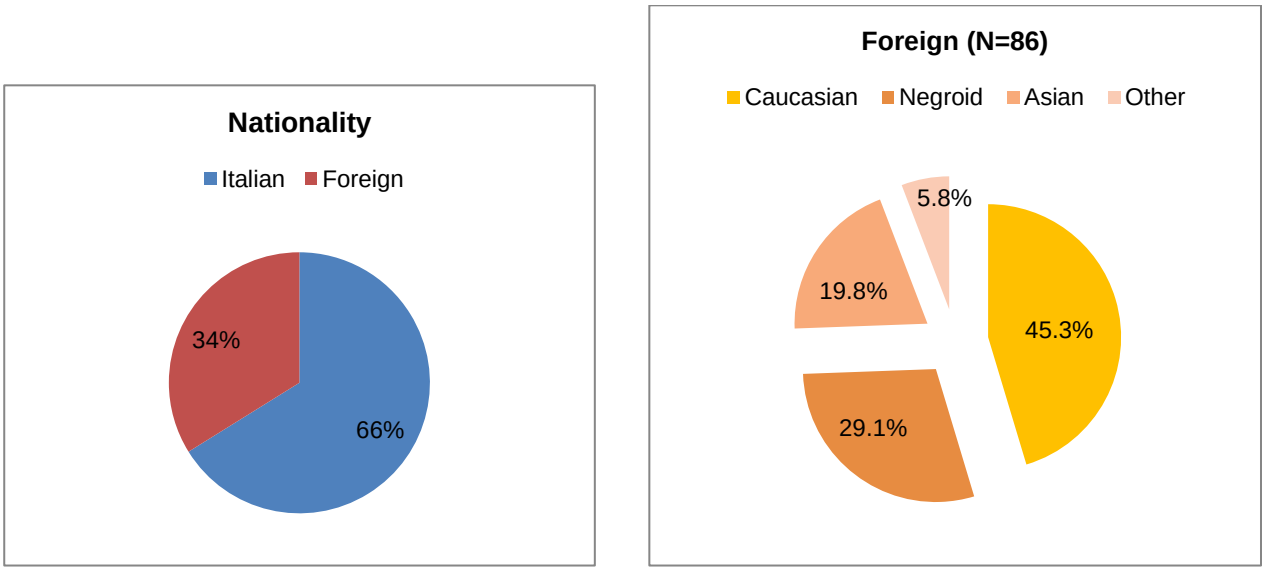


Figure 28. Nationality and ethnic group of women with sepsis, (n= 86, 1 missing)

4.4.3.2 Obstetric and medical history

Women's medical and obstetric history is shown in table 23 and 24, respectively.

A large portion of women (n=104; 40.3%) had pre-existing medical conditions consisting of 5 women with cardiac issues, 18 with diabetes, 23 with endocrine disorders, 2 with mental health problems, 17 with anemia, 8 with haematological diseases, 11 with inflammatory bowel diseases, 5 renal diseases, 5 autoimmune diseas such as Lupus, 3 with neoplastic disease and 48 with other issues such as recurrent urinary infections, varicose veins, obesity, mild Mitral valve prolapse or thrombocytopenia.

Moreover, a significant part of the sample (30.2%) had symptoms within 2 weeks before the diagnosis of sepsis and 35 (13.6%) were known to have recurrent infections (13.6%).

Medical history (N= 258)		**n**	**%**
Previous recurrent infections	No	199	77.1
	Yes	35	13.6
	Not known	24	9.3
Immunocompromised woman	No	241	93.4
	Yes	5	1.9
	Not known	12	4.7
Previous diabetes	No	225	87.2
	Yes	29	11.2
	Not known	4	1.6
STI	No	225	87.2
	Yes	16	6.2
	Not known	17	6.6
Previous medical diseases	No	147	57.0
	Yes	104	40.3
	Not known	7	2.7
Symptoms within 2 weeks before hospital admission	No	172	66.7
	Yes	78	30.2
	Not known	8	3.1

Table 24. Women's obstetric and medical history

STI: Sexually transmitted infections

There were 114 multiparous women (44.2%) and 31 (27.2%) of them had complications during their previous childbearing continuum, consisting of 5 with hypertensive disorders, 7 with gestational diabetes, 2 had an infant small for gestational age (SGA), 1 with placenta praevia, 1 had a placental abruption, 1 had a PPH with transfusion, 1 had surgery in pregnancy, 6 women experienced a neonatal death, 18 women had other issues such as I trimester miscarriage, stillbirth, hypothyroidism or infections.

A total of 36 women had a CS, of those more than half (66.7%) had a single CS.

Previous obstetric history (n=114)		N	%
Parity	Multiparous	114	44.2
Previous CS	No	78	68.4
	Yes	36	31.6
	1	24	66.7
	2+	12	33.3
Previous Obstetric complications	No	74	64.9
	Yes	31	27.2
	Not known	9	7.9

Table 25. Previous obstetric history

CS: caesarean section

4.4.3.3 Current pregnancy

The sample included 144 nulliparous women (55.8%), 13 multiple pregnancies (5.0%) and 21 (8.1%) pregnancies achieved throughout in vitro fertilization technique, of those 5 were gamete donations, 5 oocyte donations and 1 oocyte together with sperm donation, for 3 cases the ART technique was not reported (table 25). A total of 15 women underwent invasive procedures consisting of 1 cervical cerclage and 14 prenatal diagnostic tests, of those 10 (3.9) were amniocentesis and 4 were chorionic villus sampling (1.6%).

More than half of the sample had a high risk pregnancy (65.5%), due to different reasons:

- hyperemesis followed by hospital admission (1.6%)
- pathological anemia (12.8%)
- Gestational diabetes (17.4%)
- Severe infection (3.5%)
- Therapy with Immunosuppressant drugs (0.4%)
- Therapy with Corticosteroid drugs (2.3%)
- Surgery in pregnancy (1.2%)
- Placenta praevia (1.2%)
- Placenta abruption (1.2%)
- Premature rupture of membranes (13.2%)
- thromboembolic episode (0.4%)
- haemorrhage (1.6%)
- Small for gestational age infant (3.9%)
- Large for gestational age infant (1.6%)
- Stillbirth (1.6%)
- Pre-eclampsia/Eclampsia (3.1%)

- Risk of pre-term birth (7.4%)
- Antenatal corticosteroids therapy for fetal lung maturation (10.5%)
- Vaginorectal swab or urine culture test positive for group B Streptococcus (6.6%)
- Other not reported (27.9%)

History of current preganncy		N	%
Parity	Nulliparous	144	55.8
	Multiparous	114	44.2
Mutiple pregnancy	No	245	95.0
	Yes	13	5.0
ART	No	235	91.1
	Yes	21	8.1
	Not known	2	0.8
Invasive procedure	No	242	93.8
	Yes	15	5.8
ATB within the prior 2 weeks	No	176	68.2
	Yes	69	26.7
	Not known	13	5.0
Complications in pregnancy	No	88	34.1
	Yes	169	65.5
	Not known	1	0.4

Table 26. Current pregnancy history

ART: assisted reproductive technology

4.4.3.4 Birth outcomes

The mean gestational age at antenatal sepsis diagnosis was 34 weeks (interquartile range [IQR] 22–41 weeks). Among the 64 antepartum sepsis, 37 women (57.8%) gave birth pre-term, of those 19 (29.7%) occurred before 32 weeks.

The mean gestational age at birth in cases of postpartum sepsis diagnosis was 38 weeks (interquartile range [IQR] 23–41 weeks). Among the 194 postpartum sepsis, 42 women (21.6%) had a pre-term birth, of those 23 women (11.9%) delivered prior to 32 week. A total of 79 women (30.6%) gave birth before 37 weeks.

Figure 29 shows the distribution of gestational age at the time of diagnosis.

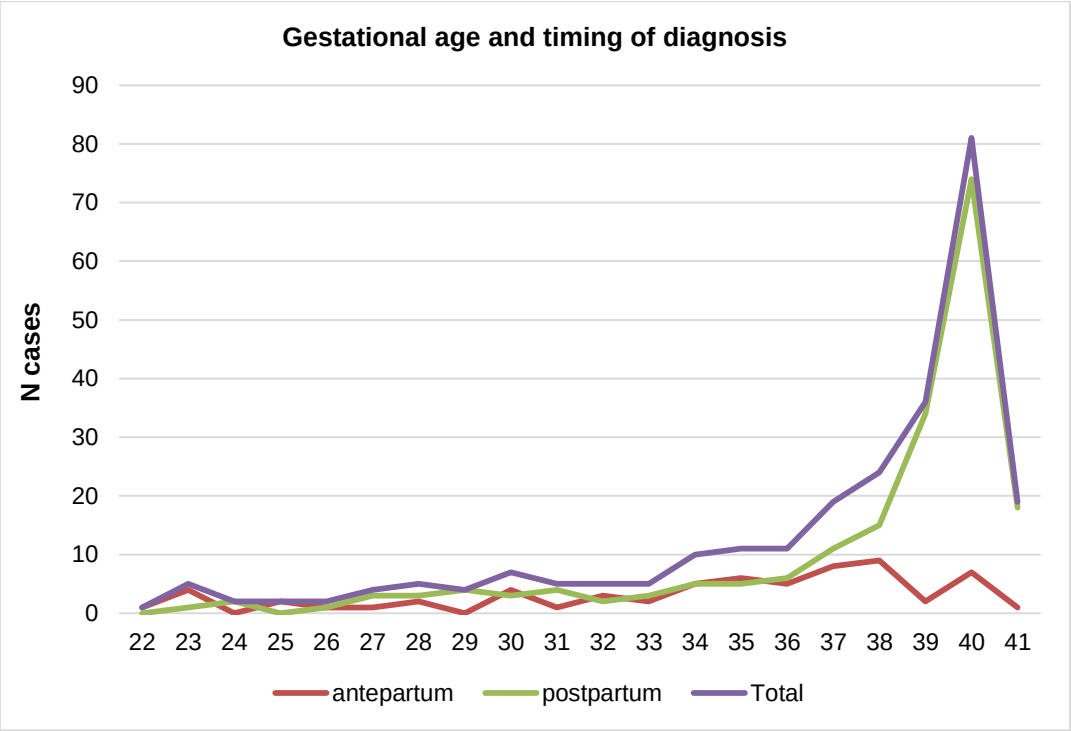


Figure 29. Distribution of gestational age at the time of diagnosis.

An induction of labour was carried out in 72 (27.9% - 14 missing= 5.43%), of those 50 (69.4%) had their labour induced with intravaginal prostaglandin E2, 1 woman (1.4%) had sublingual prostaglandins, 22 (30.6%) were given intravenous oxytocin, 12 (16.7%) underwent an artificial rupture of membranes and 8 (11.1%) had an induction of labour using mechanical methods. There were 125 labouring women (49.6%), among women who had an induction, 47 (66.2%) went into labour and 78 had a spontaneous onset.

A total of 127 women (49.2%) used an epidural analgesia, of those 60 (47.2%) were in labour. meconium-stained liquor was reported for 33 women (12.8% - 21 missing= 8.1%)

Birth outcomes are shown in Figure 30.

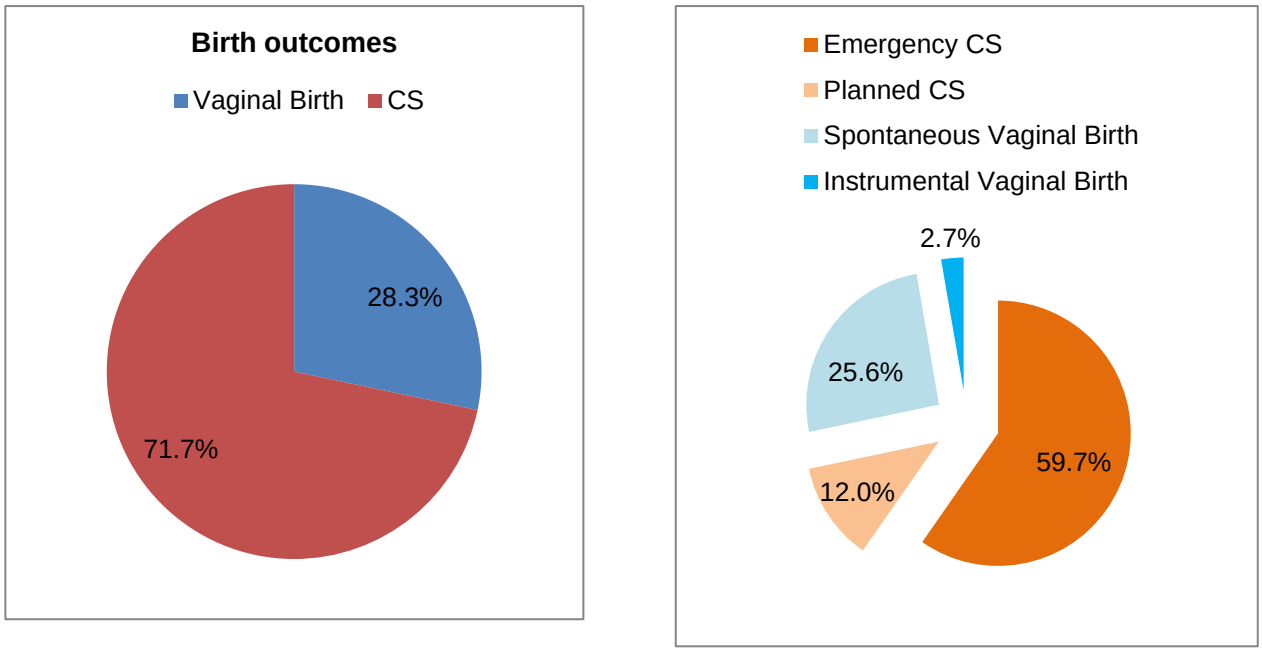


Figure 30. Birth outcomes in women who developed peripartum sepsis
CS: caesarean section

When a surgical birth was required, 150 women (81.1%) had a regional anesthesia, 33 (17.8%) were given a general one (2 missing values).

Third stage of labour outcomes in relation to mode of birth, are shown in Figure 31.
Placental delivery was spontaneous in 89 women (34.5%), of those 4 had an incomplete third stage, 153 (59.3%) underwent a manual removal and 5 had an instrumental revision of the uterine cavity.

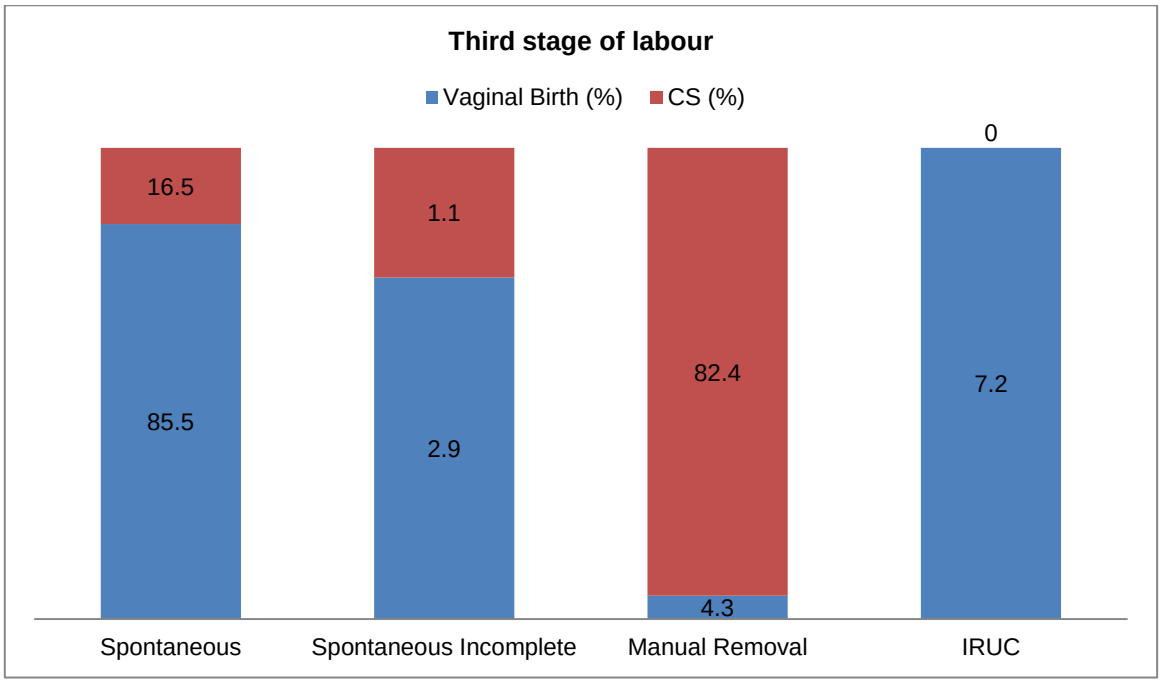


Figure 31. Third stage outcome in relation to mode of birth (7 missing values)
IRUC: Instrumental revision of the uterine cavity

A prophylaxis with antibiotics before birth was given in both vaginal and surgical deliveries as shown in Figure 32. Of note, of all women who had a CS, 98.4% of cases received prophylactic antibiotics at birth.

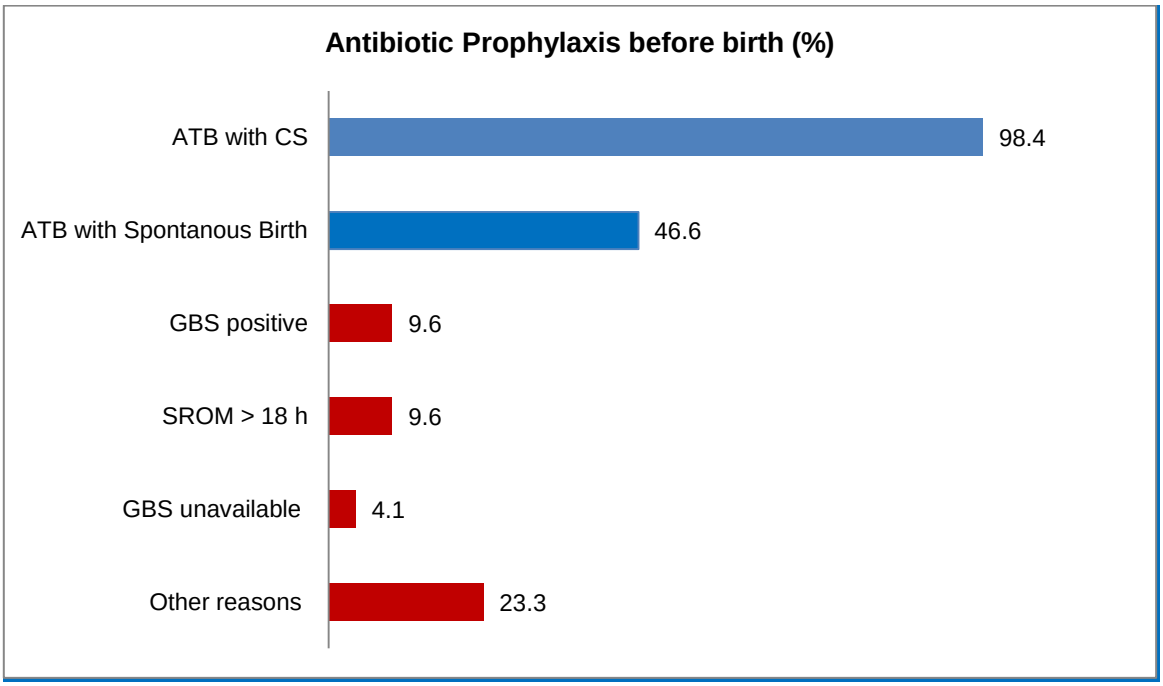


Figure 32. Antibiotic prophylaxis before birth

ATB: antibiotic; CS: caesarean section; GBS: Group B Streptococcus; SROM: spontaneous rupture of membranes

4.4.3.5 Source of infection and microorganism

The source of infection was identified in 209 women (81.3%) with peripartum sepsis, in 48 women (18.7%) none of the sources was found. Genital tract infection and respiratory infection were the most common sources of sepsis (30% and 18.3%, respectively). Identified sources of infection are shown in Figure 33. Among women with a genital tract infection, the majority (n=43; 16.7%) had chorioamnionitis, followed by endometritis (n= 32; 12.5%).

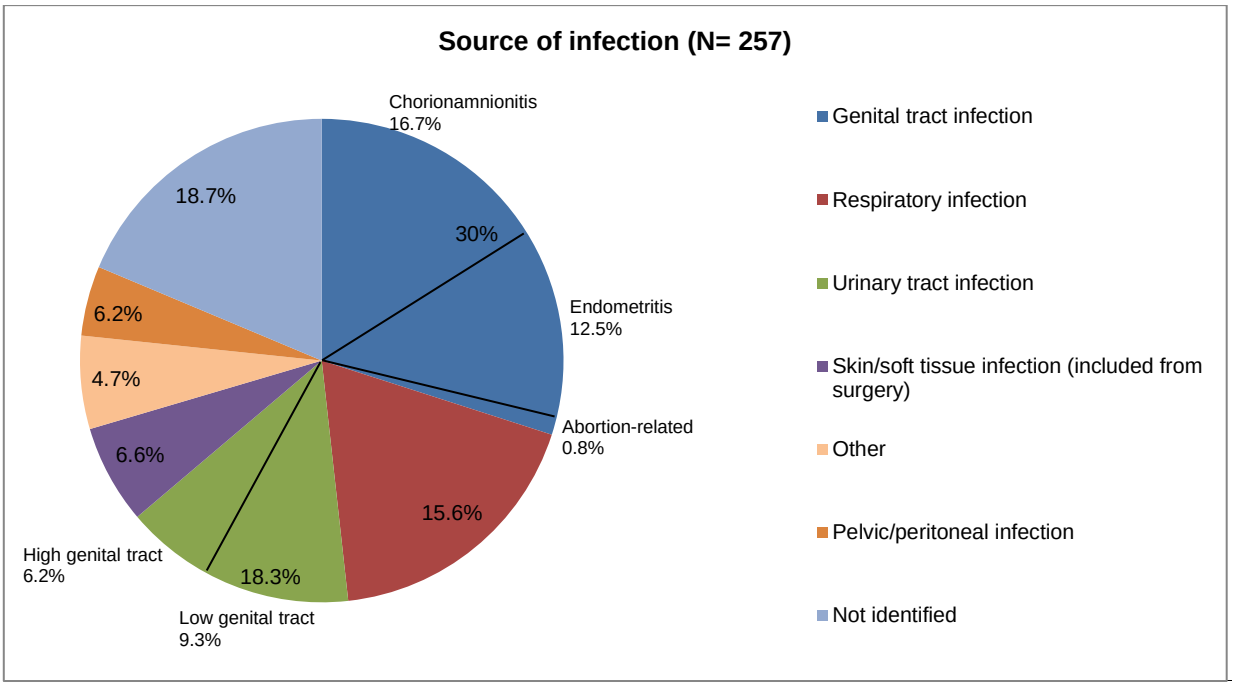


Figure 33. Source of infection (1 missing)

Sources of infection, were tabulated for all cases and stratified according to timing of diagnosis and mode of birth, as pathogenesis is known to differ between pregnant and postpartum women (Figure 34). Genital tract infection were common in both antepartum and post-partum cases, however were more likely to develop after birth. Skin and soft tissues infections, related to perineal tears or surgical incision due to CS, were reported only during the postpartum period. Pelvic and peritoneal infections were more frequent during the post-partum period. While the majority of respiratory and urinary infections occurred in pregnancy.

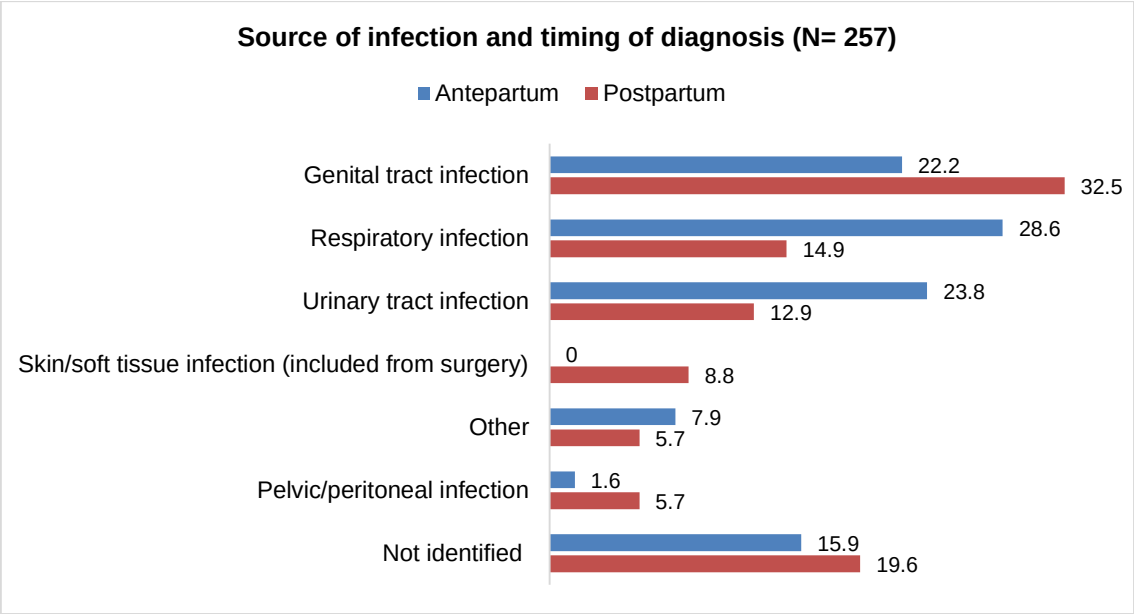


Figure 34. Source of infection according to timing of diagnosis (1 missing)

Sources of infection and causative organisms, were tabulated for all cases and stratified according to mode of birth.

Skin and soft tissue infections, peritoneal and respiratory tract infections were most frequent in CS births, while genital tract and urinary tract infections were more present when a vaginal birth occurred (Figure 35), especially if it was instrumental, confirming the infections' distribution in relation to the timing of diagnosis.

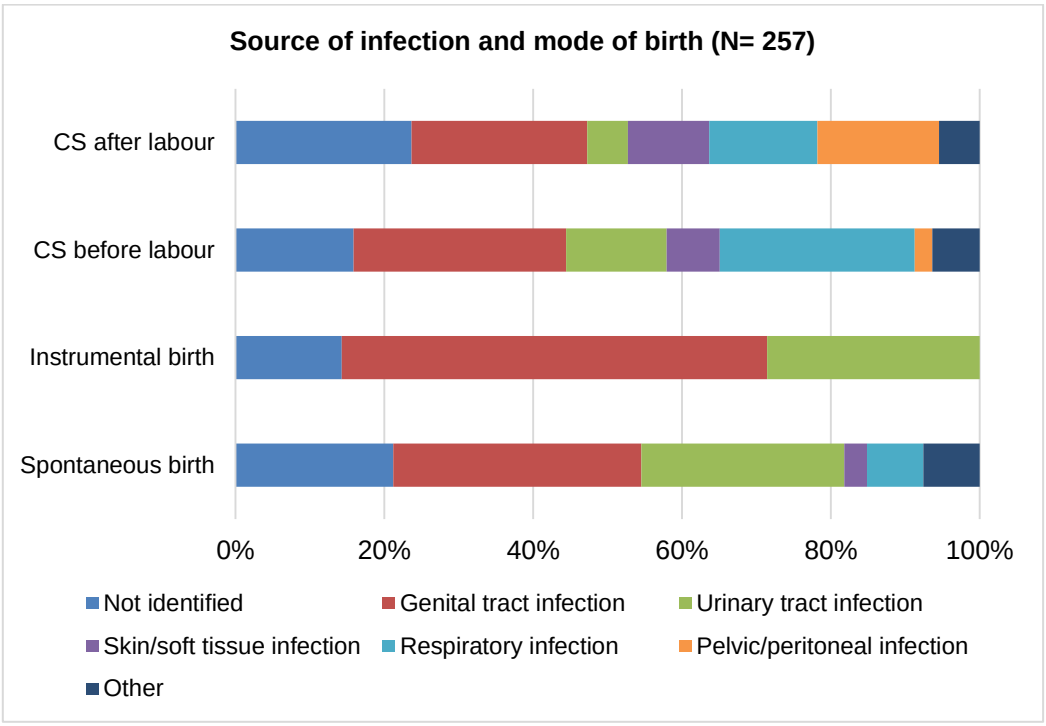


Figure 35. Distribution of source of infection according to mode of birth

CS: caesarean section

Laboratory-confirmed infection was reported for 171 (66.3%) sepsis cases (Figure 36).

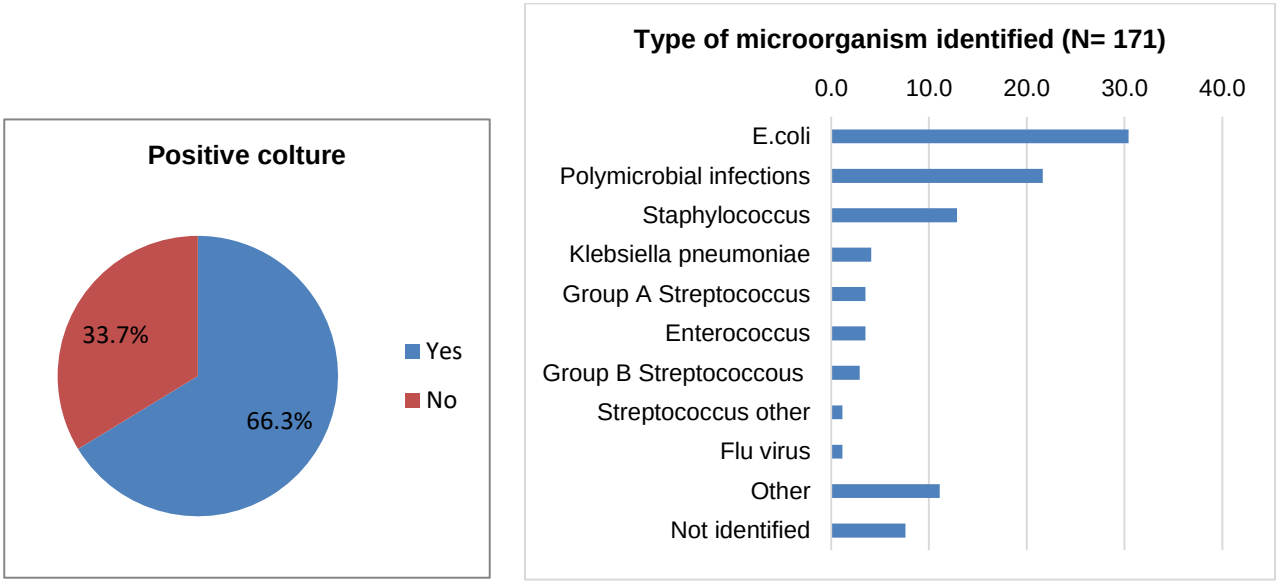


Figure 36. Type of microorganism identified

Overall, the largest proportion of cases was due to genital tract infection (30.0%), and the most common organism causing infection was Escherichia coli (n=52; 30.4%), followed by polymicrobial infections due to a combinations of microorganisms (n= 37; 21.6%). The option “other” included different type of microorganisms, all very low in frequency, such as fungal infections. The type of microorganism was not identified in 13 women (7.6%).

The distribution of microorganism according to source of infection is shown in Figure 37. Escherichia Coli was more likely to be found when a urinary infection occurred, followed by the genital tract infections. Infections caused by Streptococci were more frequent when the source of infection was the genital tract, followed by the respiratory tract infections. Staphylococci were balanced across all sources of infections, however more common when the infection was related to the skin. Polymicrobial microorganisms were largely present with genital tract infections, followed by the respiratory tract infections. The option “other”, including microorganisms such as fungal or enterococci, is more likely to be associated to genital tract infections.

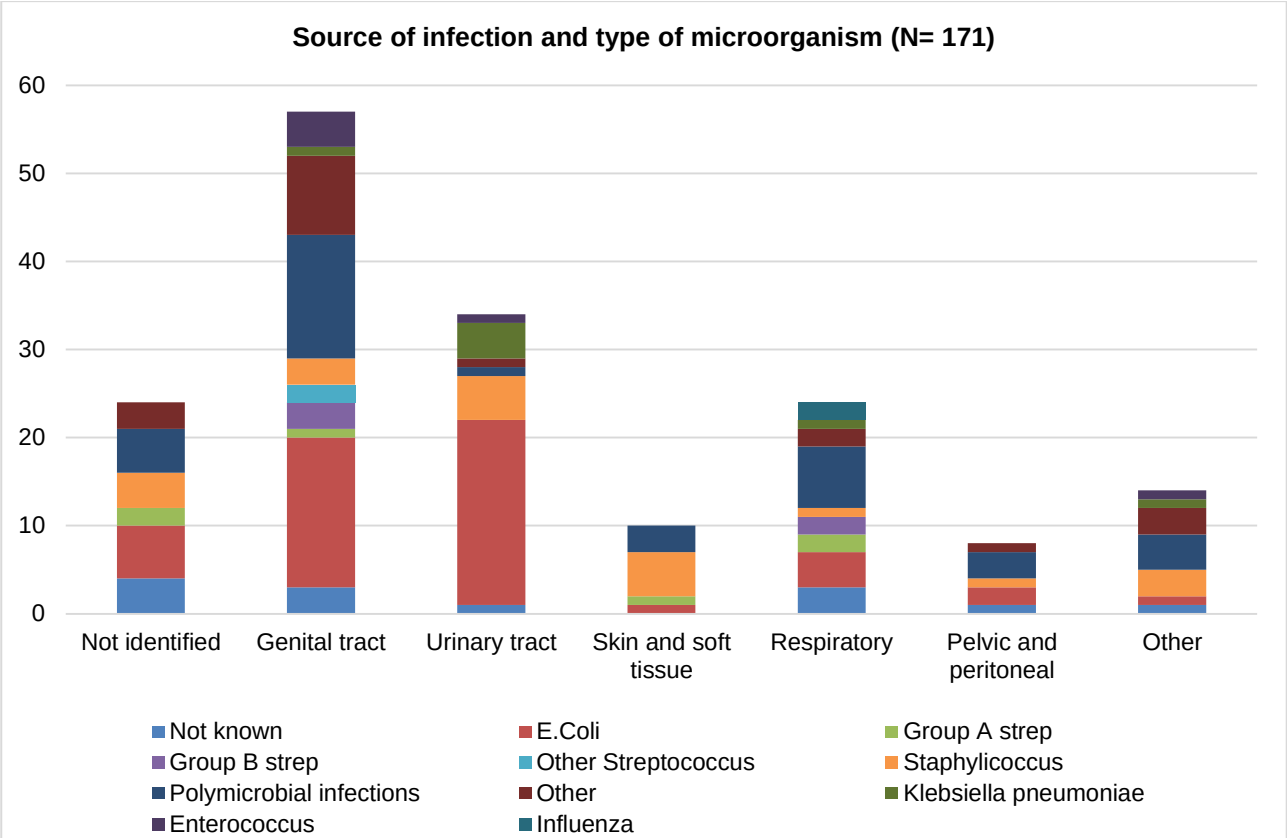


Figure 37. Distribution of source of infection according to type of microorganism

Among the infections reported, 29% occurred in women who gave birth spontaneously, 3% were reported after instrumental birth, 49.1% in women who underwent a CS before labour and 18.9% happened in women who had a CS after going into labour. Figure 38 shows the distribution of microorganism identified in relation to mode of birth.

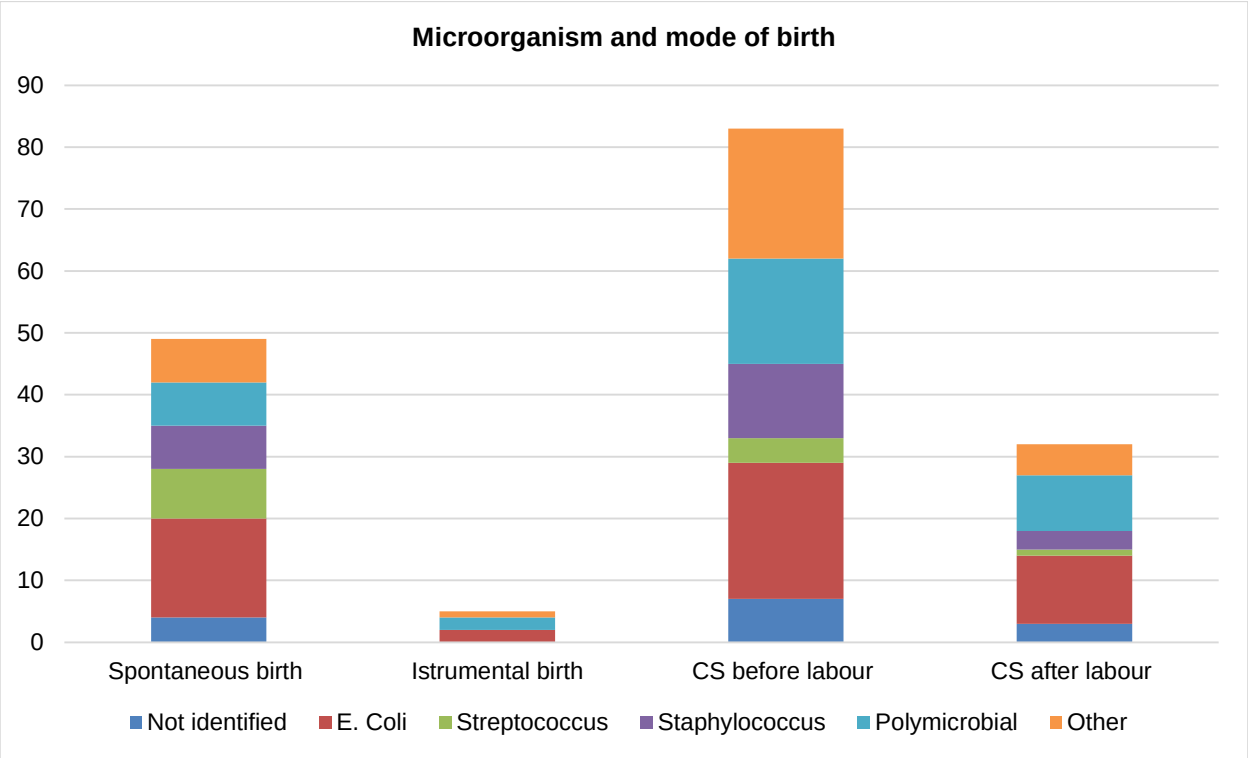


Figure 38. Distribution of causative organisms according to mode of birth

4.4.3.6 Diagnosis and treatment

Imaging for diagnosis was adopted in 86.6% of cases, blood lactate concentration was measured in 60.5% of women.

Among women with sepsis, 99.6% had antibiotic therapy, 73.2% were given a fluid challenge following hypotension, of those 92.3% started fluids 30ml/Kg and in 19.2% vasopressor drugs were required.

Antibiotics within the 'golden hour' of presumed diagnosis, were administered only in 21.3% of women (Figure 39). Timing of antibiotic administration was available for 164 women (63.6%).

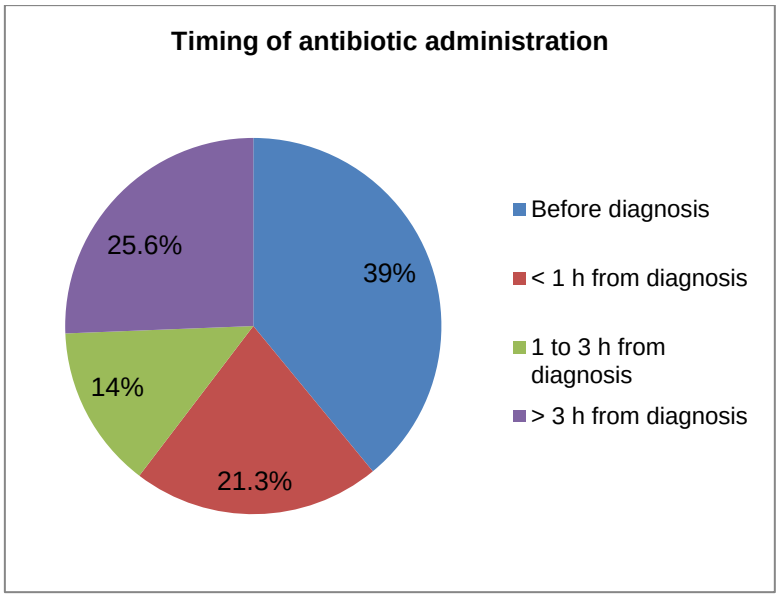


Figure 39. Timing of antibiotic administration (94 missing values)

Women were given a single antimicrobial and up to 4 or more different antibiotics as shown in figure 40. These were combined in several ways and, among the all sample, 90 different therapeutic schemes were found.

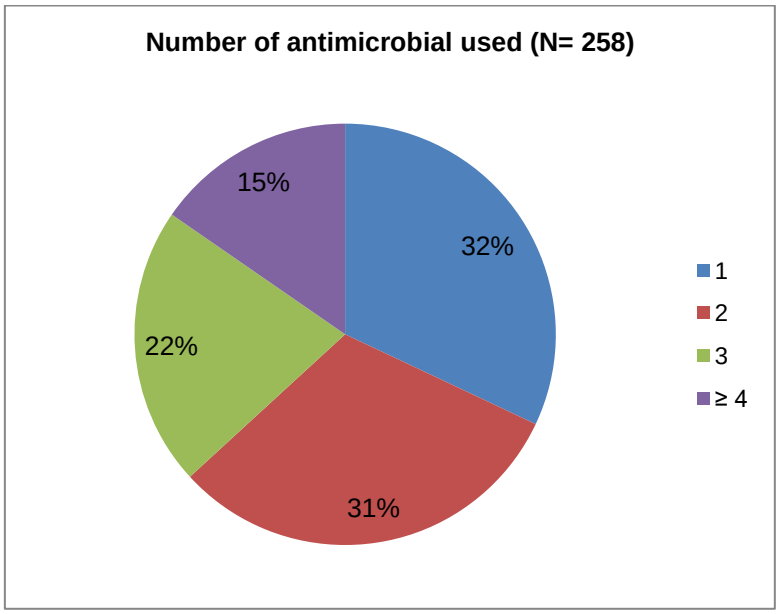


Figure 40. Number of antimicrobial adopted for a single woman

Antibiotic used, based on the total antibiotics that were administered, are shown in Figure 40. Penicillin, which is part of the initial empirical anti-infective therapy with a broad spectrum, covering both Gram-negative and Gram-positive rod bacterium while waiting for microorganism

identification, was the one most frequently administered. Penicillin was given to 160 (62.3%) women and it represented 28.0% of all antibiotics given. Beta-lactam antibiotics, could be used in association with penicillin and were the second treatment in order of frequency, administered to 79 women (30.6%), representing 13.8% of all antibiotics given. The third most common antibiotic adopted was an aminoglycoside to give Gram-negative cover, administered to 76 (29.5%) women and representing 13.3% of all antibiotics used.

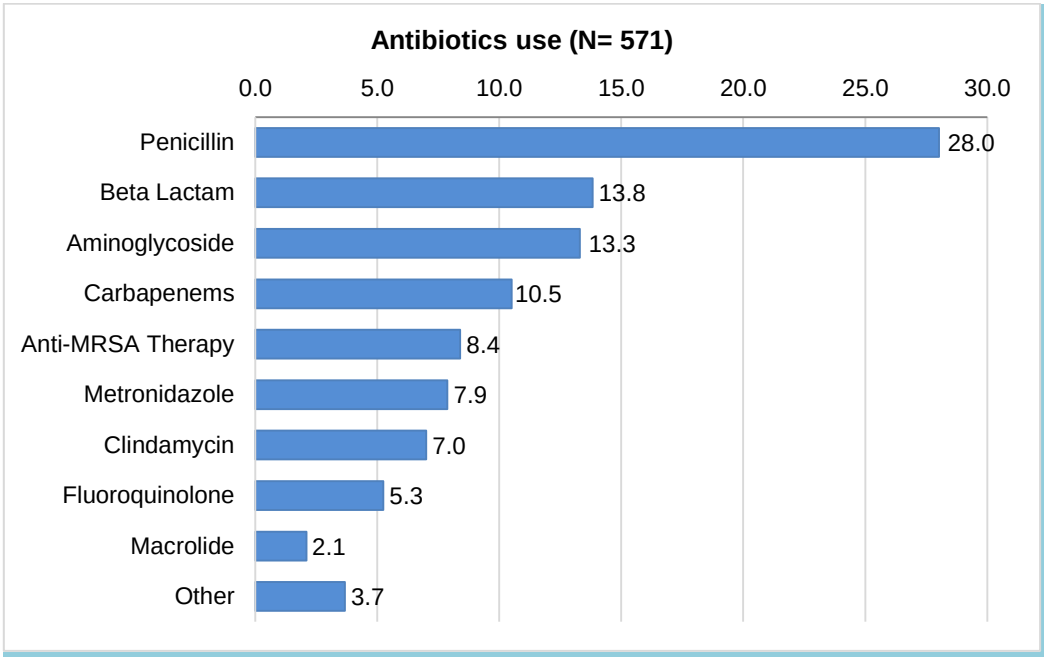
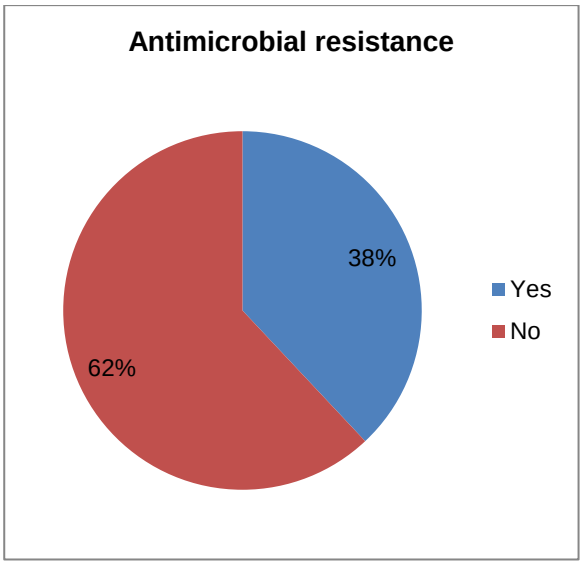


Figure 41. Antimicrobial adopeted according to the total antibiotics administered

Among the 171 (66.3%) laboratory-confirmed infections, antimicrobial resistance was reported on 65 cultures (38.0%) (Figure 42). No unusual pattern of resistance were reported, with penicillin being the antibiotic that developed more than half of the resistance identified, followed by beta-lactam (n=9), 14.1% of all the resistance confirmed.



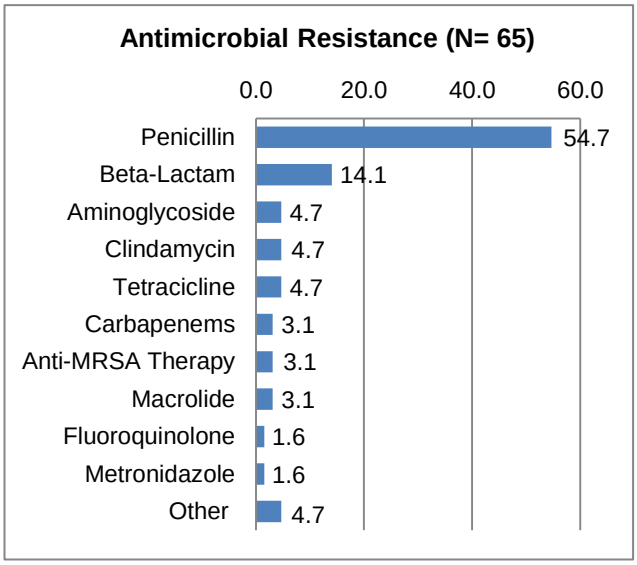


Figure 42. Antimicrobial resistance according to antibiotics classes.

4.4.3.7 Maternal outcomes

Other severe morbidities following the sepsis episode were reported in 62 women (24% - 3 missing values). Intensive Care Unit admissions were 71 (27.5% - 2 missing values). There were 16 women (6.2%) who required ventilation and 15 (5.8%) had a respiratory distress. Renal failure was reported in 10 women (3.9%), an acute thrombotic event was reported in 8 women (3.1%,) an HELLP Syndrome in 7 women (2.7%). Other morbidities observed in individual women included disseminated intravascular coagulopathy (n= 5; 1.9%) and pulmonary oedema (n=1; 0.4%). Other severe complications were specified for 28 women (10.9%), such as pleural and pericardial effusion, blood transfusion, influenza H1N1, septic emboli to the brain, kidneys, spleen, phlebitis, hypertension and hemicolectomy.

There was 1 maternal death, representing a lethality rate of 0.4%.

4.4.3.8 Neonatal outcomes

Women gave birth to 270 neonates, we have no information about 5 of them, all newborn outcomes were evaluated considering 5 missing values, then the statistical analysis was performed on 265 neonates. A number of neonates were born in poor condition with 16 (7.7%) neonates having a five-minute Apgar score less than seven. Neonates requiring admission to NICU were 80 (32.4%) and 29 (12.9%) had other severe complications (Table 26). Among neonates with complications the following issues were reported: 18 neonatal respiratory distress syndromes, 9 severe infections, 5 severe neonatal jaundice, 1 bronchopulmonary dysplasia, 1 necrotizing enterocolitis (NEC), 1 hyperglycemia, 1 Intraventricular haemorrhage, 1 encephalopathy, 1

exanguino-transfusion, 1 E. Coli and 1 Listeria positive cultures, 1 Fetal Inflammatory Response Syndrome, 2 newborns with fever, 1 newborn was transferred to a different hospital.

Neonatal Outcomes		**n**	**%**
Gender (5 missing – 1.9%)	**Female**	123	46.4
	Male	142	53.6
pH < 7mmol (34 missing – 13.2%)	**Yes**	7	3.2
5-min Apgar <7 (45 missing – 17.5%)	**Yes**	16	7.7
Admitted to NICU (5 missing – 1.9%)	**Yes**	80	32.4
	Length mean (day)	17 days (s.d.= 17.1) Min= 1 day Max= 102 days	
Severe complications (18 missing – 7.0%)	**Yes**	29	12.9
Perinatal death	**Foetal death**	13	5.1
	Neonatal death	7	2.7
Birthweight (g)	**Mean**	2938.0 g Min= 634 g Max= 4730 g	

Table 27. Neonatal outcomes

There was a significant rate of perinatal deaths, with 13 stillbirths and 7 neonatal deaths, representing a perinatal mortality rate of 7.4%

4.4.3.9 Risk factors of post-partum sepsis

The case-control design was conducted only on post-partum sepsis. The conditional logistic regression model, accounting for matching factors, considers observations without missing values. For this reason the model included cases that presented at least 1 matched control, including 183 women who experienced postpartum sepsis and 363 matched controls (Table 28).

The probability to develop sepsis was higher in nulliparous, (OR = 1.79; 95% CI = 1.02, 3.14), it was more than 3 fold higher with a history of recurrent infections (OR= 3.39; 95% CI= 1.27, 8.73), almost 3 fold higher in women who experienced a premature rupture of membranes (OR= 2.96; 95% CI= 1.07, 8.22). Complications in pregnancy accounted a risk more than 2 fold higher of developing sepsis (OR= 2.30; 95% CI= 1.02, 5.20). Risks considered were calculated both in cases and controls, respectively: anemia (10.9% - 3.3%); severe infection (2.7% - 0.3%); antibiotic

prophylaxis for fetal lung maturation (11.4% - 4.4%); risk of preterm birth (7.1% - 3.6%); positive Group B streptococcus vaginal swab or urine test (7.6% - 3.1%). An IV cannula caused a risk 13 times higher to develop sepsis (OR= 13.18; 95% CI= 2.44 – 71.31), continuous urinary catheterization was another significant risk factors (OR= 11.12; 95% CI= 2.18 – 56.7). When V.E. (vaginal examinations) in labour were performed in a number higher than 5, represented a significant risk factors for post-partum sepsis (OR= 2.25; 95% CI= 1.08- 4.7).

Although results did not reach significance, there is a trend towards a relationship between post-partum sepsis and previous medical diseases (OR= 1.85, 95% CI= 0.99 – 3.47), the same was found when an amniocentesis was performed (OR= 4.62, 95% CI= 0.54 – 25.55) and in case of complications during childbirth (OR= 2.22, 95% CI = 0.99 – 4.98).

Post-partum sepsis – risk factors			Cases (N=183)		Controls (N=363)		OR (C.I. 95%)	
			N	%	N	%	Raw	Adjusted
Socio-demographic variables	Age	<35	129	70.1	209	57.6	1	1
		>=35	55	29.9	154	42.4	0.57(0.38-0.83)	0.72(0.39-1.34)
	Citizenship	Italian	123	66.8	283	78	1	1
		Foreign	58	31.5	77	21.1	1.82(1.19-2.78)	1.43(0.7-2.92)
	Education level	Low	53	28.8	86	23.7	1.33(0.85-2.06)	1.52(0.72-3.19)
		Medium-high	121	65.8	246	67.8	1	1
Previous obstetric and medical history	Parity	Nulliparous	108	58.7	163	44.9	1.73(1.21-2.46)	1.79(1.02-3.14)
		Multiparous	76	41.3	200	55.1	1	1
	BMI	<18.5	10	5.4	21	5.8	0.94(0.41-2.12)	1.13(0.32-4.05)
		18.5-24.9	103	56	201	55.4	1	1
		25-29.9	36	19.6	71	19.6	0.99(0.63-1.57)	1.2(0.58-2.49)
		>=30	23	12.5	40	11	1.09(0.62-1.9)	0.63(0.23-1.7)
	Previous STI	No	169	91.8	349	96.1	1	1
		Yes	10	5.4	8	2.2	2.68(1.01-7.09)	3.1(0.62-15.56)
	Recurrent infection	No	148	80.4	337	92.8	1	1
		Yes	24	13	17	4.7	3.68(1.83-7.41)	3.33(1.27-8.73)
	Previous medical diseases	No	114	62	280	77.1	1	1
		Yes	70	38	83	22.9	2.14(1.43-3.19)	1.85(0.99-3.47)
Current obstetric history	Amniocentesi	No	175	95.1	357	98.3	1	1
		Yes	9	4.9	6	1.7	3.64(1.1-12.1)	4.62(0.84-25.55)
	SROM	No	159	86.4	342	94.2	1	1
		Yes	25	13.6	21	5.8	2.78(1.44-5.33)	2.96(1.07-8.22)
	Complications in pregnancy	No	131	71.2	322	88.7	1	1
		Yes	53	28.8	41	11.3	3.7(2.22-6.17)	2.3(1.02-5.2)
	PPH (≥500 ml)	No	145	78.8	328	90.4	1	1
		Yes	39	21.2	35	9.6	2.64(1.57-4.45)	2(0.75-5.35)
	Complications at birth	No	155	84.2	345	95	1	1
		Yes	29	15.8	18	5	3.95(2.04-7.66)	2.22(0.99-4.98)
	IV cannula	No	96	52.2	293	80.7	1	1
		Yes	88	47.8	70	19.3	50.34(12.27-206.59)	13.18(2.44-71.31)
	In-and-out catheter	No	168	91.3	352	97	1	1
		Yes	16	8.7	11	3	6.15(2-18.97)	4.35(0.69-27.33)
	Continuous urinary catheterization	No	98	53.3	295	81.3	1	1
		Yes	86	46.7	68	18.7	48.85(11.9-200.6)	11.12(2.18-56.7)
	V.E. > 5	No	131	71.2	274	75.5	1	1
		Yes	45	24.5	48	13.2	2.2(1.31-3.69)	2.25(1.08-4.7)

Table 28. Conditional Logistic Regression Model applied on post-partum sepsis cases.

BMI= body mass index; STI= sexual transmitted infection; SROM= spontaneous rupture of membranes; PPH= post-partum haemorrhage; IV cannula= intravenous cannula; V.E.= vaginal examination; OR= Odd Ratio; C.I. = confidence intervals

CHAPTER FIVE: DISCUSSION

5.1 Introduction

This chapter will discuss the main results of the study considering findings of other INOSS research regarding eclampsia and sepsis.

This is the first population-based study to be carried out in Italy regarding near miss cases.
This project is the first INOSS study to be conducted using the Delphi definition of eclampsia [54] and to consider the international Surviving Sepsis Campaign guideline [62] which introduced the diagnosis of sepsis throughout the criteria of suspected or confirmed infection together with organ failure.
As already demonstrated [79], population-based studies to promote an active collection of cases are more reliable than monitoring diagnosis codes using the hospital discharge databases. Those are often inappropriately adopted and their use would require a significant investment by clinicians in the accuracy of their reporting. This issue was evident also in our study, where the eclampsia ICD-9CM code was often considered to register a woman having pre-eclampsia instead. While for sepsis, the existing ICD-9CM code does not describe the real clinical situation and does not reflect the definition given by the Surviving Sepsis Campaign guideline. In both cases, a double check with clinicians was needed to confirm or to exclude episodes that were found throughout the National Hospital Discharge Database but were not reported during the data collection period, this activity required energy and time from both researchers and health professionals.

5.2 Discussion regarding eclampsia

Eclampsia is a serious obstetric disease. There are no data from Italy on this complication, neither on pre-eclampsia, the present study represents a valid source of epidemiological data with regards to the knowledge of eclampsia.

Our findings are consistent with the results found in other INOSS population-based studies [99,124], showing a slow but persistent reduction in the incidence of eclampsia. Eclampsia was a very uncommon event in Italy, being diagnosed in 1.5 women every 10'000 birth, similar to the incidence found in other high-income countries such as Australia and New Zealand with an incidence of 2.2 every 10’000 [124], and Netherland with 1.8 eclampsia episodes every 10’000 women [99].
The eclampsia Delphi definition identified any symptom or sign among high BP, proteinuria, altered AST or ALT and thrombocytopenia to make a diagnosis of eclampsia. Hypertension and

proteinuria have long been recognized as manifestations of pre-eclampsia and a warning sign for occurrence of eclampsia [125], however evidence showed controversial results [126,127]. Although, the majority of the women in our sample had hypertension and less than half had proteinuria within 24 hours before the eclamptic episode, evidence demonstrated that 40 to 60% of the eclamptic fits represent the onset of a hidden pre-eclampsia [128]. Almost half of cases considered in a population-based study conducted in Australia and Tanzania reported that proteinuria did not precede 46% of the eclamptic seizures in their sample [127], the same was found in a United States based study where women showed and absence of hypertension and proteinuria in 16-25% and 14% of the eclamptic fits, respectively [126]. A systematic review by Hastie et al. revealed that a significant number of eclamptic women had no significant prodromal symptoms before their eclamptic seizure and they had either normal or mild to moderate hypertension before the fit [101]. None of the 28 symptoms found among 11 studies considered, was able to predict imminent eclampsia. Similar results were reported by another study by Berhan Berhan [129], where nearly half of the eclampsia cases occurred in the absence of severe hypertension or warning signs. This is consistent with our findings where 41.3% of women had no premonitory signs before the eclamptic fit, of those 38.6% were already in hospital. In an population-bases study conducted in Australian and New Zealand [124] 36% of women were reported without any premonitory signs the week before the eclamptic fit. In our sample, women with 2 fits were even more asymptomatic than the women who experienced a single seizure episode.

Moreover, in our study diastolic blood pressure seemed to be a better predictor than the systolic value, both before and at the time of diagnosis. Previous evidence [130] reported the same results related to the prediction of pre-eclampsia and the UKOSS population-based study [97] stated that 37% of women had established pre-eclampsia before developing eclampsia, and of those 59% had established proteinuria and diastolic blood pressure of 100 mmHg or greater in the week before their fit.

The characteristics of women with eclampsia in relation to the general population who gave birth during the same period showed that women in our sample were more likely to be from minority ethnic groups (RR= 1.77, 95% CI: 1.16 - 2.68). The impact of technologies such as in vitro fertilisation with ovum donation may contribute significantly to an increasing incidence of pregnancies developing eclampsia (RR= 4.86%, 95% CI: 2.45 – 9.63). In addition, differences in the incidence of eclampsia between women with multiple pregnancy were also observed (RR= 4.95, 95% CI: 2.41 – 10.76). A higher risk of near miss morbidities have been previously reported in other analysis, where inequalities in the occurrence of these disorders in ethnic minority women were identified through UKOSS [131]. An Italian study by Cromi et al. [132] confirmed that increased risk of maternal potentially life-threatening conditions was found in pregnancies

conceived via ART. The same trend was described in a USA retrospective cohort study [133], where women with pregnancy achieved with ART and multiple pregnancy resulted at higher risk of severe outcomes. Evidence [134,135] suggested that multiple ART pregnancies (6% of all ART pregnancies in Italy [136]) are at higher risk of hypertensive disorders with respect to singleton ART pregnancies, that in turn are more likely to have an increased risk of hypertension when compared to spontaneous pregnancies. Multiple pregnancy was a risk factor reported in the incidence of eclampsia in the Netherland [137]. The Italian National Assisted Reproductive Techniques register in their report of 2017, stated that the Italian incidence of ART pregnancies was 3% [136]. Our findings revealed a higher rate of ART pregnancy among eclamptic women compared to the national rate, this issue may warrant further attention in future research.

Although results did not reach significance, there is a trend towards a relationship between being nulliparous (RR= 1.42; 95%: 0.96 – 2.09) and an age more than 40 years old (RR= 1.60; 95%: 0.91- 2.81).

Although characteristics such as high BMI and smoking appeared much lower compared to the rate found in other national based study [97,99], in our research these variables presented too many missing values, a recurrent problem that leads to inefficient analysis and does not allow comparison between data of the other INOSS studies.

In our sample 35.8% of women had a hypertensive disorder, of those 41.0% were multiparous; 33.0% had hypertension during the previous or the current pregnancy, among them 36.1% were women with at least a previous pregnancy; 19.3% develop pre-eclampsia, of those 52.4% were multiparous women and 2 of them (4.7%) had a pre-eclampsia also during the previous pregnancy. Our findings are quite similar to the data reported by UKOSS [97], where 37% of the eclamptic women had high blood pressure during the previous or in the index pregnancy.

Our results indicated that any previous hypertensive disorders should be carefully considered.

In regard to the treatment in pregnancy, there has been increasing focus and recommendations made to use low-dose aspirin to prevent pre-eclampsia, which in turn could prevent eclampsia, in women from moderate to high risk, especially to avoid preterm pre-eclampsia [138,139]. Only 4 women in our sample were given preventive aspirin in pregnancy before 16 weeks, as recommended by the American College of Obstetrician and Gynecologists (ACOG) [140], 2 initiated after 16 weeks and in 3 women the gestational age was not specified. Our findings regarding insufficient administration of low-dose aspirin are consistent with data from the population-based Australian study conducted in 2010-2011 [124].

Antihypertensive treatment in pregnancy was started/changed in 26.6% of women, which is very low compared to the 74.4% that occurred in the Netherland [54].

In the last 2 decades, and especially after the Magpie trial [141], magnesium sulphate has become the gold standard medication to prevent and control eclampsia, particularly in women with severe pre-eclampsia.

The present study showed that only 19 women (17.4%) had preventive magnesium sulphate, however is a higher rate compared to the 7.3% found in the Netherland data [99] and 6% in the UKOSS results [97]. Furthermore, among the 21 pre-eclamptic women, 6 (28.6%) were given magnesium, although this element should be further improved, it is consistent with the AMOSS data [124] where about one third of pre-eclamptic women were treated with magnesium and more common than in UK [97], where none of the women who had pre-eclampsia were given magnesium.

In our study 89% of women are treated with magnesium sulphate as first-line therapy to prevent recurrent fits, better results have been achieved in UK [94], Netherland [99] and Australia and New Zealand [124], where 99%, 100% and 95.5% of women, respectively, were given magnesium following their first fit. Nevertheless, our study did not investigate how many women with pre-eclampsia in Italy were treated with magnesium sulphate and did not develop eclampsia. Of note, our findings showed that, although the use of magnesium, 2 women in 10 experienced more than one single fit.

In our study almost 90% of women received hypertensive therapy after eclampsia, this was more common than in the UK, in the Netherlands or in Australia [97,99,124]. While anticonvulsant medication where still very high compared to the rate of other INOSS study. This is an important issue that should be discussed between Gynaecologists and Anaesthetists, who are probably more implicated during the administration of such drugs. The recommended therapy to be administered after an ecliptic episode should be represented by magnesium and hypertensive medications.

In accordance with the other INOSS research, also in Italy the majority of the ecliptic seizures occurred antepartum, about one third happened post-partum, while intrapartum fits were less common. The gestational age distribution is also very similar, with the majority of antepartum cases occurring preterm and having worse maternal outcomes, whereas the intrapartum and postpartum cases tend to occur at term.

In north European countries there are higher homebirths rates and women are discharged quicker from hospital, it is probably for this reason that it was more common to have the eclamptic fit at home, while in Italy are more frequently observed in hospital. However we had a higher number of women, 1 every 8 women, with fit more than 48 hours after birth, by this time a significant number of mothers could be already at home. The important rate of fits after birth, especially the rate of delayed post-partum eclampsia (more than 48 hours after birth), warrants attention towards the need of close follow-up following birth. Moreover these data gave sufficient information to state that pre-eclampsia persists after birth as well. Further research are needed to investigate whether

maternal characteristics and outcomes were different between women with delayed or early postpartum eclampsia.

Gestational age at delivery was comparable between data of UKOSS and NethOSS for both the entire group of women that developed eclampsia (38 week of gestation) as well as for the subgroup with pre-eclampsia (37^{+1} weeks and 37^{+1} weeks, respectively) diagnosed before eclampsia [98]. The Italian study reported a lower mean gestational age at delivery in both groups, 36 weeks within the entire sample and 36+1 weeks in women who developed pre-eclampsia before their fit. The same was seen for the subgroup of women who had the eclamptic seizure antepartum, the Italian women gave birth meanly at 34 weeks, in UK the mean gestational age was 37^{+5} and in Netherland 38. This could not be explained with higher rates of preventive magnesium sulphate administered in women with pre-eclampsia prior the fit, as the Italian data showed a better compliance with this recommendation than UK or Netherland. One reason could be a higher rate of women in UK and Netherland with premonitory signs (nearly 80% had at least one symptoms prior their fit), another explanation could be seen in a higher percentage of women with pre-eclampsia (ItOOS= 19.3%, UKOSS= 43%, NethOSS= 42%), who were probably under more frequent observations. Another important aspect to be noted is that similar admission were reported among Italian women and within the Dutch study, 76.1% and 65.9% of women, respectively, were already in hospital prior their fit. Authors in the NethOSS study [99] reported that an increase in antihypertensive treatment could be suggestive of more active management for all women with hypertensive disorders, including use of magnesium sulphate prophylaxis. This implies that better and continuous risk stratification during admission, including administration of antihypertensive drugs and preventive magnesium sulphate, could decrease the incidence of eclampsia. This should be done especially with women admitted in hospital, who were found to be the most during our study. The aim should be to prolong pregnancy where possible to improve fetal prognosis.

Again, the study by Schaap et al. [98] where authors compare the incidence of eclampsia between the Netherlands and the UK reported that similar proportion of women in the UKOSS and the NethOSS study were induced (NethOSS: 37.8%) or gave birth by CS (NethOSS: 40.2%). These data are very different from the Italian ones where the rate of induction of labour were lower (20%), while the CS were much higher (84.6%). Rate of induction of labour were even higher in the AMOSS study [124] (55.6%), CS was performed in 66.9% of women. When observing the rates of induction of labour and CS by the time of diagnosis of eclampsia (antepartum, intrapartum and post-partum), data showed the same trend, with the antepartum induction of labour (aIOL) and CS within the subgroup of women who experienced eclampsia during the antepartum period (aCS), making the most important difference (ItOSS: aIOL= 7.3%, aCS=100%; UKOSS: aCS=87%; NethOSS: aIOL= 18.9%, aCS= 75.7%; AMOSS: aIOL= 91.7%, aCS= 85.7%) [98,99,124].

We analysed the interval between fit and delivery to approximate the time needed to stabilise the woman and accomplish birth. The time calculate by the UKOSS and the NethOSS studies, for both the antepartum and the intrapartum eclampsia groups were much higher than the time observed during our study. This assessment offered a crucial explanation in regard to the differences we observed with the INOSS data, in women's outcomes after the fit. In our sample 3 women every 10 had severe complications after eclampsia, while the UKOSS data indicated that only 10% of their cases were reported to have severe morbidity. Also the admission to Intensive Care Unit was more common among the Italian women (62.4%) compared to UKOSS (56%) and NethOSS (30.5%). The time between the eclamptic fit and birth is important to stabilize the condition of the women giving magnesium sulphate and antihypertensive treatment. Timing observed in our study in probably insufficient and inappropriate, leading to more frequent maternal morbidities.
Only two woman was reported to have suffered from pulmonary oedema, which suggests that fluid balance in women with eclampsia is being managed effectively.

Male fetal gender is associated with an overall increased risk of pre-eclampsia in the non-Asian population, our data confirmed the literature [142]. Many variable collected regarding the neonatal birth outcomes showed many missing values, making difficult any reliable analysis.

Outcomes related to maternal and perinatal mortality were comparable between INOSS studies.

This is the first study that showed no differences between the North, the Centre and the South of Italy.

5.3 Summary on eclampsia observations

The low rate of eclampsia in our study suggests that there was a good level of antenatal care in Italy overall. We could identified some characteristics in our population that could help during practice to focus attention on particular subgroups: non-Italian women, women who conceive with ART and women who have multiple pregnancy.
About 4 women in 10 were normotensive and without any premonitory signs in the 24 hours prior to the first seizure, highlighting the unpredictable nature of eclampsia. Diastolic blood pressure seemed to be a better predictor 24 hours before the fit. There is space to improve the use of magnesium sulphate as prophylactic treatment in women diagnosed with pre-eclampsia. There is even much more room to work on the population risk stratification to administer low-dose aspirin to high risk women and at the appropriate time.

Findings shed lights on the important rate of post-partum eclampsia, which represents a challenge as this obstetric complication was believed to improve with birth, a dogma surrounding pre-eclampsia and eclampsia. However, worse outcome were seen in women with antepartum fit.
The majority of women were given magnesium sulphate as first-line therapy, however 2 over 10 had more than one fit. Anticonvulsants are inappropriately used and should be managed better.
More than 3 women in 10 developed sever complications after the eclamptic episode, this could be due to an inappropriate stabilization before birth, which could be understood observing the short interval between the first fit and birth.

Currently, there are no reliable tests to predict which women will develop eclampsia. Further research should focus on biomarkers which could enable to early predict severe pre-eclampsia with the aim to reduce this disorder, improving maternal and perinatal outcomes.

5.4 Discussion regarding peripartum sepsis

Over the past decade the incidence of maternal deaths from maternal sepsis has increased in several European countries [73,89,143], this trend has been seen also in Italy [22]. In light of increasing rates, it was important to estimate the incidence of, and describe the causative organisms, sources of infection, and risk factors for, maternal sepsis in our country.

The reported incidence of maternal sepsis varies across Countries, this is because of the absence of a standard definition that would allow to compare data between the INOSS studies. Furthermore our study is the first among the INOSS network to be conducted following the Sepsis-3 Consensus. Although we adopted a more strict definition, characterized by the suspected or confirmed infection together with the organ failure criteria, and we expected to collect a limited number of cases, the estimated incidence we found was higher compared to the one described in other European study.
This finding could be due to the increase of cases worldwide or we are probably unable to prevent the progression from infection to sepsis.
In this regard the Global Maternal Sepsis Study (GLOSS) led by WHO [69], found that the incidence of maternal infections in Italy was 71.2 every 1000 live births and 11.4‰ progressed with complications. This might reflect a later diagnosis or later treatment. Italy had an incidence of infections similar to global rate, however it did appear to have a higher rate of infection with complications compared to other European Countries.

The cases of sepsis reported by some of the participating Regions (Lazio, Campania, Puglia, Sicilia) was very low and it was considered unreliable. The criteria selected to define cases of

maternal sepsis are quite complex, it could be a challenge to identify and correctly diagnose sepsis.

Our findings showed that, as seen for eclampsia, non-Italian women were quite represented 30.2%, compared to the 20% of the general population who give birth in Italy [144], and 3 every 10 women had a language-related issue. This is consistent with previous studies [60,137], reporting that immigrant women experienced an increased risk of developing sepsis or were more likely to have severe morbidities.

In accordance with the UKOSS prospective case-control study [61], our findings showed a higher number of cases during the post-partum period. Less than one third of women in our sample gave birth vaginally, which is a lower rate compared to other studies that investigate the characteristics of maternal sepsis, where rate of vaginal births were between 40% [61] and 70% [73].

The most common sources of maternal infections were of the genital (endometritis and chorioamnionitis), respiratory and urinary tract. These findings are different from the UKOSS data [60], where the urinary tract infections were higher than the respiratory tract infections. However, in a UK based study aiming to evaluate the characteristics and risk factors for critical care admission following sepsis [145], the respiratory tract infections were observed to be the first source of infection in women with severe sepsis admitted to Intensive Care. The source of infection found during the study reflects the different patterns of infection existing between antenatal and postnatal sepsis. In fact during antenatal sepsis the respiratory tract and urinary tract infections are the predominant ones, while when the sepsis occurred post-partum the genital tract and the urinary are the most present. The different patterns of infection we observed in antenatal and postnatal women suggest that overall greater consideration needs to be given to the source of infection, and therefore the most appropriate antibiotic to prescribe. The positive culture were higher compared to the rate found during the GLOSS study, where only about half of women had a positive culture (66% vs 56%). Escherichia coli was the most frequent causative organism, this is consistent with other studies [61].
Source of infection are also different based on mode of birth, women who gave birth vaginally were observed to develop genital tract infection, together with the urinary tract in case of instrumental vaginal birth. After a CS skin/soft tissues, respiratory tract and peritoneal infection were reported. The source of infection and the mode of mode give information about the potential appropriate therapy to administer.

The international Surviving Sepsis Campaign initiative recommended to start immediate aggressive treatment in the first ‘golden hour’[62]. For every hour delay we increase the mortality

rate of 8% . The GLOSS study reported that across the all data set only 40% of women had the antibiotics within an hour [69]. The Italian data showed that very few women (21.3%) had antibiotic started within an hour as immediate response to the suspected infection and one quarter were given treatment three hours after diagnosis. This critical data could be the reason why we had so many women who developed severe complications (24%) and who were admitted to intensive care (27.5%), and might reflect the delay of diagnosis and the inappropriate therapy given. Our findings showed, in fact, that 90 therapeutic schemes where adopted, although very few are recommended by the literature [62,87]. The delay of diagnosis together with a lack of knowledge regarding the right therapy to administer, could increase the probability to develop severe maternal complications.

As reported by the GLOSS study, also the Italian data did not show any uncommon pattern of antibiotic resistance. However, the Italian Medicine Agency in the 2020 Report stated that 33.2% of pregnant women were given an antibiotic, which most of the time was observed to be appropriate.

Unfortunately we did not ask about plasma lactate measurement, which give information about the rate of women who had a septic shock. However, vasopressin infusions normally used for septic shock women not responding to fluid resuscitation, were administered to nearly 20% of cases. This information could indirectly inform about the number of septic shock developed following sepsis, that is in accordance with the literature.

The high rate of preterm births, 31% compared to a national rate of 7%, gives awareness about the severe implications sepsis could have also on neonatal outcomes. Some of the variables related to neonatal data present too many missing values, a recurrent problem that leads to inefficient analysis and does not allow comparison between data of the other INOSS studies.

The risk factors identified are in accordance with previous INOSS studies [61,73,146], and risk factors as minority ethnic group and primiparity were also showed in a US-based study [60]. This significant findings could be generalizable to other high-income countries and be the base to develop guidelines regarding maternal sepsis.

5.5 Summary on sepsis observations

Maternal sepsis represents a clinical burden, given the absence of a standard definition, the difficult identification and management and the persistent increased of this complication worldwide.

Maternal sepsis is a time-dependent disorder, prompt diagnosis, immediate intravenous antibiotic treatment within the “golden hour” and early involvement of senior midwife, obstetricians, anaesthetists and critical-care consultants, may help to achieve good maternal and neonatal outcomes.

The antibiotic resistance phenomenon should be regarded with high attention, and should be prevented giving the right and appropriate treatment.
The high rate of women who developed severe complications, demonstrated also by Italian data collected by the GLOSS study which assessed maternal infections rate worldwide, might reflect the inappropriate time of diagnosis and treatment prescribed to our population.
The high rate of pre-term births increase awareness regarding the important consequences that sepsis might have also on neonatal well-being.
The present study offers essential information for healthcare professionals on major criticisms observed during the care of women with sepsis. A delayed diagnosis and treatment, the administration of inappropriate antibiotic therapy, the high number of vaginal examinations in labour and the correct aseptic technique during all procedures, could be improved in order to reduce the risk of infections and save lives. Preventive actions are one of the most important strategy against sepsis.

The lack of diagnosis or reporting by the participating Region of the South of Italy, should be further investigated.

CHAPTER SIX: CONCLUSION

This study developed significant information concerning obstetric disorders related to the Italian population, prior to this project no Italian data were available on these life threatening complications.

Near miss studies represent a great opportunity for healthcare professionals to increase their knowledge in regard to severe and uncommon maternal morbidities. These type of projects facilitate the promotion of peer review, collaboration among colleagues, allow audit to improve quality of care, and most important they are an essential strategy to encourage to invest time and effort in creating a no-blame culture.

The present study offers an unique source of information and allows to identify the Italian system or clinical practice related-failures, in order to address strategies and strengths to improve the quality of maternal health care and promote an evidence-based practice. Furthermore, it could be the base to develop a context-specific guideline.

Population-based studies shed lights on the need to improve the appropriateness and the completeness of hospital discharge databases and the birth register certificate compilation, moreover they allow to understand which complications could be monitor using the ICD codes of diagnosis.

This research, as part of the INOSS projects, promotes a collaborative working between countries and allow international comparison which are paramount to improve the quality of midwifery and obstetric care worldwide.

Reference

[1] Peristat Monitoring and Evaluating Perinatal Health in Europe n.d.
[2] Lewis G. Saving Mothers' Lives: The Continuing Benefits for Maternal Health From the United Kingdom (UK) Confidential Enquires Into Maternal Deaths. Seminars in Perinatology 2012;36:19–26. https://doi.org/10.1053/j.semperi.2011.09.005.
[3] Harvey M. Research methods for nurses and midwives. Place of Publication Not Identified: Sage Publications; 2015.
[4] Speziale HS, Carpenter DR. Qualitative research in nursing: advancing the humanistic imperative. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2011.
[5] Harvey M, Land L. Research methods for nurses and midwives. Theory and Practice. Place of Publication Not Identified: Sage Publications; 2015.
[6] Paruk F, Moodley J. Severe obstetric morbidity: Current Opinion in Obstetrics and Gynecology 2001;13:563–8. https://doi.org/10.1097/00001703-200112000-00003.
[7] Canada, Canadian Perinatal Surveillance System, editors. Special report on maternal mortality and severe morbidity in Canada: enhanced surveillance: the path to prevention. Ottawa: Health Canada; 2004.
[8] Madsen P, Dillon RL, Tinsley CH. Airline Safety Improvement Through Experience with Near-Misses: A Cautionary Tale: Airline Safety Improvement Through Experience with Near-Misses. Risk Analysis 2016;36:1054–66. https://doi.org/10.1111/risa.12503.
[9] Geller SE, Rosenberg D, Cox SM, Kilpatrick S. Defining a conceptual framework for near-miss maternal morbidity. J Am Med Womens Assoc (1972) 2002;57:135–9.
[10] Pattinson R, Hall M. Near misses: a useful adjunct to maternal death enquiries. British Medical Bulletin 2003;67:231–43. https://doi.org/10.1093/bmb/ldg007.
[11] Say L, Pattinson RC, Gülmezoglu AM. WHO systematic review of maternal morbidity and mortality: the prevalence of severe acute maternal morbidity (near miss). Reprod Health 2004;1:3. https://doi.org/10.1186/1742-4755-1-3.
[12] Filippi V, Alihonou E, Mukantaganda S, Graham WJ, Ronsmans C. Near misses: maternal morbidity and mortality. The Lancet 1998;351:145–6. https://doi.org/10.1016/S0140-6736(05)78106-X.
[13] Fitzpatrick C, Halligan A, McKenna P, Coughlan BM, Darling MR, Phelan D. Near miss maternal mortality (NMM). Ir Med J 1992;85:37.
[14] Say L, Souza JP, Pattinson RC. Maternal near miss – towards a standard tool for monitoring quality of maternal health care. Best Practice & Research Clinical Obstetrics & Gynaecology 2009;23:287–96. https://doi.org/10.1016/j.bpobgyn.2009.01.007.
[15] Oliveira-Neto A, Parpinelli MA, Cecatti JG, Souza JP, Sousa MH. Sequential Organ Failure Assessment Score for Evaluating Organ Failure and Outcome of Severe Maternal Morbidity in Obstetric Intensive Care. The Scientific World Journal 2012;2012:1–8. https://doi.org/10.1100/2012/172145.
[16] Pattinson R, Say L, Souza JP, van den Broek N, Rooney C. WHO maternal death and near-miss classifications. Bull World Health Org 2009;87:734–734. https://doi.org/10.2471/BLT.09.071001.
[17] Knight M, INOSS. The International Network of Obstetric Survey Systems (INOSS): benefits of multi-country studies of severe and uncommon maternal morbidities. Acta Obstet Gynecol Scand 2014;93:127–31. https://doi.org/10.1111/aogs.12316.
[18] Knight M, Lindquist A. The UK Obstetric Surveillance System: Impact on patient safety. Best Practice & Research Clinical Obstetrics & Gynaecology 2013;27:621–30. https://doi.org/10.1016/j.bpobgyn.2013.03.002.
[19] Zwart J, Richters J, Öry F, de Vries J, Bloemenkamp K, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide

population-based study of 371 000 pregnancies. BJOG: An International Journal of Obstetrics & Gynaecology 2008;115:842–50. https://doi.org/10.1111/j.1471-0528.2008.01713.x.
[20] Driessen M, Bouvier-Colle M-H, Dupont C, Khoshnood B, Rudigoz R-C, Deneux-Tharaux C. Postpartum Hemorrhage Resulting From Uterine Atony After Vaginal Delivery: Factors Associated With Severity. Obstetrics & Gynecology 2011;117:21–31. https://doi.org/10.1097/AOG.0b013e318202c845.
[21] Donati S, Senatore S, Ronconi A, the Regional Maternal Mortality Working Group. Obstetric near-miss cases among women admitted to intensive care units in Italy: Obstetric near-miss in Italy. Acta Obstetricia et Gynecologica Scandinavica 2012;91:452–7. https://doi.org/10.1111/j.1600-0412.2012.01352.x.
[22] Dell'Oro S, Maraschini A, Lega I, D'Aloja P, Andreozzi S, Donati S. Primo Rapporto ItOSS. Sorveglianza della Mortalita Materna 2019.
[23] Tunçalp Ö, Souza J. Maternal near-miss audits to improve quality of care. BJOG: Int J Obstet Gy 2014;121:102–4. https://doi.org/10.1111/1471-0528.12868.
[24] World Health Organization, editor. Beyond the numbers: reviewing maternal deaths and complications to make pregnancy safer. Geneva: Dept. of Reproductive Health and Research, World Health Organization; 2004.
[25] Graham WJ. Criterion-based clinical audit in obstetrics: bridging the quality gap? Best Practice & Research Clinical Obstetrics & Gynaecology 2009;23:375–88. https://doi.org/10.1016/j.bpobgyn.2009.01.017.
[26] Lewis G. The cultural environment behind successful maternal death and morbidity reviews. BJOG: Int J Obstet Gy 2014;121:24–31. https://doi.org/10.1111/1471-0528.12801.
[27] Knight M, Lewis G, Acosta C, Kurinczuk J. Maternal near-miss case reviews: the UK approach. BJOG: Int J Obstet Gy 2014;121:112–6. https://doi.org/10.1111/1471-0528.12802.
[28] Pattinson RC, Buchmann E, Mantel G, Schoon M, Rees H. Can enquiries into severe acute maternal morbidity act as a surrogate for maternal death enquiries? BJOG: An International Journal of Obstetrics & Gynaecology 2003;110:889–93. https://doi.org/10.1111/j.1471-0528.2003.03044.x.
[29] Browne JL, van Nievelt SW, Srofenyoh EK, Grobbee DE, Klipstein-Grobusch K. Criteria-Based Audit of Quality of Care to Women with Severe Pre-Eclampsia and Eclampsia in a Referral Hospital in Accra, Ghana. PLoS ONE 2015;10:e0125749. https://doi.org/10.1371/journal.pone.0125749.
[30] Bhattacharyya S, Srivastava A, Knight M. Developing a framework to review near-miss maternal morbidity in India: a structured review and key stakeholder analysis. BMC Health Serv Res 2014;14:553. https://doi.org/10.1186/s12913-014-0553-x.
[31] Bacci A, Hodorogea S, Khachatryan H, Babojonova S, Irsa S, Jansone M, et al. What is the quality of the maternal near-miss case reviews in WHO European Region? Cross-sectional study in Armenia, Georgia, Latvia, Republic of Moldova and Uzbekistan. BMJ Open 2018;8:e017696. https://doi.org/10.1136/bmjopen-2017-017696.
[32] Okong P, Byamugisha J, Mirembe F, Byaruhanga R, Bergstrom S. Audit of severe maternal morbidity in Uganda – implications for quality of obstetric care. Acta Obstet Gynecol Scand 2006;85:797–804. https://doi.org/10.1080/00016340600593331.
[33] Lazzerini M, Richardson S, Ciardelli V, Erenbourg A. Effectiveness of the facility-based maternal near-miss case reviews in improving maternal and newborn quality of care in low-income and middle-income countries: a systematic review. BMJ Open 2018;8:e019787. https://doi.org/10.1136/bmjopen-2017-019787.
[34] Hutchinson C, Lange I, Kanhonou L, Filippi V, Borchert M. Exploring the sustainability of obstetric near-miss case reviews: a qualitative study in the South of Benin. Midwifery 2010;26:537–43. https://doi.org/10.1016/j.midw.2010.05.016.
[35] World Health Organization. Evaluating the quality of care for severe pregnancy complications. The WHO near-miss approach for maternal health. Geneva: World Health Organisation: 2011.

[36] Jabir M, Abdul-Salam I, Suheil DM, Al-Hilli W, Abul-Hassan S, Al-Zuheiri A, et al. Maternal near miss and quality of maternal health care in Baghdad, Iraq. BMC Pregnancy Childbirth 2013;13:11. https://doi.org/10.1186/1471-2393-13-11.
[37] Souza JP, Gülmezoglu AM, Vogel J, Carroli G, Lumbiganon P, Qureshi Z, et al. Moving beyond essential interventions for reduction of maternal mortality (the WHO Multicountry Survey on Maternal and Newborn Health): a cross-sectional study. The Lancet 2013;381:1747–55. https://doi.org/10.1016/S0140-6736(13)60686-8.
[38] van den Akker T, Beltman J, Leyten J, Mwagomba B, Meguid T, Stekelenburg J, et al. The WHO Maternal Near Miss Approach: Consequences at Malawian District Level. PLoS ONE 2013;8:e54805. https://doi.org/10.1371/journal.pone.0054805.
[39] Nelissen E, Mduma E, Broerse J, Ersdal H, Evjen-Olsen B, van Roosmalen J, et al. Applicability of the WHO Maternal Near Miss Criteria in a Low-Resource Setting. PLoS ONE 2013;8:e61248. https://doi.org/10.1371/journal.pone.0061248.
[40] Ngan Kee WD. Confidential Enquiries into Maternal Deaths : 50 years of closing the loop. British Journal of Anaesthesia 2005;94:413–6. https://doi.org/10.1093/bja/aei069.
[41] RCOG. Confidential Enquiry into Maternal and Child Health. Why Mothers Die 2000–2002: The Sixth Report of the Confidential Enquiries into Maternal Death in the United Kingdom. London: 2004.
[42] Knight M, Acosta C, Brocklehurst P, Cheshire A, Fitzpatrick K, Hinton L, et al. Beyond maternal death: improving the quality of maternal care through national studies of 'near-miss' maternal morbidity. Programme Grants Appl Res 2016;4:1–180. https://doi.org/10.3310/pgfar04090.
[43] Andreucci CB, Cecatti JG, Pacagnella RC, Silveira C, Parpinelli MA, Ferreira EC, et al. Does Severe Maternal Morbidity Affect Female Sexual Activity and Function? Evidence from a Brazilian Cohort Study. PLoS ONE 2015;10:e0143581. https://doi.org/10.1371/journal.pone.0143581.
[44] Fenech G, Thomson G. Tormented by ghosts from their past': A meta-synthesis to explore the psychosocial implications of a traumatic birth on maternal well-being. Midwifery 2014;30:185–93. https://doi.org/10.1016/j.midw.2013.12.004.
[45] Thompson JF, Heal LJ, Roberts CL, Ellwood DA. Women's breastfeeding experiences following a significant primary postpartum haemorrhage: A multicentre cohort study. Int Breastfeed J 2010;5:5. https://doi.org/10.1186/1746-4358-5-5.
[46] Kozhimannil KB, Jou J, Attanasio LB, Joarnt LK, McGovern P. Medically Complex Pregnancies and Early Breastfeeding Behaviors: A Retrospective Analysis. PLoS ONE 2014;9:e104820. https://doi.org/10.1371/journal.pone.0104820.
[47] Storeng KT, Murray SF, Akoum MS, Ouattara F, Filippi V. Beyond body counts: A qualitative study of lives and loss in Burkina Faso after 'near-miss' obstetric complications. Social Science & Medicine 2010;71:1749–56. https://doi.org/10.1016/j.socscimed.2010.03.056.
[48] Assarag B, Dujardin B, Essolbi A, Cherkaoui I, De Brouwere V. Consequences of severe obstetric complications on women's health in Morocco: please, listen to me! Trop Med Int Health 2015;20:1406–14. https://doi.org/10.1111/tmi.12586.
[49] Filippi V, Goufodji S, Sismanidis C, Kanhonou L, Fottrell E, Ronsmans C, et al. Effects of severe obstetric complications on women's health and infant mortality in Benin: **Effects of severe obstetric complications**. Tropical Medicine & International Health 2010;15:733–42. https://doi.org/10.1111/j.1365-3156.2010.02534.x.
[50] Hinton L, Locock L, Knight M. Support for mothers and their families after life-threatening illness in pregnancy and childbirth: a qualitative study in primary care. Br J Gen Pract 2015;65:e563–9. https://doi.org/10.3399/bjgp15X686461.
[51] Godoy SR de, Gualda DMR, Bergamasco RB, Tsunechiro MA. "Near miss": repercussões e percepção da assistência recebida por mulheres sobreviventes egressas de uma unidade de

terapia intensiva. Acta Paul Enferm 2009;22:162–8. https://doi.org/10.1590/S0103-21002009000200008.
[52] Tunçalp Ö, Hindin MJ, Adu-Bonsaffoh K, Adanu R. Listening to Women's Voices: The Quality of Care of Women Experiencing Severe Maternal Morbidity, in Accra, Ghana. PLoS ONE 2012;7:e44536. https://doi.org/10.1371/journal.pone.0044536.
[53] Souza JP, Cecatti JG, Parpinelli MA, Krupa F, Osis MJD. An Emerging "Maternal Near-Miss Syndrome": Narratives of Women Who Almost Died During Pregnancy and Childbirth. Birth 2009;36:149–58. https://doi.org/10.1111/j.1523-536X.2009.00313.x.
[54] Schaap T, Bloemenkamp K, Deneux-Tharaux C, Knight M, Langhoff-Roos J, Sullivan E, et al. Defining definitions: a Delphi study to develop a core outcome set for conditions of severe maternal morbidity. BJOG: Int J Obstet Gy 2019;126:394–401. https://doi.org/10.1111/1471-0528.14833.
[55] Ministero della Salute, Dipartimento della qualità, Direzione generale della programmazione sanitaria, dei livelli di assistenza e dei principi etici di sistema. Raccomandazione per la prevenzione della morte materna correlata al travaglio e/o parto 2007.
[56] World Health Organization, Reproductive Health and Research, World Health Organization, Special Programme of Research D and Research Training in Human Reproduction (World Health Organization). WHO recommendations for prevention and treatment of maternal peripartum infections. 2015.
[57] Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. The Lancet Global Health 2014;2:e323–33. https://doi.org/10.1016/S2214-109X(14)70227-X.
[58] Senior K. In the dark about sepsis. The Lancet Infectious Diseases 2012;12:751–2. https://doi.org/10.1016/S1473-3099(12)70233-5.
[59] Schutte J, Steegers E, Schuitemaker N, Santema J, de Boer K, Pel M, et al. Rise in maternal mortality in the Netherlands: Rise in maternal mortality in the Netherlands. BJOG: An International Journal of Obstetrics & Gynaecology 2010;117:399–406. https://doi.org/10.1111/j.1471-0528.2009.02382.x.
[60] Acosta CD, Knight M, Lee HC, Kurinczuk JJ, Gould JB, Lyndon A. The Continuum of Maternal Sepsis Severity: Incidence and Risk Factors in a Population-Based Cohort Study. PLoS ONE 2013;8:e67175. https://doi.org/10.1371/journal.pone.0067175.
[61] Acosta CD, Kurinczuk JJ, Lucas DN, Tuffnell DJ, Sellers S, Knight M, et al. Severe Maternal Sepsis in the UK, 2011–2012: A National Case-Control Study. PLoS Med 2014;11:e1001672. https://doi.org/10.1371/journal.pmed.1001672.
[62] Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med 2017;43:304–77. https://doi.org/10.1007/s00134-017-4683-6.
[63] Knight M, Kenyon S, Brocklehurst P, Neilson J, Shakespeare J, Kurinczuk JJ (Eds.) on behalf of MBRRACEUK. Saving Lives, Improving Mothers' Care - Lessons learned to inform future maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009–12. Oxford: National Perinatal Epidemiology Unit, University of Oxford: 2014.
[64] Mohamed-Ahmed O, Nair M, Acosta C, Kurinczuk J, Knight M. Progression from severe sepsis in pregnancy to death: a UK population-based case-control analysis. BJOG: Int J Obstet Gy 2015;122:1506–15. https://doi.org/10.1111/1471-0528.13551.
[65] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:801. https://doi.org/10.1001/jama.2016.0287.
[66] Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the

Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:775. https://doi.org/10.1001/jama.2016.0289.
[67] World Health Organization. Statement on Maternal Sepsis. Geneva: World Health Organisation: 2017.
[68] Royal Berkshire - NHS Foundation Trust. Maternal, Sepsis prevention, recognition and management 2016.
[69] Bonet M, Souza JP, Abalos E, Fawole B, Knight M, Kouanda S, et al. The global maternal sepsis study and awareness campaign (GLOSS): study protocol. Reprod Health 2018;15:16. https://doi.org/10.1186/s12978-017-0437-8.
[70] Oud L. Pregnancy-Associated Severe Sepsis: Contemporary State and Future Challenges. Infect Dis Ther 2014;3:175–89. https://doi.org/10.1007/s40121-014-0037-7.
[71] Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. BJOG: An International Journal of Obstetrics & Gynaecology 2011;118:1–203. https://doi.org/10.1111/j.1471-0528.2010.02847.x.
[72] Acosta CD, Knight M. Sepsis and maternal mortality: Current Opinion in Obstetrics and Gynecology 2013;25:109–16. https://doi.org/10.1097/GCO.0b013e32835e0e82.
[73] Kramer HMC, Schutte JM, Zwart JJ, Schuitemaker NWE, Steegers EAP, van Roosmalen J. Maternal mortality and severe morbidity from sepsis in the Netherlands. Acta Obstet Gynecol Scand 2009;88:647–53. https://doi.org/10.1080/00016340902926734.
[74] Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, et al. Saving mothers' lives: reviewing maternal deaths to make motherhood safer: 2006–2008. The eighth report of the confidential enquiries into maternal deaths in the United Kingdom. BJOG; 2011.
[75] Knight M, Kenyon S, Brocklehurst P, Neilson JP, Shakespeare J, Kurinczuk JJ. Saving lives, improving mothers' care: lessons learned to inform future maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-2012. 2014.
[76] Knight M, Nair M, Tuffnell D, Shakespeare J, Kenyon S, Kurinczuk JJ (Eds.) on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2013–15. Oxford: National Perinatal Epidemiology Unit, University of Oxford: 2017.
[77] Donati S, Maraschini A, Lega I, D'Aloja P, Buoncristiano M, Manno V, et al. Maternal mortality in Italy: Results and perspectives of record-linkage analysis. Acta Obstet Gynecol Scand 2018;97:1317–24. https://doi.org/10.1111/aogs.13415.
[78] Serena Donati, Alice Maraschini, Stefania Dell'Oro, Ilaria Lega, Paola D'Aloja1, and the Regional Maternal Mortality Working Group. The way to move beyond the numbers: the lesson learnt from the Italian Obstetric Surveillance System. Ann Ist Super Sanità 2019;55:363–70. https://doi.org/DOI: 10.4415/ANN_19_04_10.
[79] Chantry AA, Berrut S, Donati S, Gissler M, Goldacre R, Knight M, et al. Monitoring severe acute maternal morbidity across Europe: A feasibility study. Paediatr Perinat Epidemiol 2020;34:416–26. https://doi.org/10.1111/ppe.12557.
[80] Acosta C, Bhattacharya S, Tuffnell D, Kurinczuk J, Knight M. Maternal sepsis: a Scottish population-based case-control study: Maternal sepsis: population-based case-control study. BJOG: An International Journal of Obstetrics & Gynaecology 2012;119:474–83. https://doi.org/10.1111/j.1471-0528.2011.03239.x.
[81] Chebbo A, Tan S, Kassis C, Tamura L, Carlson RW. Maternal Sepsis and Septic Shock. Critical Care Clinics 2016;32:119–35. https://doi.org/10.1016/j.ccc.2015.08.010.
[82] Buppasiri P, Lumbiganon P, Thinkhamrop J, Thinkhamrop B. Antibiotic prophylaxis for third- and fourth-degree perineal tear during vaginal birth. Cochrane Database of Systematic Reviews 2014. https://doi.org/10.1002/14651858.CD005125.pub4.
[83] Elton R, Chaudhari S. Sepsis in obstetrics. BJA Education 2015;15:259–64. https://doi.org/10.1093/bjaceaccp/mku062.

[84] Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early Goal-Directed Therapy in the Treatment of Severe Sepsis and Septic Shock. N Engl J Med 2001;345:1368–77. https://doi.org/10.1056/NEJMoa010307.
[85] Rivers EP, Katranji M, Jaehne KA, Brown S, Abou Dagher G, Cannon C, et al. Early interventions in severe sepsis and septic shock: a review of the evidence one decade later. Minerva Anestesiol 2012;78:712–24.
[86] Rusconi AM, Bossi I, Lampard JG, Szava-Kovats M, Bellone A, Lang E. Early goal-directed therapy vs usual care in the treatment of severe sepsis and septic shock: a systematic review and meta-analysis. Intern Emerg Med 2015;10:731–43. https://doi.org/10.1007/s11739-015-1248-y.
[87] Royal College of Obstetricians and Gynaecologists. Bacterial Sepsis in Pregnancy. 2012.
[88] Yoon BH, Romero R, Park JS, Kim CJ, Kim SH, Choi J-H, et al. Fetal exposure to an intra-amniotic inflammation and the development of cerebral palsy at the age of three years. American Journal of Obstetrics and Gynecology 2000;182:675–81. https://doi.org/10.1067/mob.2000.104207.
[89] van Dillen J, Mesman J, Zwart J, Bloemenkamp K, van Roosmalen J. Introducing maternal morbidity audit in the Netherlands: Audit of severe acute maternal morbidity in the Netherlands. BJOG: An International Journal of Obstetrics & Gynaecology 2010;117:416–21. https://doi.org/10.1111/j.1471-0528.2009.02480.x.
[90] World Health Organization. WHO recommendations for prevention and treatment of preeclampsia and eclampsia. Implications and Actions. 2013.
[91] Shennan AH, Redman C, Cooper C, Milne F. Are most maternal deaths from pre-eclampsia avoidable? The Lancet 2012;379:1686–7. https://doi.org/10.1016/S0140-6736(11)60785-X.
[92] Sibai BM. Diagnosis, Prevention, and Management of Eclampsia: Obstetrics & Gynecology 2005;105:402–10. https://doi.org/10.1097/01.AOG.0000152351.13671.99.
[93] Royal College of Obstetricians and Gynaecologists. Management of severe pre-eclampsia/eclampsia. 2006.
[94] Douglas KA, Redman CWG. Eclampsia in the United Kingdom. BMJ 1994;309:1395–400. https://doi.org/10.1136/bmj.309.6966.1395.
[95] Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews 2010. https://doi.org/10.1002/14651858.CD000025.pub2.
[96] Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. The Lancet 1995;345:1455–63.
[97] Knight M. Eclampsia in the United Kingdom 2005. BJOG: An International Journal of Obstetrics & Gynaecology 2007;114:1072–8. https://doi.org/10.1111/j.1471-0528.2007.01423.x.
[98] Schaap T, Knight M, Zwart J, Kurinczuk J, Brocklehurst P, van Roosmalen J, et al. Eclampsia, a comparison within the International Network of Obstetric Survey Systems. BJOG: Int J Obstet Gy 2014;121:1521–8. https://doi.org/10.1111/1471-0528.12712.
[99] Schaap TP, van den Akker T, Zwart JJ, van Roosmalen J, Bloemenkamp KWM. A national surveillance approach to monitor incidence of eclampsia: The Netherlands Obstetric Surveillance System. Acta Obstet Gynecol Scand 2019;98:342–50. https://doi.org/10.1111/aogs.13493.
[100] Senatore S, Donati S, Andreozzi S. (Ed.). Studio della cause di mortalità e morbosità materna e messa a punto di modelli di sorveglianza della mortalità materna. Istituto Superiore di Sanità; 2012.
[101] Hastie R, Brownfoot FC, Cluver CA, Walker SP, Hesselman S, Tong S, et al. Predictive Value of the Signs and Symptoms Preceding Eclampsia: A Systematic Review. Obstetrics & Gynecology 2019;134:677–84. https://doi.org/10.1097/AOG.0000000000003476.

[102] Sibai B. Diagnosis and Management of Gestational Hypertension and Preeclampsia. Obstetrics & Gynecology 2003;102:181–92. https://doi.org/10.1016/S0029-7844(03)00475-7.
[103] Fitzpatrick K, Tuffnell D, Kurinczuk J, Knight M. Incidence, risk factors, management and outcomes of amniotic-fluid embolism: a population-based cohort and nested case-control study. BJOG: Int J Obstet Gy 2016;123:100–9. https://doi.org/10.1111/1471-0528.13300.
[104] Pacheco LD, Saade G, Hankins GDV, Clark SL. Amniotic fluid embolism: diagnosis and management. American Journal of Obstetrics and Gynecology 2016;215:B16–24. https://doi.org/10.1016/j.ajog.2016.03.012.
[105] Clark SL, Romero R, Dildy GA, Callaghan WM, Smiley RM, Bracey AW, et al. Proposed diagnostic criteria for the case definition of amniotic fluid embolism in research studies. American Journal of Obstetrics and Gynecology 2016;215:408–12. https://doi.org/10.1016/j.ajog.2016.06.037.
[106] Sultan P, Seligman K, Carvalho B. Amniotic fluid embolism: update and review. Current Opinion in Anaesthesiology 2016;29:288–96. https://doi.org/10.1097/ACO.0000000000000328.
[107] Fitzpatrick KE, van den Akker T, Bloemenkamp KWM, Deneux-Tharaux C, Kristufkova A, Li Z, et al. Risk factors, management, and outcomes of amniotic fluid embolism: A multicountry, population-based cohort and nested case-control study. PLoS Med 2019;16:e1002962. https://doi.org/10.1371/journal.pmed.1002962.
[108] Knight M, Berg C, Brocklehurst P, Kramer M, Lewis G, Oats J, et al. Amniotic fluid embolism incidence, risk factors and outcomes: a review and recommendations. BMC Pregnancy Childbirth 2012;12:7. https://doi.org/10.1186/1471-2393-12-7.
[109] Overview of the Nationwide Inpatient Sample (NIS). n.d.
[110] National hospital morbidity database (NHMD). n.d.
[111] Kramer M, Rouleau J, Liu S, Bartholomew S, Joseph K, for the Maternal Health Study Group of the Canadian Perinatal Surveillance System. Amniotic fluid embolism: incidence, risk factors, and impact on perinatal outcome: Amniotic fluid embolism. BJOG: An International Journal of Obstetrics & Gynaecology 2012;119:874–9. https://doi.org/10.1111/j.1471-0528.2012.03323.x.
[112] Bonnet M-P, Zlotnik D, Saucedo M, Chassard D, Bouvier-Colle M-H, Deneux-Tharaux C. Maternal Death Due to Amniotic Fluid Embolism: A National Study in France. Anesthesia & Analgesia 2018;126:175–82. https://doi.org/10.1213/ANE.0000000000002511.
[113] Clark SL, Hankins GDV, Dudley DA, Dildy GA, Porter TF. Amniotic fluid embolism: Analysis of the national registry. American Journal of Obstetrics and Gynecology 1995;172:1158–69. https://doi.org/10.1016/0002-9378(95)91474-9.
[114] Yentis S. Amniotic fluid embolism. Can J Anesth/J Can Anesth 2001;48:829–829. https://doi.org/10.1007/BF03016710.
[115] Dean LS, Rogers RP, Harley RA, Hood DD. Case Scenario: Amniotic Fluid Embolism. Anesthesiology 2012;116:186–92. https://doi.org/10.1097/ALN.0b013e31823d2d99.
[116] Benson MD. A hypothesis regarding complement activation and amniotic fluid embolism. Medical Hypotheses 2007;68:1019–25. https://doi.org/10.1016/j.mehy.2006.09.052.
[117] Kaur K, Bhardwaj M, Kumar P, Singhal S, Singh T, Hooda S. Amniotic fluid embolism. J Anaesthesiol Clin Pharmacol 2016;32:153. https://doi.org/10.4103/0970-9185.173356.
[118] Lier MCI, Malik RF, Ket JCF, Lambalk CB, Brosens IA, Mijatovic V. Spontaneous hemoperitoneum in pregnancy (SHiP) and endometriosis — A systematic review of the recent literature. European Journal of Obstetrics & Gynecology and Reproductive Biology 2017;219:57–65. https://doi.org/10.1016/j.ejogrb.2017.10.012.
[119] Brosens IA, Lier MC, Mijatovic V, Habiba M, Benagiano G. Severe spontaneous hemoperitoneum in pregnancy may be linked to in vitro fertilization in patients with endometriosis: a systematic review. Fertility and Sterility 2016;106:692–703. https://doi.org/10.1016/j.fertnstert.2016.05.025.

[120] Brosens IA, Fusi L, Brosens JJ. Endometriosis is a risk factor for spontaneous hemoperitoneum during pregnancy. Fertility and Sterility 2009;92:1243–5. https://doi.org/10.1016/j.fertnstert.2009.03.091.
[121] Glavind MT, Forman A, Arendt LH, Nielsen K, Henriksen TB. Endometriosis and pregnancy complications: a Danish cohort study. Fertility and Sterility 2017;107:160–6. https://doi.org/10.1016/j.fertnstert.2016.09.020.
[122] Vigano P, Corti L, Berlanda N. Beyond infertility: obstetrical and postpartum complications associated with endometriosis and adenomyosis. Fertility and Sterility 2015;104:802–12. https://doi.org/10.1016/j.fertnstert.2015.08.030.
[123] Lier MCI, Brosens IA, Mijatovic V, Habiba M, Benagiano G. Decidual Bleeding as a Cause of Spontaneous Hemoperitoneum in Pregnancy and Risk of Preterm Birth. Gynecol Obstet Invest 2017;82:313–21. https://doi.org/10.1159/000468933.
[124] Pollock W, Peek MJ, Wang A, Li Z, Ellwood D, Homer CSE, et al. Eclampsia in Australia and New Zealand: A prospective population-based study. Aust N Z J Obstet Gynaecol 2020;60:533–40. https://doi.org/10.1111/ajo.13100.
[125] Bell MJ. A Historical Overview of Preeclampsia-Eclampsia. Journal of Obstetric, Gynecologic & Neonatal Nursing 2010;39:510–8. https://doi.org/10.1111/j.1552-6909.2010.01172.x.
[126] Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. The Lancet 2005;365:785–99. https://doi.org/10.1016/S0140-6736(05)17987-2.
[127] Cooray SD, Edmonds SM, Tong S, Samarasekera SP, Whitehead CL. Characterization of Symptoms Immediately Preceding Eclampsia: Obstetrics & Gynecology 2011;118:995–9. https://doi.org/10.1097/AOG.0b013e3182324570.
[128] Sibai BM, Abdella TN, Spinnato JA, Anderson GD. Eclampsia. American Journal of Obstetrics and Gynecology 1986;154:581–6. https://doi.org/10.1016/0002-9378(86)90605-8.
[129] Berhan Y, Berhan A. Should magnesium sulfate be administered to women with mild pre-eclampsia? A systematic review of published reports on eclampsia: Systematic review of reports on eclampsia. J Obstet Gynaecol Res 2015;41:831–42. https://doi.org/10.1111/jog.12697.
[130] Walsh CA, Baxi LV. Mean arterial pressure and prediction of pre-eclampsia. BMJ 2008;336:1079–80. https://doi.org/10.1136/bmj.39555.518750.80.
[131] Nair M, Kurinczuk JJ, Knight M. Ethnic Variations in Severe Maternal Morbidity in the UK– A Case Control Study. PLoS ONE 2014;9:e95086. https://doi.org/10.1371/journal.pone.0095086.
[132] Cromi A, Marconi N, Casarin J, Cominotti S, Pinelli C, Riccardi M, et al. Maternal intra- and postpartum near-miss following assisted reproductive technology: a retrospective study. BJOG: Int J Obstet Gy 2018;125:1569–78. https://doi.org/10.1111/1471-0528.15308.
[133] Martin AS, Monsour M, Kissin DM, Jamieson DJ, Callaghan WM, Boulet SL. Trends in Severe Maternal Morbidity After Assisted Reproductive Technology in the United States, 2008–2012. Obstetrics & Gynecology 2016;127:59–66. https://doi.org/10.1097/AOG.0000000000001197.
[134] Sibai BM, Hauth J, Caritis S, Lindheimer MD, MacPherson C, Klebanoff M, et al. Hypertensive disorders in twin versus singleton gestations. American Journal of Obstetrics and Gynecology 2000;182:938–42. https://doi.org/10.1016/S0002-9378(00)70350-4.
[135] Jackson RA, Gibson KA, Wu YW, Croughan MS. Perinatal Outcomes in Singletons Following In Vitro Fertilization: A Meta-Analysis: Obstetrics & Gynecology 2004;103:551–63. https://doi.org/10.1097/01.AOG.0000114989.84822.51.
[136] Italian Ministry of Health. RELAZIONE DEL MINISTRO DELLA SALUTE AL PARLAMENTO SULLO STATO DI ATTUAZIONE DELLA LEGGE CONTENENTE NORME IN MATERIA DI PROCREAZIONE MEDICALMENTE ASSISTITA (LEGGE 19 FEBBRAIO 2004, N. 40, ARTICOLO 15). 2018.

[137] Zwart JJ, Richters A, Öry F, de Vries JIP, Bloemenkamp KWM, van Roosmalen J. Eclampsia in the Netherlands: Obstetrics & Gynecology 2008;112:820–7. https://doi.org/10.1097/AOG.0b013e3181875eb3.
[138] Tolcher MC, Chu DM, Hollier LM, Mastrobattista JM, Racusin DA, Ramin SM, et al. Impact of USPSTF recommendations for aspirin for prevention of recurrent preeclampsia. American Journal of Obstetrics and Gynecology 2017;217:365.e1-365.e8. https://doi.org/10.1016/j.ajog.2017.04.035.
[139] Poon LC, Wright D, Rolnik DL, Syngelaki A, Delgado JL, Tsokaki T, et al. Aspirin for Evidence-Based Preeclampsia Prevention trial: effect of aspirin in prevention of preterm preeclampsia in subgroups of women according to their characteristics and medical and obstetrical history. American Journal of Obstetrics and Gynecology 2017;217:585.e1-585.e5. https://doi.org/10.1016/j.ajog.2017.07.038.
[140] American College of Obstetrician and Gynecologists (ACOG). Low-dose aspirin use during pregnancy. ACOG Committee Opinion N 743 2018;132:e44-52.
[141] Magpie Trial Follow-Up Study Collaborative Group. The Magpie Trial: a randomised trial comparing magnesium sulphate with placebo for pre-eclampsia. Outcome for women at 2 years. BJOG: An International Journal of Obstetrics & Gynaecology 2006;114:300–9. https://doi.org/10.1111/j.1471-0528.2006.01166.x.
[142] Jaskolka D, Retnakaran R, Zinman B, Kramer C. Fetal sex and maternal risk of pre-eclampsia/eclampsia: a systematic review and meta-analysis. BJOG: Int J Obstet Gy 2017;124:553–60. https://doi.org/10.1111/1471-0528.14163.
[143] Vincent J-L, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, et al. Sepsis in European intensive care units: Results of the SOAP study*: Critical Care Medicine 2006;34:344–53. https://doi.org/10.1097/01.CCM.0000194725.48928.3A.
[144] Basili, Messia, Montorio, Tamburini. Certificato di assistenza al parto (CeDAP) Analisi dell'evento nascita - Anno 2015 2018.
[145] Acosta CD, Harrison DA, Rowan K, Lucas DN, Kurinczuk JJ, Knight M. Maternal morbidity and mortality from severe sepsis: a national cohort study. BMJ Open 2016;6:e012323. https://doi.org/10.1136/bmjopen-2016-012323.
[146] Bakhtawar S, Sheikh S, Qureshi R, Hoodbhoy Z, Payne B, Azam I, et al. Risk factors for postpartum sepsis: a nested case-control study. BMC Pregnancy Childbirth 2020;20:297. https://doi.org/10.1186/s12884-020-02991-z.
[147] Chief Nursing Officers of England, Northen Ireland, Scotland and Wales. Midwifery 2020: Delivering Expectation, 2010 2010.
[148] World Health Organization. WHO recommendations: intrapartum care for a positive childbirth experience. 2018.
[149] Royal College of Midwives. Reaching out: Involving Fathers in Maternity Care 2011.
[150] Schytt E, Bergström M. First-time fathers' expectations and experiences of childbirth in relation to age. Midwifery 2014;30:82–8. https://doi.org/10.1016/j.midw.2013.01.015.
[151] Rijnders M. Perinatal Factors Related to Negative or Positive Recall of Birth Experience in Women 3 Years Postpartum in the Netherlands 2008.
[152] Hildingsson I. Women's birth expectations, are they fulfilled? Findings from a longitudinal Swedish cohort study. Women and Birth 2015;28:e7–13. https://doi.org/10.1016/j.wombi.2015.01.011.
[153] Mei JY, Afshar Y, Gregory KD, Kilpatrick SJ, Esakoff TF. Birth Plans: What Matters for Birth Experience Satisfaction. Birth 2016;43:144–50. https://doi.org/10.1111/birt.12226.
[154] Fair CD, Morrison TE. The relationship between prenatal control, expectations, experienced control, and birth satisfaction among primiparous women. Midwifery 2012;28:39–44. https://doi.org/10.1016/j.midw.2010.10.013.

[155] DeLuca RS, Lobel M. Diminished Control and Unmet Expectations: Testing a Model of Adjustment to Unplanned Cesarean Delivery: Adjustment to Cesarean Delivery. Analyses of Social Issues and Public Policy 2014;14:183–204. https://doi.org/10.1111/asap.12040.
[156] Iles J, Pote H. Postnatal posttraumatic stress: A grounded theory model of first-time mothers' experiences. Journal of Reproductive and Infant Psychology 2015;33:238–55. https://doi.org/10.1080/02646838.2015.1030732.
[157] D'Cruz L, Lee C. Childbirth expectations: an Australian study of young childless women. Journal of Reproductive and Infant Psychology 2014;32:199–211. https://doi.org/10.1080/02646838.2013.875134.
[158] van Bussel J, Spitz B, Demyttenaere K. Childbirth expectations and experiences and associations with mothers' attitudes to pregnancy, the child and motherhood. Journal of Reproductive and Infant Psychology 2010;28:143–60. https://doi.org/10.1080/02646830903295026.
[159] Haines H, Rubertsson C, Pallant JF, Hildingsson I. Womens' attitudes and beliefs of childbirth and association with birth preference: A comparison of a Swedish and an Australian sample in mid-pregnancy. Midwifery 2012;28:e850–6. https://doi.org/10.1016/j.midw.2011.09.011.
[160] Christiaens W, Verhaeghe M, Bracke P. Childbirth expectations and experiences in Belgian and Dutch models of maternity care. Journal of Reproductive and Infant Psychology 2008;26:309–22. https://doi.org/10.1080/02646830802350872.
[161] Cipolletta S, Sperotto A. From the hospital organisation to the childbirth practice: Italian women's experiences. Journal of Reproductive and Infant Psychology 2012;30:326–36. https://doi.org/10.1080/02646838.2012.707777.
[162] Rota A, Antolini L, Colciago E, Nespoli A, Borrelli SE, Fumagalli S. Timing of hospital admission in labour: latent versus active phase, mode of birth and intrapartum interventions. A correlational study. Women and Birth 2017. https://doi.org/10.1016/j.wombi.2017.10.001.
[163] Euro-Peristat Project. European Perinatal Health Report. Core indicators of the health and care of pregnant women and babies in Europe in 2015. 2018.
[164] International Confederation of Midwives. Core Document International Definition of the Midwife 2017.
[165] Sanders RA, Crozier K. How do informal information sources influence women's decision-making for birth? A meta-synthesis of qualitative studies. BMC Pregnancy and Childbirth 2018;18. https://doi.org/10.1186/s12884-017-1648-2.
[166] Young K, Miller YD. Keeping it Natural: Does Persuasive Magazine Content Have an Effect on Young Women's Intentions for Birth? Women & Health 2015;55:447–66. https://doi.org/10.1080/03630242.2015.1022690.
[167] Soriano-Vidal FJ, Vila-Candel R, Soriano-Martín PJ, Tejedor-Tornero A, Castro-Sánchez E. The effect of prenatal education classes on the birth expectations of Spanish women. Midwifery 2018;60:41–7. https://doi.org/10.1016/j.midw.2018.02.002.
[168] Preis H, Chen R, Eisner M, Pardo J, Peled Y, Wiznitzer A, et al. Testing a biopsychosocial model of the basic birth beliefs. Birth 2018;45:79–87. https://doi.org/10.1111/birt.12313.
[169] Takács L, Seidlerová JM, Šulová L, Hoskovcová SH. Social psychological predictors of satisfaction with intrapartum and postpartum care – what matters to women in Czech maternity hospitals? Open Medicine 2015;10. https://doi.org/10.1515/med-2015-0022.
[170] Bar-On S, Benyamini Y, Ebrahimoff M, Many A. Mother knows best? Comparing primiparous parturients' expectations and predictions with actual birth outcomes. Journal of Perinatal Medicine 2014;42. https://doi.org/10.1515/jpm-2013-0236.
[171] Raphael-Leff, J. Psychological processes of childbearing. London, United Kingdom: Ann Freud Centre. 2005.
[172] Brodrick A. Exploring women's pre-birth expectations of labour and the role of the midwife. Evidence Based Midwifery 2008.

[173] Fleming SE, Donovan-Batson C, Burduli E, Barbosa-Leiker C, Hollins Martin CJ, Martin CR. Birth Satisfaction Scale/Birth Satisfaction Scale-Revised (BSS/BSS-R): A large scale United States planned home birth and birth centre survey. Midwifery 2016;41:9–15. https://doi.org/10.1016/j.midw.2016.07.008.
[174] Bayes S, Fenwick J, Hauck Y. A Qualitative Analysis of Women's Short Accounts of Labour and Birth in a Western Australian Public Tertiary Hospital. Journal of Midwifery & Women's Health 2008;53:53–61. https://doi.org/10.1016/j.jmwh.2007.07.021.
[175] Goldbort J. Women's Lived Experience of Their Unexpected Birthing Process. MCN 2009;34.
[176] Moore MF. Multicultural Differences in Women's Expectations of Birth. ABNF J 2016;27:39–43.
[177] Morrow, R., Rodriguez, A. and King, N. . Colaizzi's descriptive phenomenological method. The Psychologist 2015;28:643–4.
[178] Hollander MH, van Hastenberg E, van Dillen J, van Pampus MG, de Miranda E, Stramrood CAI. Preventing traumatic childbirth experiences: 2192 women's perceptions and views. Archives of Women's Mental Health 2017;20:515–23. https://doi.org/10.1007/s00737-017-0729-6.
[179] Glaser BG, Strauss AL. The discovery of grounded theory: strategies for qualitative research. 4. paperback printing. New Brunswick: Aldine; 2009.
[180] Fenwick J, Bayes S, Johansson M. A qualitative investigation into the pregnancy experiences and childbirth expectations of Australian fathers-to-be. Sexual & Reproductive Healthcare 2012;3:3–9. https://doi.org/10.1016/j.srhc.2011.11.001.
[181] Young E. Maternal expectations: do they match experience? Community Pract 2008;81:27–30.
[182] Mattern E, Lohmann S, Ayerle GM. Experiences and wishes of women regarding systemic aspects of midwifery care in Germany: a qualitative study with focus groups. BMC Pregnancy and Childbirth 2017;17. https://doi.org/10.1186/s12884-017-1552-9.
[183] Gadamer, Hans Georg. Philosophical hermeneutics. David E. Linge, Ed. & Trans. Berkeley, CA: University of California Press.: 1976.
[184] Paterson, Higgs. Using hermeneutics as a qualitative research approach in professional practice. The Qualitative Report 2005:339–57.
[185] Borrelli SE, Spiby H, Walsh D. The kaleidoscopic midwife: A conceptual metaphor illustrating first-time mothers' perspectives of a good midwife during childbirth. A grounded theory study. Midwifery 2016;39:103–11. https://doi.org/10.1016/j.midw.2016.05.008.
[186] World Health Organization. Standards for improving quality of maternal and newborn care in health facilities. 2016.
[187] Bélanger-Lévesque M-N, Pasquier M, Roy-Matton N, Blouin S, Pasquier J-C. Maternal and paternal satisfaction in the delivery room: a cross-sectional comparative study. BMJ Open 2014;4:e004013. https://doi.org/10.1136/bmjopen-2013-004013.
[188] Lewis L, Hauck YL, Ronchi F, Crichton C, Waller L. Gaining insight into how women conceptualize satisfaction: Western Australian women's perception of their maternity care experiences. BMC Pregnancy and Childbirth 2016;16. https://doi.org/10.1186/s12884-015-0759-x.
[189] Johnson RB, Onwuegbuzie AJ, Turner LA. Toward a Definition of Mixed Methods Research. Journal of Mixed Methods Research 2007;1:112–33. https://doi.org/10.1177/1558689806298224.
[190] Chin R, Daiches A, Hall P. A qualitative exploration of first-time fathers' experiences of becoming a father. Community Pract 2011;84:19–23.
[191] Porrett L, Barkla S, Knights J, de Costa C, Harmen S. An Exploration of the Perceptions of Male Partners Involved in the Birthing Experience at a Regional Australian Hospital. Journal

of Midwifery & Women's Health 2013;58:92–7. https://doi.org/10.1111/j.1542-2011.2012.00238.x.
[192] Walsh D, Downe S. Appraising the quality of qualitative research. Midwifery 2006;22:108–19. https://doi.org/10.1016/j.midw.2005.05.004.
[193] M Reiners G. Understanding the Differences between Husserl's (Descriptive) and Heidegger's (Interpretive) Phenomenological Research. J Nurs Care 2012;01. https://doi.org/10.4172/2167-1168.1000119.
[194] Stewart, Shandasani. Focus groups. Theory and practice. London: Sage Publications. London: Sage Pubblication: 1990.
[195] Carlsen B, Glenton C. What about N? A methodological study of sample-size reporting in focus group studies. BMC Med Res Methodol 2011;11:26. https://doi.org/10.1186/1471-2288-11-26.
[196] Cleary M, Horsfall J, Hayter M. Data collection and sampling in qualitative research: does size matter? J Adv Nurs 2014;70:473–5. https://doi.org/10.1111/jan.12163.
[197] Rees,C. Introduction to Research for Midwives. Great Britain: Elsevier; 2011.
[198] Parahoo, K. Nursing Research. Principles, Process and Issues. 2nd Edition. Basingstoke.: Palgrave Macmillan.; 2006.
[199] Shenton, Andrew K. Strategies for ensuring trustworthiness in qualitative research projects. Education for Information 2004:63–75.
[200] Johansson M, Fenwick J, Premberg å. A meta-synthesis of fathers′ experiences of their partner′s labour and the birth of their baby. Midwifery 2015;31:9–18. https://doi.org/10.1016/j.midw.2014.05.005.
[201] Longworth HL, Kingdon CK. Fathers in the birth room: What are they expecting and experiencing? A phenomenological study. Midwifery 2010. https://doi.org/10.1016/j.midw.2010.06.013.

II PART | PARENTS' BIRTH EXPECTATIONS AND THEIR FULFILMENT

PREMISE

The present study involved two steps. The first step consisted of conducting focus groups with parents' to be between 36 to 40 week of gestation. Focus groups were conducted on the 17th of July 2019. The second step consisted of conducting semi-structured interviews with both parents, individually. This phase was expected to take place at least 6 weeks after the women gave birth. However, due to different time-related issues, interviews are in progress. Data will be analysed when all participants will be interviewed.

ABSTRACT

Background: Literature suggests that the majority of women expect to have a straightforward birth, however as events during labour and birth could also go differently than expectations, women are also aware that sometimes they will need to go with the flow. Fathers-to-be expect to be present, to share the experience with their partner and to have a natural process and a healthy baby. However there are also men who feel pressured to attend, could express overwhelming feelings and inadequacy in their ability to support their partner. In addition, the literature highlights that women exposed to a more medicalized birth-culture are less likely to view birth as a natural event and make women more prone to interventions

Aim: To explore parents' expectations of labour and birth during pregnancy and to investigate whether their expectations are fulfilled following birth.

Method: A qualitative methodology is proposed, using a descriptive approach. Data collection was undertaken in the form of focus groups during pregnancy and semi-structured interviews after birth.

Anticipated results: Women will probably expect to have a normal birth and to be with their partner during labour and childbirth, as they had a low risk pregnancy. Father's to be will probably expected to be with their partners and to know their baby immediately after birth. The high risk culture around the Italian birth-context and the place of birth choose by couples could make the differences, leading to different expectations compared to the ones found in the literature.

Conclusions: A positive experience and satisfaction with birth can be influenced by expectations' fulfilment. However, it has been demonstrated that maternal expectations could be influenced by a high risk culture surrounding childbirth and the mass media negative information, and that women's attitudes towards obstetric interventions have become more positive.

Midwives have a key role to empower women to experience feelings of fulfilment after their childbirth, in order to have a positive experience of the process. Midwives, however, should also support fathers-to-be, in order to avoid feelings of isolation, to encourage a family centred approach and to promote benefits for the mother and the newborn, that result from fathers being involved in the maternity care.

Keywords: birth expectations; paternal expectations; parent's-to-be expectations; satisfaction with birth; satisfaction of midwifery care

CHAPTER ONE: PARENTS' EXPECTATIONS CONTEXT

1.1 Introduction

This chapter introduces a research study focused on parental expectations of childbirth, it documents the proposed research question and provides a rationale for its selection. In addition, the research design is outlined and a brief background is presented to explain the relevance of the topic.

1.2 Research question

What are parents' expectations regarding childbirth and are these expectations fulfilled?

1.3 Context study

Pregnancy, childbirth and the postnatal period are important phases in the parenthood pathway. Childbirth is a family event and, in the recent years, maternity care has emphasized the importance of family-centered care [147]. The presence of fathers can help to improve women's birth experience by providing emotional support and reassurance during labour and delivery [148,149]. However father's expectations are not well documented. To facilitate a positive birth experience for the father, it is essential that midwives include him in conversations and in the support and caring actions of his partner [150]. Research evidence indicates that childbirth expectations influence childbirth experience [151–153]. Although some research identifies that there is no correlation between them [154]. However fulfilment of maternal expectations, i.e. aiming for a positive experience and satisfaction with birth, appears to be associated with lower depressed mood [155] that could potentially influence the relationship with the baby [156]. Women's beliefs and perceptions seem to be based on an expectation that pregnancy and labour is either a normal, natural process or that it is a medical condition with risks [157–159] and that these beliefs related to the way care is organized [159,160]. Assisted vaginal delivery and unplanned caesarean section appear as factors contributing to a negative experience of childbirth [151,161]. Others argue that one of the most powerful influence is the attitude and behaviours of caregivers [152,154]. Considering the trend that intrapartum interventions are rising everywhere in Europe, it should be considered that in Italy this dramatic rise of intrapartum interventions is more evident [162,163]. Therefore, an exploration of parental childbearing expectation before and after birth offers useful information about current maternity care provision, with potential implications for midwifery practice.

1.4 Rationale of the study

Midwives play a key role promoting the health and wellbeing of women and their newborn.

Midwifery is a profession that is based upon a partnership between women and midwives aimed at promoting healthy outcomes [164]. Midwives are in an ideal position to empower both women and men during pregnancy, to monitor expectations, aiming for a positive childbirth experience [152]. Quality of care is increasingly recognized as a critical aspect for maternal and newborn wellbeing, mainly with respect to care around labour and delivery and in the immediate postnatal period [148]. Birth satisfaction is one of the most important outcomes by which quality of maternal care can be assessed. From the literature it appears there is a relationship between maternal birth expectations

and ultimate satisfaction [151–153]. A family centred care approach, appears to be the most effective when considering maternal and paternal expectations. This study has the potential to explore parents' expectations regarding childbirth and to help midwives improve the care they provide to a couple in order to achieve positive birth experiences.

1.5 Overview of research designs

A qualitative methodology and a phenomenological approach was adopted for this study. Purposive sampling was used to select participants. Between eight and ten couples were recruited from antenatal classes. Childbirth expectations were explored using a focus group for women and a focus group for men during the third trimester of pregnancy.

After birth, three to four couples that meet the inclusion criteria were randomly selected. Semi-structured interviews were conducted with mothers and fathers individually, to explore if expectations have been met. The focus groups discussions and interviews were audio recorded, will be transcribed verbatim and analysed using a thematic approach.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

In this chapter the literature exploring maternal and paternal expectations of childbirth and whether these are being fulfilled.

The Literature review was divided in two major themes regarding both research questions. These are parents' expectations on childbirth and fulfilment in relationship with satisfaction with the birth experience. Sub-themes were included to further explore the individual themes and develop a more in depth understanding.

Search criteria are provided with the most relevant evidence included in the review.

2.2 Search strategy

A systematic search of the Literature was undertaken using PubMed, Cinahl, PsychInfo and Cochrane Library (Database of Systematic Review) (Appendix 1), between the 22nd of March and the 5th of April 2018 during my visiting period at the University of Surrey (UK).

2.3 Parents' Expectations on childbirth

2.3.1 Role of information and education

Women have access to many information sources that could influence their view of childbirth. Women also access informal information that can increase their level of anxiety and challenge their existing attitudes and aspirations of personal birth process. They often seek informal information as a way to mitigate the experience of discordant data provided by maternity staff [165]. Professionals are often unaware of women's information seeking behaviour and this could create a barrier to women-centred care and support [165]. Various forms of media continue to provide narrative and images of birth promoting the benefits of medicalized birth and drama. Thus, this will be an ongoing issue for the foreseeable future, in the climate of expanding technologies and access to birth related media and information. Sander Crozie's [165] meta-synthesis highlights the significant impact of informal information sources on women's decision making for birth. Midwives should provide individualised information and develop their understanding of women's expectations to improve experiences of childbirth for women and their families. This meta-synthesis used the term "informal information sources" to capture all the individual sources of data (the internet, television documentaries, visual media, newspaper reports, childbirth magazines, mobile phone apps, social media and birth stories). This offered an opportunity to form a holistic understanding of the different information that women utilise. Although the Meta-synthesis is acknowledged to be an effective way of collating, interpreting and representing synthesised qualitative data and authors checked papers using the National Institute of Health and Care Excellence quality appraisal checklist for qualitative studies, the evidence was collected over a relatively short period of time. Due to the expanding speed of information accessible to women, it provides only a contemporary view of women's influencing factors, which could evolve very quickly.

Young and Miller [166], conducted a randomized controlled trial with non-pregnant women who wished to have children in future. They demonstrated that exposure to magazine articles that

endorse childbirth as a normal physiological event, significantly reduces women's intentions for a medicalized birth. The researchers concluded that women exposed to positive communication regarding childbirth, are more likely to change their intention towards a more physiological birth compared to those who were not exposed to these type of magazines. This study [166] used a three-group experimental design. Participants (N = 180) were allocated via computer randomization to one of three conditions: celebrity endorsement of non-medicalized birth, non-celebrity endorsement of non-medicalized birth, or a control condition (endorsement of organic eating). Using a quantitative methodology was appropriate to establish a causality relationship between an intervention (women reading magazine articles focusing on normal birth) and the outcome (intention towards childbirth). Researchers used several Scales to test the pre and post exposure women's birth attitude: Intention for medicalized birth, Perceived risk of birth, Expectations for labour and birth, Attitudes toward medicalized and non-medicalized birth. However, validated scales were not available to measure the theory-based constructs of interest in a population of women who were not pregnant and had not given birth, so the scales used were either developed specifically for this study or adapted from previously validated scales. It means that measures used may not have adequately reflected the complexity of attitudes toward birth by forcing participants to report one dimensional attitudes toward non-medicalized and medicalized birth. Furthermore a high proportion of recruited participants were lost to follow-up and differed slightly in pre-exposure measures (greater women with intentions for medicalized birth were lost). This may have resulted in participants' bias, which could affect the accuracy and generalizability of the results. The present study was unable to examine whether outcomes have a short term effect or could predict future birth choices, but it has implications for informing mass strategies to reduce unnecessary intervention in labour and birth.

Preconceived expectations could also be influenced by communication and education through antenatal classes [167]. A prospective, multicentre, observational study of Soriano-Vidal et al. [167] measuring variables in pregnant women attending antenatal classes, showed that midwives could make a difference during the antenatal care, giving women evidence-based information to shape their birth plans. The present study had a valuable approach to establish association between variables, however it has a limitation because the researcher was the same one conducting the antenatal class. Researchers, in order to reduce this bias, used the same educational material for all antenatal sessions. Moreover, the research evaluated only standardized care throughout a proposed birth plan, than other preferences could not be considered. This could impact especially on women who were in their subsequent pregnancy, less represented than primiparous participants, and could also affect the results of the study.

2.4.2 Women's expectations

The importance of women's expectations on the experience of birth has been studied and questioned. Some researches argue that fulfilled maternal expectations increase a more positive overall childbirth experience [151–153]. Alternatively other research showed there is no correlation between them [154].

D'Cruz and Lee [157] recruited young childless Australian women to respond to an on-line survey measuring their expected preferences for delivery mode, for birth attendant (midwife or obstetrician), reasons for their preferences, childbirth self-efficacy, childbirth fear, general anxiety, depression and life satisfaction. They found that childless women have a multitude of aspirations and expectations. The majority of participants would prefer a vaginal delivery and obstetric-led care, the latter was associated with higher childbirth fear and general anxiety. In addition, these women would prefer midwife led-care for emotional support. This study suggests that young childless women are already influenced by cultural factors due to the medicalization of childbirth, overestimation of childbirth risks and mass media's influence. These could be the reasons why some women reported high levels of fear and low level of self-efficacy. The authors [157] used a mixed method design. An on-line survey with different Scales was provided to examine General anxiety and depression, Life satisfaction, Childbirth preferences, Childbirth self-efficacy and Childbirth fear. Open-ended comments were add on reasons regarding the expected preference for delivery mode and for birth attendant. The final sample size was of three hundred and thirty-four participants. Although a qualitative methodology would be the most appropriate to explore childless women's expectations on childbirth, as it would allow one to gain an understanding of behaviour and beliefs, this research aimed to find in childless women, potential predictors already known to be correlated with birth choices. Therefore the mixed method appeared correct for the purposes of D'Cruz and Lee's research as it provides a complete and comprehensive understanding of the research problem than the qualitative approach alone. Probing and prompting, essential during a focus groups discussion or during face to face interviews, was not possible. This could limit participants' answers. Factors, identified by authors to be associated with birth choices, have been measured throughout the Scales mentioned above. It is important to underline that, because the study focused on women who are neither pregnant nor contemplating pregnancy in the immediate future, relationships amongst variables may attenuate. Moreover attitudes and expectations may change when women move from expressing a general desire to have children, towards having more definite plans and then to pregnancy and birth.

There are also other studies [158,168] even before they are pregnant and that it is possible that the dominance of a medical model of care contributes to these factors. Medicalization has influences women's definition of pregnancy and women's willingness to accept medical interventions [161,168,169].

A study by Preis et al. [168] was part of a larger prospective project that examined birth choices and experiences. This observational study included four hundred and thirteen primiparae at ≥ 24 weeks, recruited in medical centers and in natural birth communities in Israel. The women completed a questionnaire which included the Birth Beliefs Scale and a variety of biopsychosocial characteristics such as obstetric history, birth environment, optimism, health-related anxiety, and maternal expectations. They explored factors that might contribute to the development of beliefs about birth as a medical or natural process among first-time mothers. The use of a biopsychosocial theoretical framework allowed to understand the origins of the beliefs, if they are associated with psychological characteristics or with sociocultural and obstetric features. Because authors aimed to understand the underlying factors associated with the basic birth beliefs, a quantitative descriptive study that establishes only associations between variables is appropriate. However qualitative studies using in-depth interviews could stimulate a richer understanding of women's beliefs and attitudes.

Long exposure to the medical obstetric system and becoming dependant on medical staff and technology may have influenced beliefs [168,169].

The study of Takàcs et al. [169] belongs to a broader research project aimed at evaluating the climate in Czech maternity hospitals as perceived by women. Within this project, an instrument for measuring the quality of climate in maternity hospitals was developed and validated. The data reported in this study were obtained by the final psychometric validation of the questionnaire. To identify the social psychological factors affecting women's evaluation of care provided in Czech maternity hospitals, a quantitative methodology was used and the questionnaire was completed by seven hundred and sixty-two women. This is a valuable methodology for the purpose of the study, results reported are based on large sample size that is representative of the population and the research question has been clearly defined. Authors did not set a limit to fill out the questionnaire after delivery, the majority of women (80%) evaluated the care between the second and twenty-ninth month after delivery. The study is unable to establish if the time between delivery and the answers could influence how women assessed the care.

In addition, Haines et al. [159], in their cross cultural cohort study, found that women exposed to a more medicalized culture are less likely to view birth as a natural event, resulting in a higher preference to have a caesarean section and a passive attitude in expressing their views. They reported that a high risk culture around childbirth may change expectations and make women more prone to interventions. This work [159] is part of a broader investigation of aspects of the pregnancy, birth and early parenting experiences of rural and regional women in Sweden and Australia. To compare attitudes and beliefs towards birth in a sample of Australian (n= 386) and

Swedish (n= 123) women in mid-pregnancy, a questionnaire was used to collect data, after validation in both Countries. Levels of agreement or disagreement were indicated on sixteen attitude and belief statements regarding birth. The prospective design allowed women to express their views directly at the time of mid-pregnancy, rather than retrospectively after giving birth. It cannot reflect the views of all Australian or all Swedish women in mid-pregnancy, however it adds to the existing literature motivations and beliefs of women at this stage of pregnancy. A larger cohort of women to determine if findings are more generalizable, would be needed. In addition, a qualitative approach could better explore how women come to form their attitudes and beliefs about birth.

The evidence appraised above should give maternity stakeholders the opportunity to examined services offered, as a pessimistic pre-birth perception may also affect outcomes of labour and delivery [170]. However, van Bussel et al. [158] in their study concluded that women approach childbirth in many different ways: as a natural event, as a dangerous and exhausting process or without any specific orientation or attitude towards it. These differences in maternal attitudes before pregnancy, contribute, to some extent, to maternal childbirth satisfaction and to women's experience of the birth process [158]. Both studies [158,170] used a prospective observational cohort design, that is appropriate to determine if maternal expectations and beliefs could be associated with birth outcomes [170] or if maternal antenatal views of pregnancy and motherhood could predict childbirth experience [158], but they used a different approach.

In Shikma Bar-On et al.' s study [170], researchers asked women to fill in a questionnaire in which they rated their chances to have a vaginal delivery or a caesarean section and responses were compared to actual outcomes. Findings indicate that pre-birth perceptions of delivery by a caesarean section were significantly higher among women who had a vacuum extraction or caesarean section, however a larger sample size (N= 280) is needed to determine if maternal optimism and pessimism affect these and other obstetric outcomes or if there is a relationship between several factors. Moreover the criteria to assess participants women as low risk, were very strict, limiting the generalizability of the results to other populations. In addition, the number of participants combined with the low rates of caesarean section and vacuum extraction might have not allowed to detect additional reasons for the caesarean section deliveries.

Van Bussel et al. [158] used a model of antenatal orientations of pregnancy and motherhood as described by Raphael-Leff [171] (the Facilitator, Regulator, Reciprocator, and Conflicted or Bipolar mother), to investigate whether this could influence the maternal expectations and experiences of childbirth. They [158] asked two hundred and ninety-eight expectant mothers to complete a booklet with questionnaires at 30–36 gestational weeks and at 8-12 weeks postpartum. They found that the intrapartum childbirth feelings of fulfilment, distress, and difficulty clearly predicted the

postpartum recollection of these intrapartum experiences. However, generalisation of results is difficult because the population consisted of educated and employed Caucasian women. In addition, more specific information about labour and delivery (e.g. length of labour) was not available to control for. The maternal childbirth experience was measured at only one time point, at 8–12 weeks, a woman's childbirth experience could change over time. Moreover, many of the registered obstetric interventions are interdependent, making it difficult to investigate the real contribution of a specific intervention. For both studies [158,170], a qualitative methodology would restrict the sample size, but could support and gain more in-depth understanding of women's attitudes, expectations and satisfaction with birth.

Specifically considering pre-birth views of primiparous women in relation to childbirth, Brodrick [172] shows that, although women expect labour and birth to be achievable without intervention, many stated a need to keep their mind open and to be able to go with the flow. The aim of this study was to explore the values, beliefs, behavioural, knowledge systems and the role of the midwife of women during pregnancy and childbirth and required a qualitative methodology. This enables the researcher to gain an in-depth understanding of the women's perceptions. The objectives of the study needed an explorative descriptive design to discover and describe the topic. A total of eight low-risk primigravid women were recruited and interviewed using semi-structured interviews. A thematic analysis was adopted and two global themes emerged from the data: maintaining internal control and external control factors. These were supported by six organising themes: facilitating a birth without interventions, going with the flow, faith in the system, fear of the unknown, role of support partner and role of the midwife. Women expect and hope for a birth free of intervention and place considerable faith in the hospital's ability to provide appropriate and safe care.

As with all small scale qualitative work, findings may not always be replicated, but it adds a further dimension and depth to the volume of evidence already published. In this sort of study, the researcher plays a very visible role, and participants could answer positively due to the presence of the interviewer. Participants were not asked to provide feedback of findings, although a senior midwifery colleague verified codes and emerging themes.

In other research [173] women expressed faith that their bodies would cope with the experience, reaching a spontaneous delivery, although the strongest emotion stated by participants was fear. They reported the fear of having to cope with a frightening experience and the need to know as much as possible about the body changes, probably to reduce their fear. In fact, several participants were active in seeking information from different sources to obtain satisfactory answers. As reported from other research (Young and Miller, 2015), women change their vision of childbirth and think about a different birth plan when reading about benefits of normal birth. In the

study by Fleming et al. [173], this was especially noted for those who got in touch with association promoting physiological birth. Some women visualized birth as the outcome of personal preparation, feeling responsible for the outcome of childbirth and viewing a potential caesarean section as a personal failure. These women tended to give birth outside the hospital setting. As in Brodrick's [172] study, Swiss women reported faith in the system and would trust healthcare professionals also to make a final decision about mode of birth, if needed. In addition, participants reported the wish for more continuity of care.

Fleming at al. [173] aimed to describe the emerging expectations of giving birth of healthy primigravid women in the early second trimester of pregnancy in Switzerland. The qualitative methodology is appropriate for its purpose and, throughout the thematic analysis, authors identified, analysed and reported patterns within data. They clearly explained the way they put aside their own beliefs and viewpoints, so as not to influence interpretation of data, a process known as bracketing for descriptive phenomenological research. While a vast amount of data were generated, as fifty-eight healthy primigravid women were interviewed, qualitative research can never be truly representative of the population as a whole. Although Switzerland is a small country, the strength of this study is the presence of three major language regions each with its own culture and customs.

The most frequent and relevant expectation women reported was to being in control over their experience of birth [152,154,172,174–176]. Personal control is an important aspect for women, but it can also be a source of negative expectations, because they fear losing control during such an overwhelmingly physical event [176]. The review by Moore, surveyed qualitative and quantitative studies to explore expectations around birth that are held by women from different cultures. Studies identified were grouped according to expectations of personal control: expectations of support from partner/others/family; expectations of care; behaviour from providers; expectations about the health of the baby; expectations about pain in childbirth. Many of the studies included, had predominantly White populations and involved people who do speak only the native language of the researcher. Another gap in the research papers relates to the well-educated, with a good socio-economic status of sampled women. The author argues that studies regarding expectations should make efforts to include the viewpoint of women who are less educated or from lower socioeconomic groups.

To describe the essence of women's unexpected birthing experiences, Goldbort [175] used a qualitative methodology with a phenomenological approach, citing Husserl's philosophy, which encourages the process of bracketing. However the author did not disclose any pre-conceptions or how they may have affected the quality of the data collection and interpretation. Thematic analysis was conducted using Colaizzi's method (1978) [177]. The limitation in this study was the

homogenous population of participants. Interviewing women with more diverse backgrounds, such as adolescents and women of different cultures and ethnic backgrounds, would be informative to discern what effects an unexpected birthing process had on them.

Lack and/or loss of control is often perceived as a major cause of emotional trauma [178]. In this study authors aimed to investigate the association between women's characteristics and their attributions of the trauma, what they feel their caregivers could have done differently, what they themselves could have done to prevent the trauma, and differences between primiparous and multiparous women. Authors adopted a quantitative methodology with a retrospective survey conducted on line among 2192 women with a self-reported traumatic childbirth experience. This is a valuable methodology to determine the association existing between variables and to compare population groups. The questionnaire was designed specifically for the purpose of this study and validated, was based on qualitative research studies and it contained thirty-five items, the most important were: self-reported attributions of the trauma and how women believed the traumatic experience could have been prevented by the caregivers or by themselves.
Women attribute their traumatic childbirth experience primarily to lack and/or loss of control, issues of communication and low practical and/or emotional support. They believed that in many cases, their trauma could have been reduced or prevented by better communication and support by their caregiver or if they themselves had asked for or refused interventions. Participants were recruited through online invitations posted on a website created for the purpose of this study, a Facebook page and a Twitter account. Although the study had a large sample size, the self-selection of the participants and the language barrier, due to the questionnaire only available in Dutch, make the findings hard to be generalized. Certain groups of women may have responded in disproportionate numbers to the recruitment posts. For instance, women with strong convictions about mismanagement of their labour, as well as women who had sought psychological help, could have been more attracted to fill out the survey than women who had found a way to successfully process their experience. In addition, there is a possibility that some women, who experienced physical trauma during their delivery, misunderstood the invitation and filled out the questionnaire, although authors stated that in the Netherlands the term trauma is generally understood to mean psychological trauma. Furthermore, the fact that the study took place in the Netherlands, with its unique midwifery model, may impact on its generalizability as well.

The concept of control could have several meanings. For some women the concept is about having personal control, while for others it is about being able to cope with pain [152]. Women's loss of control is associated with lack of or limited participation in decision-making, which is another significant element for them [152,156].

Iles & Pote [156] conducted a qualitative grounded theory design to explore the experiences of first-time mothers who found labour or childbirth traumatic, and reported trauma symptoms within the first 18 months postpartum. The qualitative methodology used, provides insight into the feelings and lived experiences of women, thus the methodology is appropriate for the purpose of the study. Research was based on interviews with eleven first-time mothers (six reporting full trauma symptoms, five reporting partial symptoms), five overall themes emerged (with further sub-codes), describing significant aspects of maternal experiences in the antenatal and postnatal periods, as well as during labour and birth itself. Semi-structured interviews were conducted until both authors agreed data reached saturation: six with fully symptomatic mothers and five partially symptomatic. Authors followed grounded theory methodology, in which data collection and analysis occurred simultaneously. Codes were arranged into a preliminary theoretical model, to assist understanding of mothers' postnatal trauma symptoms. A number of factors were identified which contributed to maternal postnatal trauma symptoms, including pre-existing anxieties, expectations for labour and birth, the way postnatal narratives were developed about the birth and the meaning of trauma symptoms in their role as a new mother. This qualitative design involved a relatively small number of women were, this makes difficult the transferability of findings. A mixture of mothers reporting full and partial symptoms were included, this strategy led the inclusion of a wide range of mothers, but also deviated focus on women with severe symptoms. Moreover, the sample was not representative of a multicultural background. In this research pre-existing beliefs appeared to be particularly relevant to postnatal trauma symptoms as anticipatory birth-related anxieties and fears were influential. Having control and be able to make choices was important for women. Although support was valued from a range of sources, healthcare providers were particularly important and mothers were disappointed if midwives seemed uninterested, having lasting impacts on mood and symptoms.

With control playing a key role, healthcare professionals need to consider their actions and behaviours very carefully to ensure women are supported during labour in a way that minimises unnecessary intervention and allows them to maintain control and integrity [172]. A strong emotion expressd by women in much research is fear of the unknown [172,173] and of the pain [161,173] that often leads to loss of control [152,161]. For some women labour and birth are scary, potentially dangerous and stressful. Fear plays a central role as do childbirth interventions, women's feeling to lose control over the birth process and childbirth pain [174].

Cipoletta & Sperotto [161] in their study explored women's perception and their satisfaction with the childbirth management stated by the hospital. They adopted a qualitative grounded theory approach, conducting semi-structured interviews until saturation. This was achieved by interviewing twenty first-time Italian mothers. Participants were recruited while in the post-natal ward, from soon after delivery to three day following birth. Authors started the analysis by reading

through the firsts interviews for a primary general view, identifying categorises and themes. The methodology of the study is appropriate for the aim, as authors wanted to gain in-depth understanding from the women's lived experiences. However the research may have achieved greater rigour if authors would have mentioned the need to remain open-mind, in order to avoid bias due to preconceptions. In addition authors stated that they identified themes, but, as per grounded theory [179], analysis and data collection needed to proceed simultaneously in order to constantly check that developing insights are grounded in all parts of the analytical process [179], there was not a clear explanation about it. The main themes emerging from the interviews were: Expectations, Control and medicalisation and the Relationship with the caregivers. Women expressed the wish to deliver in that particular hospital because was a II level Maternity Department with a NICU for sick babies, this was reported also from women with a low risk pregnancy. Moreover, they expected to have a women-centred care, the hospital's mission affirmed to provide it. Women's expressed a high level of fear which led to a loss of internal control with the external control established by the healthcare professionals. The loss of internal control was related to a sense of personal failure that established women's passive role throughout the process. Midwives were often described positively, some women reported a low level of satisfaction in the relationship with the obstetrician. If the caregivers had a human approach, women reported to be satisfied with the overall experience. Women place considerable faith in the hospital's ability to provide appropriate and safe care, which is consistent with Brodrik [172] and Fleming [173], and willingness to give up internal control in order to accept medical interventions and to preserve their child's and their own safety. Although the hospital philosophy was to focus on the humanisation of service and provision of women-centred care, women did not experience these elements. While authors reassured women that they could express themselves freely and without fear, women still reported it was difficult for them to communicate their feelings and their experience. This could be the reason why interviews do not last more than thirty minutes each, this could affect research's findings.

2.3.3 Paternal expectations

Many women expected their partners to be at the birth. Some of them expressed concern that their partner would not cope [172]. Research suggests that some women report their partner to be very important and supportive, whilst others find their presence annoying [161]. Primiparas and women with positive feeling about being pregnant were more likely to expect a significant support from their partner [152].

Nowadays in western countries, fathers are encouraged to be involved and actively participate during labour and birth. There is substantial evidence of the health and wellbeing benefits that

result from fathers being involved in their partner's maternity care. Most women want their partners to be involved and this desire to be engaged is shared by most expectant fathers [149].

Compared with past generations, society's expectations are increasingly for fathers to play a significant role throughout pregnancy, labour, childbirth, the postnatal period and beyond [149]. When fathers are well prepared and involved during pregnancy, birth and a child's early years, there are many health and wellbeing benefits for themselves, their partner, baby and family. RCM Guide published in 2011 and endorsed by the Father Institute and the Royal College of Obstetrician and Gynaecologist, recommended to include expectant fathers in all aspects of maternity care.

Despite the increase in the fathers' birth attendance, their feelings and experiences have not been extensively studied. Some research reveals that fathers have their own expectations regarding birth.

In Fenwick et al.'s qualitative study [180], all men interviewed viewed pregnancy and childbirth as a shared experience, wanted to be part of the process and to support their partner. Early in pregnancy they have no idea what to expect and, as the pregnancy progressed, they were often aligned with their partner's expectations. By the end of the third trimester of pregnancy men expected to have a natural labour and delivery with a healthy baby. Some men were anxious about the partner's pain, especially those that were second time fathers, although their partner went through labour without pain relief during the first birth. They appeared more relaxed if their partner agreed to have epidural during this second labour. Fathers also expected to have female support during labour, either throughout friends or a family member of the family to help them to support the woman in labour [180]. In this research Fenwick et al. (2012) aimed to explore and describe men's experiences of pregnancy and childbirth expectations. A qualitative descripted design was adopted which is consistent with the aim, in order to describe and explore the phenomena. A convenience sample of twelve expectant fathers consented to participate in the study. Data collection consisted of thirty-two interviews conducted across three time points (second and third trimester and approximately eight weeks after birth). All of the men were offered the opportunity to keep also a diary during the pregnancy and encouraged to make regular entries, six men agreed to participate also to this activity. Although the interviews were conducted at a time and place convenient to participants, often men were interviewed by phone. This could influence researcher's ability to probe and prompt, affecting the quality of results. Interpretations of findings could be also influenced by experiences of men who kept also a diary. Results could be more representative of them than of other men who underwent only the interview. A thematic approach was used to analyse the data. To ensure trustworthiness of data and rigour, authors regularly discuss and debate concepts, themes and sub-themes.

In the study by Schytt & Bergstrom [150] expectant first time fathers' feelings and expectations varied by age. Older men had more negative feelings, fear and worry, than the younger ones. The

increased risk of complications and interventions during labour and birth caused by biological ageing, may also have caused worry and fear in men. Younger men, instead, would like to have received more support from midwives. Although their feelings and despite having partners who had a more difficult labour, men of advanced age were more satisfied with overall intrapartum care compared with men of average and young age. Authors gave few interpretations for it: men's feelings of gratitude for having a healthy partner and child, more attention from the staff, as there were more medically demanding situations or better communication with the midwives because the older fathers were more prepared, may have found it easier to interpret the information and signals from the staff or were knowledgeable to pose questions. Schytt & Bergstrom's study was part of a larger project, a randomized controlled trial designed to test the effect of two models of antenatal education. Participants were randomly allocated to a standard care programme, or to natural childbirth preparation techniques. For the purpose of Schytt & Bergstrom's study, that aimed to establish a relationship between experience and paternal age, the quantitative methodology is correct. Furthermore, it was possible to merge the randomised groups for secondary analyses as participants did not present any differences between the two groups in terms of primary outcomes of the trial (labour outcomes, experience of childbirth and early parenthood). The sample was than divided into three groups on the basis of paternal age by the breakpoints for the lower and upper quartiles for age. Men were defined young when they were ≤ 27 years old, average if 28–33 years old and of advanced age if ≥ 34 years old. Participants filled in two questionnaires, at baseline in mid-pregnancy and at follow-up three months after birth. Fearful expectations of the upcoming birth were measured by the Wijma Delivery Expectancy Questionnaire that was originally developed for women. Authors for this reason conducted a piloted study to assess the relevance of the instrument also for fathers. This led to the exclusion of eight of the thirty-three items as they were irrelevant for men. Participants were 777 fathers and, although this is a large sample size, the fact that these men took part in a trial on antenatal education, may create a bias because all fathers were highly engaged within the maternity pathway. Moreover, this sample is not representative for men of more than 40 years old, as the age of participants has been divided bases on the lower and upper quartile identified in the sample. Old men were defined to be of ≥ 34 years old, this appear to be a strict limit. However, knowledge about age-related differences in the experiences of first-time fathers may help midwives and doctors give more individualised information and support.

Studies indicate the need to consider the father's birth satisfaction and needs as a future parent, and not solely as the mother's partner. In order to support families as a whole, the importance of the father in a supportive role and as an important parent himself should be addressed [181].

2.3.4 Role of the midwife

Many studies report women would like to receive more continuity of care and support from the midwife. Primiparas and women with negative feelings about birth, have higher expectations on the midwife role and they expect her to be present most of the time [152,169,173,182].

In recent years the importance of a midwife's presence has been identified in many study [148,154,161,169,182], indicating that it reduces the need of interventions, decreases the amount of pain relief used and influenced a positive birth experience. In a medicalized environment where midwives take care of more than one woman in labour, appears difficult to provide one-to-one midwifery care. This could affect the birth process and women's experience.

In the study by Brodrick [172] women viewed the midwife as a specialist in terms of pregnancy and childbirth, but none of them during the interviews could describe the role of the midwife intrapartum or the process of care within the hospital. While women expected reassurance and support from the midwife, they were unable to contextualise midwife's skills further, preferring instead to talk about clinical activities performed by them, such as checking blood pressure. Women underestimated the role of the midwife (in terms of skills), and her value and significance throughout the entire maternity pathway, is realised postnatally when reflecting on the birth process [172]. Women trust the expertise of the midwife during the intrapartum period and want a birth devoid of intervention, for this reason is the midwifery profession responsibility to reducing intervention rates [172].

The research by Brodrick [172] is consistent with a study conducted in Germany [182], where women seem to lack knowledge regarding midwives competencies, skills and scope of practice. Due to this, women have different expectations of midwifery care: some women would like a proactive support of midwife, some expect a support on-demand and others believe they don't need any midwifery care [182]. Women would prefer midwifery care in order to avoid unnecessary interventions and would expect to be able to deliver in a non-hospital setting where they could receive continuity of midwifery care. Women expressed they would like more from midwife than just medical care, they would like a holistic respectful approach and they would like midwives to be their advocate for normal birth offering evidence-based information [182].

The study by Mattern et al. [182], explored pregnant women's and mothers' experiences, needs and wishes regarding systemic aspects of midwifery care (access, availability, choices, model of midwifery care, maternity care in the healthcare system). The qualitative methodology of the project was designed according to Gadamer's hermeneutic approach [183]. Gadamer's approach refers to Heidegger's philosophy, that emphasized the ontological perspective of hermeneutics by suggesting that researchers are concerned with an inquiry of the theory of being, in addition he stressed the idea of understanding of being, that happens prior to reflection [184]. Gadamer believed that the hermeneutic circle of interpretation is never closed but is ongoing, with movement

of understanding from the whole, to the part, and back to the whole. He emphasized the need for researchers to acknowledge their biases and prejudices as part of the interpretive process of hermeneutics [184]. During the study by Mattern et al. [182], authors had an open approach, conducted a reflective discussion between them that focused on each team member's own views on midwifery care for women during pregnancy, labour and birth and the post-natal period in Germany. This provided an awareness of individual preconceptions and allowed reflections and interpretation of participants' experiences. In addition the reflection and openness were called for during the focus groups' interviews: women were allowed to relate their views without interruption by the researcher, and to converse amongst themselves without restrictions. They made very clear each step in data collection and analysis. In accordance with Gadamer's hermeneutic approach the analysis was performed in a cyclical manner involving a first analysis by two member of the team independently, memos and code were identified and grouped according to themes and sub-themes, relationship between themes was found and they were gathered in common thematic subjects. Double checks of data and interpretation was constant throughout the process. The methodology is appropriate for the purpose of the study which is rigorously conducted. The research included fifty women participated in ten focus groups in five federal states of Germany. Fifteen women were pregnant and thirty-five women had given birth during the past twelve months. The focus groups were heterogeneous with regard to age, parity, model of maternity care used, and rating of satisfaction. Authors included women with different level of education. In the focus groups with women who had a similarly high level of education, the conversations seemed uninhibited and free flowing as the women communicated their experiences, needs and wishes. This made it easier for the researchers to grasp narrative and meaning of argumentation. In contrast, analysis of the conversations of women with lower levels of education, or those who did not complete formal schooling, proved to be more challenging. The women didn't seem at ease to discuss on a particular subject. It means that was probably hard for authors to adequately understand the participants' viewpoints, making it difficult to be sure the meaning was fully comprehended. There is a possibility that the experiences of women with a higher level of education are more represented in this study. Moreover, only German women had been included in the focus groups, the study is not generalizable to women with different origin.

Borrelli et al. [185] conducted a study with the aim to conceptualise first-time mothers' expectations and experiences of a good midwife during childbirth in the context of different birth places. They adopted a qualitative Straussian grounded theory methodology, which is appropriate for the purpose of the research. Authors proceeded interactively and inductively and data analysis included a constant comparison between the literature, collected data, codes, categories and memos. The Straussuan's approach is not a linear process as data collection and analysis proceed simultaneously in order to constantly check that developing insights are grounded in all parts of the

analytical process. The aim of grounded theory is to generate theory that seeks not only to explore, but also to explain a phenomenon of interest, going beyond descriptive data [179]. The importance of theoretical sensitivity in Grounded Theory means that, the researcher should enter the field work with a general awareness of the topic, but without any prejudice about what might be discovered. Authors remained open minds during the data collection and the analysis, in order to limit preconceptions given by their midwifery background. Fourteen women's expectations and experiences of a good midwife during childbirth were explored in the context of three different planned places of birth (home, Freestanding Midwifery Unit and Obstetric Unit). Data were collected through two semi-structured interviews for each participant before and after birth. A purposive theoretical sampling strategy was adopted and the sample size was determined by data saturation, which was achieved for both antenatal and postnatal interviews independently from the place of birth. The theory achieved by authors is a conceptual metaphor model named “The Kaleidoscopic midwife” that illustrated first-time mothers’ perspectives of a good midwife during childbirth. The model identified the intrapartum care priorities that enable first-time mothers to feel supported and assisted by midwives who fit the criteria of good, during labour and birth across different birth settings. Four pillars of intrapartum care for a good midwife from first-time mother perspectives have been identified: promoting individuality, supporting embodied limbo, helping go with the flow and providing information and guidance. In Borrelli et al. [185] women from minority ethnic groups were not included, as well as a high risk population, therefore the applicability of the findings to these groups is limited. Moreover, few first time mothers usually plan for a home birth, the sample had more women planning to give birth in a Freestanding Midwifery Unit, but only two actually delivered in this setting. Due to a high transfer rate, was not possible to compare the experience of women giving birth where planned, during the post-natal interview. The principal investigator was a midwife and she declared her background before the first interviews to all participants. Women may have felt inhibited to share a negative experiences about their midwives, though few participants recounting midwives’ undesirable language and manners. Findings in Borrelli et al. study reported that women would like to establish a trusting relationship with the midwife in order to be understood and listened to; the midwife should be present most of the time during labour and be immediately available; she should be knowledgeable. The midwifery care should be shaped based on women’s birth plan rather than fitting the women’s preferences around maternity care policies. Authors stated that when a woman is cared for by a midwife with these characteristics, she is likely to have a positive experience of birth.

2.4 Expectations’ fulfilment and satisfaction with childbirth experience

Understanding and improving a woman’s experience of midwifery care is increasingly important and an integral component of the quality of maternity care [147]. The experiences of people who use health services are as important as measures of clinical effectiveness. Although many

outcomes are already measured by existing datasets, it is more difficult to measure the care that women actually receive [147]. Maternal satisfaction with birth has become more and more important and is now considered one of the most important indicator in the evaluation of the quality of maternity services [186]. Measures of experience will become more widely used as they provide results that are more practical. This would support midwives to understand needs of women, babies and their families to improve their experience with maternity services [147]. WHO [148] also argued that whilst much is known about clinical aspects of labour and birth, less attention is paid to what women need, to have a positive experience of childbirth. Knowledges on how to observe and monitor the physiological changes during the childbirth process has led to an important medicalization of it. This approach could make women feel less confident in their ability and could negatively impact on the experience of childbirth. For this reason WHO [148] recently published guidelines focusing on evidence-based recommendations to promote the emotional wellbeing of women in labour and a positive experience of childbirth.

A positive experience and satisfaction with birth could be influenced by expectations' fulfilment. Difference between expectations and experience of childbirth can unfortunately occur, both for women and for men. Research suggests that women whose expectations were not met were more dissatisfied, not because their expectation were too great but because they had experienced too little control [155]. As already mentioned, control is a relevant expectation for women and it appears to be a significant predictor of birth satisfaction, with high level of control correlated with greater satisfaction with birth process. Perceived control is also significantly associated with postpartum depressed mood [155].

DeLuca and Lobel [155] conducted a longitudinal study to examine the association between delivery method and postpartum adjustment, with mediation by two variables: perceived control over labour and delivery and unmet expectations of control over childbirth. A quantitative methodology with an observational approach is appropriate to evaluate the association between variables, based on the research hypothesis. Authors observed the same participants over a period of time to test their hypothesis. They hypothesized that women delivering by unplanned caesarean section will experience greater postpartum depressed mood and lower childbirth satisfaction. Moreover they assumed that the relationship between method of delivery with postpartum mood and childbirth satisfaction will be mediated by two factors: by perceived control during labour and delivery and by unmet expectations of control during labour and delivery. One hundred and twenty-four participants (76%) delivered vaginally and forty (24%) by unplanned caesarean section. They filled in two questionnaires at two time points. The first between twenty-eight and thirty-six weeks of pregnancy, because by this time, pregnant women have formed opinions about childbirth, and they are focused on the event. The second questionnaire was administered between four and eight weeks after birth, during this period of time women would

have recent memories of childbirth, but be able to relate negative as well as positive impressions of their delivery. The two questionnaires contained different Scales measuring Perceptions of control, Expectations about Childbirth and the Experience of Childbirth. Findings showed that participants who delivered by caesarean section reported lower childbirth satisfaction than those delivering vaginally. Women most satisfied with their childbirth experience held their baby less than thirty minutes after birth, perceived lower threat to themselves and their babies during childbirth, delivered vaginally, perceived higher control during labour and delivery and had expectations of control closer to what they experienced than women who were least satisfied. It should be noted that authors did not rich a large sample size for a longitudinal study, moreover they recruited predominantly White women, well-educated, with middle to upper class income, and the majority were giving birth for the first time. Therefore future studies would benefit from larger sample size and from the inclusion of women with wider characteristics in order to make findings generalizable. Moreover, the study had limited power to detect an effect of delivery type on postpartum depressed mood. A larger sample size would provide more information about the association between mode of birth and depressed mood.

Findings from Fair et al. [154], reported the same association between control and experience, however this study found no relation between satisfaction and birth expectations. Their findings indicate that women cared for by midwives have significantly higher experienced control and birth satisfaction than women cared for by obstetricians. Same results were found in caesarean section deliveries suggesting that, despite differences in birth mode, midwives tend to facilitate greater experience of control during birth and therefore greater satisfaction [154].
The study by Fair et al. [154] aimed to evaluate the relationship between perceptions of prenatal control, expectations for childbirth, and experienced control in labour and birth and how they individually and collectively affect birth satisfaction. Authors adopted a quantitative methodology with a longitudinal prospective approach. This is a reliable methodology to asses a potential correlation between variables considered by the researcher. Participants were interviewed before and after giving birth by surveys administered orally. The prenatal interview assessed demographic information, prenatal control, and expectations for control. The postpartum interview assessed control experienced in the delivery room, birth satisfaction levels, and whether the participant delivered with an obstetrician or a midwife. The sample size was very small for a longitudinal study, with thirty-one participants. Although participants varied widely in race, age, and socio-economic status, all participants were from the same geographic location and attended the same midwifery/obstetric practice, therefore findings cannot be generalized to other populations. Results presented by authors could be seen only as exploratory, as the sample size was insufficient to test the true relationships between variables. Although the limited sample, experienced control in the delivery room was a significant predictor of birth satisfaction. No correlations between prenatal

control, expectations, and experienced control was found. It seems that the most important issue of control is what is actually experienced by women during labour and birth. A mother's perception of experienced control will significantly affect her assessment of her birth experience. Experiencing complications during labour and birth were shown to decrease experienced control and birth satisfaction. It would be important to explore what midwives and obstetrician are doing differently to account for the increased control and birth satisfaction among women cared for by midwives, despite the mode of birth, by interviewing women and providers.

Mei et al. [153] contradicts the above findings in terms of birth expectations as concludes that, although having a high number of maternal requests was associated with an 80% reduction in overall satisfaction, having expectations fulfilled is positively associated with birth experience satisfaction. In addition, the antenatal expectations of the intrapartum fulfilment, distress and difficulty, clearly predicted the recollection of the experience.
Authors [153] aimed to categorize individual birth plan requests and to determine if number of maternal requests and request fulfilment is associated with birth experience satisfaction. This study is a sub-analysis of a prospective cohort study of women admitted to the Delivery Suite of a large urban tertiary care medical center. The original prospective cohort study analysed the effect that birth plans had on the mode of birth, perinatal interventions, and birth experience satisfaction. A cohort study is an observational design, which does not implies interventions by researcher and it is appropriate to establish links between variables and health outcomes. The sub-analysis of Mei et al. was performed concurrently to analyse women's satisfaction. The study included women having a pre-written birth plan at the admission to the Delivery Suite. In the post-natal period, while they were still into the hospital, women completed a satisfaction survey that asked them to evaluate their hospital birth experience in three domains: the overall satisfaction with their birth experience, if the birth experience was what they expected, and if they felt in control during the birth process. Participants were one hundred and nine women admitted to the Delivery Suite, among these, 86% completed also the post-natal survey. During the analysis, authors found twenty-three distinct maternal requests into the different birth plans, ranging from a minimum of one to a maximum of twenty-three, with a mean of ten requests. They considered more than fifteen maternal requests a high number of requests, as it would be more than one standard deviation (SD) above the mean (> 80th percentile). Findings showed that mothers who had a high number of requests on their birth plan, specifically more than fifteen (a SD above the mean), had a significantly reduced overall satisfaction with the birth experience. The population of this research is quite small for a cohort study and is limited to women delivered at one hospital, therefore generalizability is affected. However, authors underlined the importance of take women birth plans seriously as mothers can feel down if their plans are not looked and considered. Birth plan fulfilment can lead to an overall more positive birth experience.

Bélanger-Lévesque et al. [187] evaluated and compared maternal and paternal satisfaction with birth, and reported that global satisfaction scores were similar for both women and men, but the analysis of sub-themes showed a difference between factors related to mothers' and fathers' satisfaction. Women appeared to be more distressed than men and reported lower satisfaction in case they required an epidural analgesia and experiencing a long labour, spinal anaesthesia was significant for a positive experience in case of a caesarean section occurred. Fathers reported dissatisfaction when epidural analgesia was required and when an instrumental delivery occurred. If the delivery was through caesarean section, men reported a worse experience in case it was a primary section and if baby was born with an Apgar score < 7 at 5 mins. Men reported greater dissatisfaction with care and that they felt less support than their partner. There was a single variable that remained significant to predict lower satisfaction for both men and women, it was the use of epidural analgesia. As other studies suggested (van Bussel et al.), the level of pain does not affect fulfilment or overall satisfaction with childbirth.

The study of Bélanger-Lévesque et al. [187] aimed to evaluate and compare the birth satisfaction of mothers and fathers. They conducted a comparative cross-sectional study, as parents' satisfaction was measured once after birth. Authors adopted the Birth Satisfaction Scale (BSS) [173] to evaluate women's and men's satisfaction with birth, which is an appropriate instrument for a quantitative methodology. However, the BSS has been originally developed for the evaluation of maternal satisfaction exclusively. Although authors justified that they used this Scale for men due to the low amount on evidence on fathers' birth experience, a rigorous study would need a validation of the instrument before administering it. Based on the literature, authors required a sample size that detected a 10% difference in satisfaction between mothers and fathers. The sample size required was a minimum of one hundred and twenty-eight couples, using a standard deviation of sixty points and an α of 0.05, in order to achieve a statistical power of 80%. Participants were 200 mothers and 200 fathers/mother's partner recruited from twelve hours to twenty-four hours after birth, only cases of major infant malformations or death in utero were excluded. Although this time was chose to maximise survey completion, women often feel a sense of relief and euphoria following birth and their post-birth feelings may not be so positive following a period of reflection [172], the same could happen to men. The response rate was higher than expected, but questionnaires were not completed for one-third of the births recruited, those parents might constitute the least satisfied group that authors were unable to include. Surveys were completed by parents and returned in envelopes before discharge, parents were left alone while completing the survey and they could consulted each other, this could lead to a contamination of data.

Research that focus on professionals, reported that women could have issues many years after delivery [151,181] and that they could feel the need to deal with them before having another child

[181]. Studying the perinatal factors related to the experience three years after birth, Rijnders et al. [151], found that women in the Netherlands had negative recall of birth when: delivered through assisted vaginal birth or unplanned caesarean section, did not have a home birth as planned, have been referred during labour, did not have choice in pain relief or were not satisfied in coping with pain, gave a negative description of the caregivers and had fear for the baby's or their own life. These results are consistent with many researches that indicate lower women's satisfaction when obstetric interventions occurred and felt disempowered during the birth process [152,158,161,188].

Rijnders et al. [151] in their study aimed at investigating Dutch women's views of their birth experience three years after the event. This study was originally conducted to investigate women's long-term perception of birth in relation to mode of delivery in the Netherlands compared with the United Kingdom. It was hypothesized that women's appraisals of their birth experience would be different in cultures with different birth norms. Authors adopted a quantitative methodology, using a questionnaire that was mailed to all women who had given birth in 2001 and who had at least one prenatal, perinatal, or postnatal visit from one of the eight participating midwifery practices randomly selected. The methodology is appropriate for the aim of the study as authors wanted to establish an association between a variable (mode of birth) and the outcome (birth experience three years after delivery) and to compare results among two different populations.
Women were excluded if it was known to the midwife, either from the perinatal record or from any other source, that they had experienced a perinatal death or a deceased child in the past three years. Women who had a subsequent birth after the index birth in 2001 were not excluded, but respondents were asked to reflect on the birth that occurred in 2001. Women were asked to say how they felt looking back on their labour and birth, with five response options from "very happy" to "very unhappy". The recruitment started three years after birth and no reminders were sent. Authors estimated to have at least forty percent of response rate, they achieved forty-four percent with 1.309 questionnaires received back from participants. It is possible to assume that with a reminder to nonresponders, the sample size could be larger. In addition, two midwifery practices had more than thirty percent of non-Dutch clients. The fact that the questionnaire was issued only in Dutch also might have contributed to a low response rate from non-Dutch women. For this reason the sample was fairly representative with respect to the mode of delivery, place of birth, and obstetric interventions compared with the total Dutch population of pregnant women, but not for ethnicity and initial caregiver. This could affect the generalizability of findings in non-Dutch women. Three years after delivery, most women looked back positively on their birth experience, but more than 16 percent looked back negatively. More than one in five primiparas looked back negatively compared with one in nine multiparas. Despite a self-reported good memory, recall bias might still be a problem in the study, especially for women who had another child after 2001.

Lewis et al.'s [188] study confirmed the relevance of concepts of loss of control and disempowering when events went not as planned. They aimed to investigate women's experiences of maternity care in an urban tertiary obstetric setting, to gain insight into conceptualization of satisfaction across the childbirth continuum. Authors adopted a mixed method study design to provide insight and understanding into a complex issues where further in-depth knowledge is required. Mixed methods have been described as an evolving research paradigm which build on triangulation between methods rather than within methods [189]. This methodology gives qualitative researchers the opportunity to utilize quantitative research to give a more comprehensive overview and deeper understanding of the investigated phenomenon. The data collection process used a questionnaire that was sent to seven hundred and seventy-three women two weeks after birth, which included an invitation to participate in a semi-structured, audio recorded, telephone interview with a research midwife. This option was removed after six weeks of data collection, when 18% of women (63 of 342) had been interviewed and data saturation achieved with no new information being identified. English speaking women, who received scheduled antenatal care, birthed a live baby and were cared for by the visiting midwives service, were invited to participate at the moment of discharge from hospital. The self-selection of women for qualitative interview could resulted in responders at both extremes of satisfaction. Frequency distributions and univariate comparisons were employed for quantitative data. Thematic analysis for the qualitative arm of the study was undertaken, to extract common themes. A higher proportion of women having a spontaneous vaginal birth were more likely to feel involved with their birth than the women having an assisted or caesarean birth (91% vs 83% and 81%; p= 0.020). During their birth a higher proportion of women having a spontaneous vaginal or assisted birth felt supported by a midwife compared to women who had a caesarean birth (83 % versus 63 %; p= <0.001). Three main themes emerged from the data: how care is provided; attributes of staff; and engaged in care. The thematic analysis revealed that organisation of care, resources and facilities influenced women's satisfaction and that personal characteristics of individual staff contributed to women's experience. Women wanted to be listened, to make their own choices and to be informed about events. Withholding information can disempower women, so if things did not go as planned, they perceived a profound loss of control. This is particularly important for women who had a caesarean section or experienced interventions, especially those women needed information to make sense to the all process. Dissatisfied women had the impression of not having their wishes listened to and that their expectations of care could not be addressed.

Sometimes women's experience could be reported as negative because women felt they did not have enough support during the post-natal period and they felt alone, scared and unprepared for the emotional impact of motherhood, for the changes in their relationship with partner and for the new role of their partner as a father [181]. The latter study of Young (2008) is a qualitative research

project and aimed to explore maternal expectations toward motherhood and compare these to actual experience, in order to identify where expectations were not being met and inform the improvement of services. A qualitative research method was used to gain in-depth information about mothers' experiences and perceptions. The author used a combination of two focus groups with professionals, and semi-structured interviews with first-time mothers. The aim of the first focus group was to discuss the professionals' experience of mothers whose expectations for delivery and early parenting had not matched their experience. Another aim was to examine the interview guide prepared for the semi-structured interviews. For the individual interviews with mothers, a purposive sample of eleven first-time mothers, with a baby up to approximately one year, was used. Participants were recruited by health visitors from the area and, as sensitive issues were discussed, care was offered in case they felt they need support after words. The aim of the second focus group was to share the results of the interviews and to look at solutions to the problems that were identified. The interview data was analysed by identifying the themes that emerged from the interviews, and by highlighting important statements made by the interviewees. Data were double checked by participants, sending them the audiotaped interviews, confirming the accuracy of data collected. Findings indicated that there were some areas for which parents did not feel well prepared and where care could be more focused. Supporting other researches [153] findings of Young's study [181] suggested that women could experience feelings of failure because things went differently than their birth plans, and that they would expect to have the opportunity to debrief with professionals about labour. The study involved a small sample, and the practice discussed within the study relates to a local area and may not reflect the national pattern, therefore transferability of results is limited.

Many women report their positive experience to be shaped by a combination of feelings, as feeling safe, secure and supported, respected, confident of their abilities and in control. The reverse occurs when women felt to be treated disrespectfully [174].

Bayes et al. [174] reported the findings of the postnatal qualitative arm of a larger study, which investigated women's prenatal and postnatal levels of childbirth fear. The researchers employed a qualitative descriptive approach for this part of the study to describe women's experiences of labour and birth in a Western Australian public tertiary hospital. This is an appropriate methodology which provided insight through a process of identifying and describing the major themes women chose to write about in their postnatal narratives. Participants were recruited from the midwife and obstetrician-led normal and high risk care antenatal clinics. The larger study required completion of two questionnaire designed to assess women's prenatal and postnatal childbirth fear, at 35 to 37 weeks' gestation and at six weeks postnatally, respectively. One hundred and forty-one (57%) women completed and returned the postnatal questionnaire, which included an open-ended question. This question was analysed throughout the approach of Crabtree and Miller named editing analysis style. This approach implies the researchers to act as interpreters reading through

accounts, identifying meaningful statements to code and defining themes. As the analysis progress, researchers need to constant go back and forward, from data to themes in order to identify categories and sub-categories. This study used a single open-ended question after a structured tool, this may have created bias into the responses. Moreover a qualitative methodology most of the times adopts interviews or focus groups, where researchers could use their skills to gain an in-depth understanding of the participants' experience throughout probe and prompting. This approach was not an opportunity for this study, women's narratives could be richer and more reliable if face to face interviews would be adopted. However, the analysis showed important findings. Childbirth was either perceived to be a normal, natural process that women can and should achieve themselves, or to be a pathologically event, with risks, that needs medical control. Authors reported that childbirth fear is certainly an issue for women before and after birth. The actions and interactions women shared with health care professionals during labour and birth contributed significantly to how women perceived their childbirth experience. Clearly, labour and birth can have an extreme effect on future birth choices and plans, particularly for women whose experience was not so positive. When midwives during the intrapartum care are confident, sensitive and respectful, women's satisfaction is high, residual negativity is low, and belief in birth is maintained. Where care is suboptimal and/or women's fears, distress or disappointment are not identified or adequately addressed, women's satisfaction is low, negative psycho-emotional thoughts occurs and confidence about future birth is dented.

Midwives appear to play a central role for women's and men's experiences, making a difference in both negative and positive recalls [152,174]. Women see midwife as an advocate to empower them to gain control over the birth process [175,182]. The relationship between parents and midwife during childbirth have an important impact on their experience and for future family decision-making [174].

Midwives should support also fatherhood and men's expectations [180,190], as involvement of partners is also associated with maternal emotional well-being, a positive perinatal experience and child development [180]. For this reasons midwives should help fathers to feel accepted and involved during labour as they often reported to experience a lack of utility during the process and to feel physically detached from their partner and the baby [180,190].

Chin et al. [190] aimed to explore first-time fathers' experiences of becoming a father, focusing on their expectations, experiences, and how they are coping with this transition. An interpretative phenomenological analysis epistemology and methodology were adopted, this is valuable for the purpose of the study as researchers aimed to focus on understanding the meaning and experiences of the transition to fatherhood. Investigating how phenomena are experienced and given meaning requires interpretative activity on the part of the researcher. This approach combines phenomenological ("how has this phenomenon been understood by this person?") and

interpretative ("what does this mean for this person, in this context?") components. Nine participants were recruited from seven NCT antenatal classes. Individual semi-structured interviews were conducted with participants, predominantly in their homes, between four and eleven weeks after birth. This research could not to produce results generalizable to all fathers, due to the small sample that a qualitative methodology uses. Expectations have been explored retrospectively. Considering men's expectations before becoming a father, could have gave more in-depth understanding of the beliefs and needs that men have before birth. The findings of this interpretative analysis reported that first-time fathers (aged 30 to 46) experienced an array of psychological responses during each stage of their transition to fatherhood, as they searched for their place as father in relation to their partner, child and work. It is crucial that professionals who work within antenatal and postnatal services discuss the various narratives of fatherhood with men and support them to consider realistic expectations. These findings have significant implications especially for midwives, as supported also by Porret et al. [191], who showed that men's positive experience is influenced by the extent of feeling involved during the birth process, promoting a positive impact on the relationship with their partner and with the child.

This research by Porret et al [191] is a cross-sectional study which aimed to document men's self-reported perceptions of their partners' antenatal, labour, and birthing experiences and to determine whether these perceptions influenced their feelings that their presence during birth was beneficial to the birthing woman. A cross-sectional study is a quantitative descriptive methodological study, which could establish only associations between variables. Although this is appropriate to determine the hypothesized correlation between men's perceptions and their feeling to be helpful for their partner during birth, a qualitative methodology would had better explore first-time fathers' perceptions and feelings. Thus a mixed methodology could be useful. The study population consisted of men whose female partners began labouring spontaneously, who were fluent in English, not health professionals, experiencing for the first time their partner giving birth and who were present throughout the birth regardless of whether this was a vaginal birth (normal or assisted) or an emergency caesarean. A self-administered fourteen-item questionnaire was used to collect data; 163 of 200 eligible participants returned completed questionnaires. The research design did not include potential confounding factors, such as socioeconomic status and different ethnicities. Moreover, all participants attended an antenatal classes, which could mean they were already more involved into the entire maternity pathway, than men who did not undertake them. This could limit the generalizability of results.

Findings showed that the antenatal experience and birth experience were positively and significantly correlated with male partners' feelings to be useful in labour and birth. The more that men viewed their antenatal experience and their experience of their partners' births as positive, the more they perceived that their presence had been beneficial to the women. Moreover, this was

regardless of whether the birth was vaginal or a caesarean section. These results highlight the roles that antenatal education and supportive midwifery practice can play in shaping male partners' perceptions that their partners benefited by their presence. Although men were concerned at times by aspects of the labour, they felt well informed and supported by staff and did not consider that their ability to help their partners through the experience was diminished by their own concerns.

The research reviewed suggested that midwives have a responsibility to empower both women and men regarding their expectations and ensuring that the birth process is a fulfilling experience, especially when women have expressed a fear of childbirth [152]. Helping women to manage anxiety and develop flexible birth plans may be important in decreasing vulnerability to birth-related trauma symptoms that could interfere with bonding with the baby and could affect relationship with the partner [156]. Further studies are needed to understand men's expectations and feelings of fulfilment after the birth process.

The aim of Hildingsson's [152] study, was to describe pregnant women's expectations of birth and to investigate if these expectations were fulfilled. An additional aim was to determine if unfulfilled expectations were related to the mode of birth, use of epidural analgesia and the birth experience. This study is one part of a prospective regional cohort study where women were recruited in mid-pregnancy and followed up after birth. A quantitative methodology with a longitudinal design allowed to have a large sample size (1042 women antenataly and 936 women following their birth) and to collect data for the same subjects repeatedly over a period of time (from early in pregnancy to one year after birth). Women completed four questionnaire: the first with background information, the second assessed fears related to childbirth and expectations, the third collected data about the delivery and evaluate women's satisfaction with birth and the fourth after one year was not considered in this study. Regarding women's expectations about the upcoming birth, five areas of expectations were focused on: support from midwife, support from partner, participation in decision making, feelings of being in control and midwife's presence in the labour room.

The main findings of this study were that certain background characteristics were associated with expectations and with experiences. For example primiparas expected to have high support from the midwife and their partner. Younger women (<25 years) were more likely to expect greater support from their partner, to participate in decision making and to be in control compared to the other age groups. A high level of education was associated with higher expectations on support from midwife, which also was relevant in women who preferred to have a caesarean section. Fearful women had higher expectations in all areas compared to non-fearful women.

Women valued as important their participation in decision making and control, which were strongly associated with mode of birth; these factors were assessed as low with mode of birth other than vaginal. An experience worse than expected, was also associated with a less positive birth

experience. Being younger than 25 years, expecting the first baby and suffering from childbirth-related fear were associated with higher birth expectations.

Women undergoing caesarean sections reported lower mean scores in their experiences of midwife support, of being in control and in participation in decision making. Epidural was associated with lack of control. High expectations regarding the support from the midwife, was less likely to be achieved. This study [152] was conducted in one single region in Sweden. There was a large dropout rates from late pregnancy until after birth, this could have affected the results and the sample's characteristic. Participants were, in fact, healthier women compared to the general population and with a higher level of education. Therefore, for these reasons, it is difficult to generalize findings. Women not knowing Swedish language were not invited to participate, this could have affected the results. Although a quantitative methodology allowed to evaluate correlation between variable, a qualitative studies with participants' interviews might be a better design for a more in-depth investigation in the area.

The concept of maternal satisfaction is challenging, as women's and clinician's expectations and experiences may differ. Women appear to be satisfied when are in control over the birth process, are involved in their care and in decision-making; they value sensitive, respectful and shared relationship with healthcare professionals ensuring women-centred care [152,169,172,185,188].

2.5 Summary of Literature Review

Most of the cited studies used a quantitative methodology to assess parents' expectations of childbirth and a retrospective analysis, examining women's views, beliefs and attitudes immediately post birth. Women however often feel a sense of relief and euphoria following birth and their post-birth feelings may not be so positive following a period of reflection. There has been extensive research carried out looking into maternal expectations and into women's satisfaction with birth. However, none of the studies considered, explored using a qualitative methodology and a prospective approach women's expectations on childbirth during pregnancy and whether the expectations identified were fulfilled after birth.

Moreover, the qualitative studies appraised, due to the small sample size, could not be transferalised to a different population, a different culture or a diverse midwifery model of care.

Compared with research into women's expectations, fathers' expectations, perceptions and experiences regarding the pregnancy and birth, have not been extensively studied.

Research highlights that women want a spontaneous birth, in order to preserve their integrity, their control over the process and to be able to participate in decision-making. They value women-centred midwifery care and would like more continuity throughout the childbearing continuum. They want their partner to be with them, to share the experience. The partner's presence is to support

the maternal well-being, to establish an early bonding with the neonate and to promote parenthood.

A positive experience and satisfaction with birth can be influenced by expectations' fulfilment.
However, it has been demonstrated that maternal expectations could be influenced by a high risk culture around childbirth and the mass media negative information and that women's attitudes towards obstetric intervention have become more positive.
Midwives have a key role to empower women to experience feelings of fulfilment after their childbirth, in order to have a positive experience of the process. Midwives, however, should also support fathers-to-be, in order to avoid feelings of isolation, to encourage a family centred approach and to promote benefits for the mother and the newborn, that result from fathers being involved in the maternity care.

A gap in research evidence is therefore evident, research is needed to gain a deep understanding of Italian parents' expectations around childbirth, within a country with a high medicalization of the maternity childbearing continuum. A qualitative methodology is sought to explore whether expectations are fulfilled, in order to improve midwifery care and to ensure a positive parents' experience of birth.

CHAPTER THREE: RESEARCH PROPOSAL

3.1 Introduction

This chapter describes the proposed research design, including methodology and data collection approach. The research question is justified, followed by an outline of the recruitment and

sampling, data collection and data analysis method which will be presented. In addition, criteria to maintain the quality within a research and ethical considerations, will be discussed.

3.2 Research question

What are parents' expectations regarding childbirth and are these expectations fulfilled?

3.3 Justification for research

The literature review has shown that pregnant women expect to have a spontaneous labour, to be supported by partner and midwives, to be in control over the process and to have a role in decision-making [161,172,173,182]. A strong emotion expressed by women in many research papers is fear of the unknown [172,173] and fear of pain in childbirth [161,173] that often led to loss of control [152,161]. In addition, research reveals a high risk culture surrounding the childbearing continuum, especially around labour and birth, may change expectations and make women more prone to interventions [159,168,169].

Research on men's expectations and satisfaction with birth is limited, but it has been shown that they often feel isolated during the process, feel detached during labour from their partner and their child and would like to receive more support from the midwife [150,180,190].

The literature has also demonstrated that midwives appear to play a central role in women's and men's experiences, making a difference in both negative and positive recalls [152,174]. Women see the midwife as an advocate to empower them to gain control over the birth process [175,182]. The relationship between parents and midwife during childbirth have an important impact on their experience and for future family decision-making [174].

Satisfaction with birth experience is one of the most important outcomes to monitor the quality of maternity services. From the Literature it appears there is a relationship among maternal expectations of childbirth and satisfaction with the birth [151–153].

Further research is required to better understand women's and men's expectations in a medicalized environment. In addition the researcher should explore further to comprehend if these expectations are fulfilled, in order to accurately ascertain if midwifery care delivers what matters to parents-to-be.

This study has the potential to support midwives to improve their daily practice and to empower women in order to ensure a positive experience of birth.

3.4 Primary aim and objectives of the study

The aim of this study is to explore parents' expectations of labour and birth and to investigate whether their expectations were fulfilled.

The objectives of the study are:

- to gain insight into first time parents' beliefs, needs and wishes regarding labour and birth
- to explore whether the expectations expressed by parents have been fulfilled
- to highlight any potential opportunity to improve midwifery care to enable a positive childbirth experience for parents

3.5 Methodology

There are two main research methodologies: quantitative and qualitative.
In Italy there is no published evidence focusing on maternal or paternal expectations on labour and birth.
In order to explore this phenomenon, within the Italian context, a qualitative methodology is proposed.

Qualitative research allows the researcher to gain an understanding of the behaviours, interactions, attitude, beliefs, experiences and opinions of individuals, enabling an approach to interpret life experiences and to provide meaning [192].
People experiences are subjective and cannot be adequately accounted for in a numerical way. Therefore a qualitative methodology using focus groups or semi-structured interview allows the perspective and the emotions of the individual experiencing the phenomena to be explored [4]
This research methodology is also coherent with the fundamental elements of midwifery, which are: a holistic approach to care, empathy and woman/family-centred care [5]. In relation to this study, a structured questionnaire with closed-ended questions would not produce the information required. It would not generate an in-depth views from the participants' lived experience and would not create an in-depth understanding of the participants' beliefs and feelings, needed to answer the research question.

Qualitative research enables the understanding of behaviours, interactions, attitudes, beliefs, experiences and opinion of individuals or groups of people [5]. This methodology usually starts with a broad research question, in regard to the topic that the researcher wants to consider, and it is suitable to explore phenomena about which little is previously known or reported [4]. Research methods adopting qualitative methodology have flexible, evolving research designs. This means that the researcher does not always know at the beginning of a qualitative study exactly how they will conduct the research [5].

The researcher needs to maintain an open-mind approach, in order to be sure that the knowledge about the phenomenon do not influence the way in which the study will be conducted. Before

starting a qualitative study, it is in the researcher's interest to make clear his own thoughts, ideas, suppositions and preconceptions about the topic and the potential impact of these on the findings. The purpose of this process, called reflexivity, is to bring to consciousness and reveal what is believed about a topic, in order to be in a better position to approach the topic honestly and openly [4]. Participants recruitment, data collection and data analysis, often occurs simultaneously.

Studies using a qualitative methodology usually involve small, relevant samples. Non-probability sample methods are used and participants are recruited because they have lived an experience of interest that the researcher is exploring [4]. The researcher is able to understand that the sample size is enough when saturation is reached. This is a feature that is used in qualitative research to refer to the repetition of discovered information and confirmation of previously collected data [4].

The most commonly used qualitative data collection methods are interviews, diaries, focus groups, participant and non-participant observation, case studies and life histories.

3.6 Research Approaches

There are three main approaches within qualitative research, which are: Ethnography, Grounded Theory and Phenomenology [5]. Within Phenomenology, there are considered to be two main schools of thought: Husserlian and Heideggerlain. These two theoretical underpinnings determine two different approaches to phenomenology: descriptive and interpretative respectively.

The main purpose of this research is to gain the lived experience of participants. A phenomenological approach aims to discover the meaning of a person's life and this is based on the premise that a person's reality is determined by their interpretations of their world [5].
The aim of this study is to describe phenomena in its purest sense, and to report participants' views.
Therefore, the study adopted a descriptive approach, the researcher strived to bracket all conscious preconceptions and predeterminations regarding parents' expectations and their fulfilment.

Phenomenology has its foundation in the ideologies of Husserl and Heidegger [193], the purpose is to gain insight into the experience of individuals and is based on the notion that a person's reality is determined by their participations of their world. This approach describes particular phenomena, or the appearance of things, as lived experience [192]. The overall aim of using a phenomenological approach is to develop knowledge within the disciplinary interest [192].

Phenomenology as a research approach is rigorous, critical and a systematic investigation of phenomena [4]. This approach requires participants who have encountered the events or experiences that the researcher is investigating. Therefore non-probability, purposive sampling is required. The researcher usually has an idea of the number of participants that will be recruited, however data saturation will determine final sample size. This occurs when data collection and data analysis do not reveal any new findings and so the recruitment of further participants is deemed unnecessary [5]. A variety of data collection methods may be used, as interviews and focus groups, during which participants are encouraged to reflect upon their experience and feelings. There are also different method of data analysis, the most commonly used is thematic analysis [5]. Data are coded to identify themes, which may contain sub-themes.

Husserl's descriptive phenomenology focuses on the concept of a lived world and lived experience [5]. With this approach, the researchers step out of their natural attitude and "brackets" their world from consciousness [192], in order to set aside, suspend prior knowledge, assumptions, preconceptions and beliefs. Bracketing is usually done before the study begins, by reflecting on what researchers know about the phenomenon they want to explore. It also assists data collection and analysis by increasing the likelihood that the reported findings describe the participants' experiences and are not influenced by the researcher's ones, this would increase trustworthiness within results.
A rigorous process of data analysis is a key feature of descriptive phenomenology. Particular attention is paid to the research design and the steps taken in data analysis, which emphasizes the importance they place on rigour [192].

The underpinning philosophy of midwifery is congruent with that of phenomenology as it is both person-centred and a holistic approach and require skills of communication, observation and interpersonal interaction [192]. Midwifery is concerned with delivering quality care, understanding women and their environmental and personal factors. The researcher is able to focus on the whole person and gain insight into their lived experience. Midwives need to understand the perceptive, beliefs and attitudes of women and their families in order to care after them effectively [5]. For these reasons and due to the purpose of this research, which is to gain the lived experience of participants, a phenomenological approach was undertaken.

3.7 Sampling and recruitment

Phenomenology requires participants who have encountered the events or experiences that the researcher is investigating. This strategy is used in qualitative research where there is no intention to generalise the findings to the study population [5]. The strategy commonly used in non-probability sampling are: convenience, purposive, quota, snowball and theoretical sampling.

Purposive sampling is commonly used to allow the researcher to include participants with a lived experience of the topic that needs to be explored. For this reason a purposive sampling strategy was adopted.

Participants recruited met the study's inclusion criteria and experienced the phenomenon under investigation. Therefore non-probability, purposive sampling strategy was used for the purpose of this study.

The recruitment process lasted five months, following the ethic approval. Parents were approached to participate in the study during the third trimester of pregnancy by the midwives who conducted the antenatal classes. Midwives were fully informed about the study and were asked to help by giving brief information about the study to parents, providing them with the participant information sheet (Appendix 2). Four different groups of antenatal classes were approached and asked to participate into the study, however none of the parents' to be agreed to participate. The fifth group of mothers accepted to participate and from them were selected primiparous and low risk women. My contact details were available in case clarification from both midwives and parents was required. Those who wanted to participate in the study contacted the researcher by telephone, text or email. Otherwise, the woman or her partner left their contact details with the midwife using a participant's contact details form. In this case, the researcher contacted them by telephone. For the first part of the study, participants were asked to attend a focus group, one for men and one for women. During the focus groups I explored parents' expectations of labour and birth. Therefore the researcher arranged a suitable time and venue for all participants to attend the focus groups.

The second step of the study is in progress.

Following birth, parents were asked to participate to an interview to gain parents' experience of expectations' fulfilment. The researcher checked the birth register for the date of birth, and get in contact with parents, in order to meet the inclusion criteria of the study. As the period following the birth of their babies is a time when parents make the transition to parenthood and, in order to leave time to reflect on their experience, participants were left time to build the new family and think about their experience. I then contacted both parents by phone, to arrange a suitable place and time for the interview.

3.7.1 Setting

The research setting is a consultant-led maternity unit delivering approximately 2500 babies per annum; this has been chosen, even if low risk women were recruited, due to the absence of a Midwifery Led Birthing Unit in the trust affiliated to the University. However, this hospital has a historical underpinning philosophy which seeks to maintain birth as a normal process. Hospital midwives conduct antenatal classes, which start around 28 of gestational age and finish when

women are at 38 weeks gestation. They attend ten classes during pregnancy, at least four with their partners, and one last meeting when all babies are born.

Women in active labour are admitted to the Delivery Suite, which facilitates four delivery rooms, where women and their birth partner stay during labour and delivery and two hours after birth with the baby. Labour ward midwives provide one-to-one midwifery care to all women.

Following two hours after birth, women and babies are transferred to the post-natal ward. They are discharged 24 to 48 hours after a spontaneous delivery and at least after 72 hours if a caesarean section occurred.

3.7.2 Sample

Consent forms was obtained from all participants (Appendix 3).

This qualitative research used combination of focus groups and semi-structured interviews.

The inclusion criteria for the focus groups and fro the interviews are reported in Table 3 and Table 4, respectively.

Inclusion	Exclusion	Rationale
Primigravida women and their partners.	Multiparous women and their partners.	The first birth experience is known to shape future reproductive choices (Borrelli, 2016).
Women with a straight-forward pregnancy (single fetus) anticipating a normal birth and their partners.	Women with medical/obstetric conditions or multiple pregnancy and their partners.	Complications during pregnancy could lead to change in expectations and greater worries (Fenwick, 2012).
Participants need to be able to read and speak Italian sufficiently to understand the information leaflet and to participate in the interview.	Women and their partners who cannot read or speak Italian sufficiently to understand the information leaflet and to participate in the focus group.	To eliminate translation biases.
Gestational age between 36 and 40 weeks.	Gestational age prior than 36 weeks	By this time, pregnant women and their partner have formed opinions about childbirth, and they are focused on the event (DeLuca and Lobel, 2014; Fenwick, 2012).

Table 3: Inclusion and Exclusion Criteria for the focus groups

Inclusion	Exclusion	Rationale
Primigravida women and their	Multiparous women and their	The aim of the study is to

partners, who participated in the focus groups discussion.	partners or primigravida women and their partners, who did not participate in the focus groups discussion.	explore whether parents' expectations were fulfilled.
Participants need to be able to read and speak Italian sufficiently to understand the information leaflet and to participate in the interview.	Women and their partners who cannot read or speak Italian sufficiently to understand the information leaflet and to participate in the interview.	To eliminate translation biases.
Women and their partners at least six weeks following birth.	Women and their partners prior than six weeks following birth.	Parents often feel a sense of relief and euphoria following birth, but they could change their feelings following a period of reflection (Brodrick, 2008; Fenwick 2012)

Table 4: Inclusion and Exclusion Criteria for interviews

Eight couples took part into the study and two focus groups were conductd, one with eight women and the other one with eight men.
Before conducting the interviews, three couples were randomly selected from the participants of the focus groups. Individual interviews are ongoing.

Many phenomenological studies require in-depth data with time-consuming methods of data collection, for these reasons, sample size are typically small in number and selective in nature (Harvey and Land, 2017). Data collection usually end when data saturation has occurred or depending on the number of participants available.

3.8 Method of data collection

There are a vast array of data collection methods available to the researcher. When deciding which method of data collection to use, the most important factors to consider is the need to achieve the aim and objectives of the study [5]. The choice of data collection should be determined by the research question. Other elements could influence the choice of data collection method, such as: time available, the research setting, researcher skills, resources required and available, costs, acceptability to participants [5].
Data collection was undertaken in the form of focus groups during pregnancy and semi-structured interviews after birth.

3.8.1 Focus groups

The focus groups took place on the 17th of July 2019, during the third trimester of pregnancy of the participants, between 36 and 40 weeks of gestational age. By this time women and their partners formed opinions about childbirth, and they were focused on the event [155,180]. Couples were recruited from antenatal classes and they were divided, in order to have a focus group with women and another focus group with their partners. Both focus groups were audio-recorded.

Focus groups were employed rather than individual interviews to ensure that wide ranging ideas emerged and debate among participants follows. Group settings are known to have a synergistic effect over one-to-one interview settings [194]. Group size is an important consideration in focus group data collection method.

According to Carlsen and Glenton's review [195] of 220 focus group research publications, almost half failed to mention the minimum and maximum number of participants. A focus group should generate sufficiently extensive relevant information; benefit from group interactivity; prevent socially correct responses; avoid non-conducive activities such as the researcher holding the floor; or stop participants feeling shy about contradicting a fellow interviewee [196]. Therefore a focused group of two to four people cannot achieve these purposes. At the other end the interviewer should have deep skills to manage in-depth focused information gathering from more than twelve participants (even with a digital recorder/note taker) who are unknown to each other, within a timeframe of 90 minutes [196].

Fundamentally, for focus group methods of data gathering, the phenomenon being investigated should determine how many participants in each group to optimize interactivity; and the research question itself guides researchers to decide how many focus groups are needed and why [196].

Participants should be likely to generate rich, dense, focused information on the research question to allow the researcher to provide a convincing account of the phenomenon [192]. Stewart & Shamdasani [194], suggest that is better to slightly over-recruit for focus group and potentially manage a slightly larger group, that under-recruit and risk having to cancel the session or having an unsatisfactory discussion. They advise that each group would probably have two non-attenders. The optimum size of a focus group is between five and ten participants [5]. Therefore, in order to promote discussion, to be able to manage the group and considering potential withdraw, eight participants were recruited for each focus group.

The strength of approaching parents from antenatal classes is that women and men already knew each other, this should facilitate communication and make participants uninhibited to participate in discussion. This would facilitate narrative and meaning of argumentation for the researcher. The time and place for the focus groups were arranged with each participant, guaranteeing privacy and confidentiality. The purpose of a focus group is that participants not only respond to the questions asked by the researcher, but that they also discuss issues raised by fellow participants.

The researcher conducted the focus groups using a topic guide (Appendix 4), which consists of key open questions and probes, in order to encourage participants to share their expectations of labour and birth. However, they also need to enable a balance between an open interview and focusing on significant areas [197].

Conducting a focus group could be also challenging, as the researcher needs to be able to balance participants' interventions, in order to give all people the same chance to speak and to contribute to the discussion and to the study [5].

3.8.2 Interviews

Qualitative interviews may vary based on the level of control the interviewer has over the participants' answers [4]. The structure of the interview depends on the type of investigation being conducted and the purpose of the study, so it can range from structured, to semi-structured and unstructured.

Structured interviews are best used when the topic is already known and the researcher want to generalize data to the population. They standardized data that can be easily analysed, however they reduce the extent to which individual circumstances and differences can be explored [5]. Unstructured interviews are useful when exploring new topic and ideas or when the phenomenon is not known or not well understood. They allow participants to express themselves freely and the research should not interfere, in order to gain the most information possible [5].

For the purpose of this study, semi-structured interviews were adopted, in order to encourage participants to speak freely having an interview schedule as a guide. Probes and prompts to gain deep understand of the topic were added.

The topic guide (Appendix 5) reported the semi-structured interviews, characterised by open questions to stimulate discussion and enable participants to respond as comprehensively as possible. The interview started with an initial broad opening question, but the order of the subsequent questions could change. This helped to follow the interviewee discussion and enables flexibility in the semi-structured interviews. The topic guide enabled exploration of the topic initially raised by the participant, in order to gain a deeper understanding enrich information. The researcher must be extremely vigilant throughout the interview to ensure that, by the end, all of the questions on topic guide have been addressed [5].

Before meeting with parents after childbirth, the interviewer re-read the transcripts of the focus groups. At the time of the interview, references made to the topics previously discussed with the participant, stimulating the comparison between expectations and experiences.

Interviews took place sometime following the birth of the baby, to give time to parents to settle in their new role and because, often, parents feel a sense of relief and euphoria following birth, but they could change their feelings following a period of reflection [172,180]. The purpose of these interviews was to gain perceptions, feelings and lived experience of participants regarding the

fulfilment of their expectations, for this reason parents had a period of time to reflect on their experiences.

3.8.3 Reflective accounts

The researcher is a midwife undertaking a PhD in Public Health. Both Supervisors are midwives as well by background, Midwifery Teaching Fellows and experienced researchers; they contributed to the design of the study and provided insights during all project stages. The researcher declared to participants that she is a midwife before the focus group discussions. It is acknowledge that parents may have difficulties to report negative experience about midwifery care that they received, this could impact on the fulfilment of expectations [152,154,161,169,173,182]. Whether this element could be a limitation in the research, will only be identified after data analysis.

3.9 Method of data analysis

The purpose of qualitative data analysis is to understand meaning and to provide an accurate portrayal of that meaning for others [5]. Qualitative data analysis is an iterative process, as the researcher will deeply engage with data, in order to facilitate her understanding and interpret the findings.

Qualitative data analysis differs from quantitative approaches as it is characterized by the ongoing interpretation of data while collecting is still taking place [4].

Although qualitative methodology generally involve small samples, they generate vast quantities of data, therefore the researcher needs to decide how the data will be organizes and managed [5].

The transcription of audio-recorded data usually takes a long time and can be seen as the first step of the data analysis process [5]. The researcher, while transcribing, will be listening to participants' discussion and will be processing the data.

There are numerous ways in which qualitative data can be analysed and there are frameworks to support the process. The most commonly used method to analyse qualitative data is thematic analysis [5]. Several procedural interpretation of phenomenological method are available, such as Colaizzi (1978), Giorgi (1985), Petrson & Zderard (1976) and van Kaam (1984) [4].

In this study a thematic analysis will be adopted using Colaizzi's method (1978). This framework has been chosen for this research due to its simple, accessible format and compatibility with semi-structured interviews analysis [198].

The process of data analysis will begin with the researcher transcribing verbatim the audio-recorded participants' discussion and reading and re-reading the text, in order to become familiar

with the data and to begin to develop an understanding of the phenomenon. Relevant and important statements will then be extracted. Meaning from these statements will be interpreted with the intent to highlight unknown aspects of the phenomena. Meanings will be aggregated into clusters that will form themes, with each theme capturing the essence of the data it contains [5]. Similarities, differences, links, patterns and contradictions between themes could emerged, this process will originate sub-themes. From themes, categories will emerge to describe the phenomenon under study.

The last step of Colaizzi's method (1978) is to return to participants with findings, in order to validate the description.

During this study, the researcher will not undertake this final step as it can be a very long process, participants can change their minds and it is difficult to collect experiences again and incorporate them together in order to achieve a new exhaustive description of the phenomenon.

This study, alternatively, performed member checking [199] during the focus groups and during the interviews, in order to validate participants' expressions and be sure to understand what participants intended.

NVivo software package will be used to manage, organize and to sort data in one place in order to see them more clearly.

3.10 Ethical considerations

3.10.1 Informed consent

Informed consent means that participants have adequate information regarding the research, are capable to understand the information and have the power of free choice, in order to consent to participate in the study, to decline or to withdraw at any time [4]. Therefore, informed consent was gained from all participants involved in the study. A consent form is provided in appendix 4.

3.10.2 Confidentiality and anonymity

A researcher has a duty to discover potential benefits of the research while minimising harm during the process by adhering to principles of beneficence and non-maleficence [4]. The sensitive topic of this study could potentially trigger participants' feelings of disappointment or sadness (Harvey and Land, 2017), therefore it is crucial to reduce emotional stress. For this reason the researcher, in the Participant Information Sheet (Appendix 3), made clear that support and debriefing could be provided at any time to participants, if required.

The researcher will not discuss or share data collected with others, rather than supervisors and her research team; during the study any information will be stored safely within university premises and data will not be accessible. Audio-taped discussions will be stored securely on laptops that will be password protected and at the completion of the study disposed of properly (Data Protection Code, 2003; GDPR, 2018).

3.10.3 Ethical approval

Ethical approval for the study was given by the Brianza Ethics Committee (N°2918, 13/12/2018*).*

CHAPTER FOUR: DISCUSSION

4.1 Introduction

In this chapter the Italian culture around midwifery care is discussed, this supports a better understanding of the context where the study will be conducted and potential findings indicated. Limitations of the research design and implications for the future of Midwifery practice have also been described.

4.2 Anticipated findings

Literature suggests that the majority of women expect to have a straightforward birth [157,172,173], however as events during labour and birth could also go differently than expectations, women are also aware that sometimes they will need to go with the flow [172,185]. Fathers-to-be expect to be present, to share the experience with their partner and to have a natural process and a healthy baby [180,200]. However there are also men who feel pressured to attend, could express overwhelming feelings and inadequacy in their ability to support their partner [200]. In addition, the literature highlights that women exposed to a more medicalized culture are less likely to view birth as a natural event, resulting in a higher preference to have a caesarean section and a passive attitude in expressing their views. A high risk culture around childbirth may change expectations and make women more prone to interventions [161,166,168,169]. Evidence also suggests the role of the midwife to support and address couple's expectations and that women would like midwives to be their advocate for normal birth offering them evidence-based information [152,175,182].

In Italy the midwifery care is provided mainly during labour and birth in consultant-led units; maternity care during pregnancy is led by obstetricians, during the postnatal period women are cared for by midwives or nurses and the newborn care (either healthy or sick) is provided by nurses.

There is high degree of medicalization during the childbearing continuum [163].

Although the Italian Midwifery Council recognizes the midwife as the healthcare professional who should provide care to the family during pregnancy, labour and birth and the postnatal period, she is also the professional who conducts antenatal classes, should be involved in the prevention of women's cancers, during sexual education and care for women in the menopause, she has a marginal role during these processes.

The hospital where the study was conducted, has a historical underpinning philosophy which seeks to maintain birth as normal process and midwives are the main professionals providing the care when women undergo a physiological pathway.

These considerations lead to different potential findings that will be presented.
Italian women, as the literature suggests [161,168,169], could feel disempowered and unable to give birth naturally, due to the influence of the medicalized culture around the childbearing continuum and especially around birth. Conversely, women are normally aware about the mission of each hospital and would chose consequently [161]. This means that women delivering in the hospital where the study took place, could be more conscious about their competencies to give birth naturally and they would want to maintain the process as physiological as possible. Their partners could share the same thoughts at the end of pregnancy [180]. However, when women desire a natural process, fathers could experience fear to cope with their partners' pain and feel unable to support them [180,190,200]. The Italian society, as other western countries, expect fathers to play a significant role throughout pregnancy, labour, childbirth, the postnatal period and beyond [149].

Findings regarding a feeling of fulfilment depend on parents' expectations as the evidence suggests that fulfilled maternal expectations increase a more positive overall childbirth experience [151–153].
Italian women, due to the culture surrounding childbirth, could accept many interventions during the process [166,168,169] and see their experience as normal, therefore they could express feelings of fulfilment. Otherwise, they could accept the healthcare professionals' control, but feel disempowered during the process when interventions occur [152,158,161,188].

In addition, hospital midwives do conduct antenatal classes and this could impact on parents' views [167].

4.3 Limitations

There are a few limitations associated with this study.
The small predicted sample size and parents planning their midwifery care in a single hospital will generate findings that could not be generalised.

Participants were recruited from antenatal class groups, this reflects a study population that could be more involved during pregnancy [167,190,201]. In addition, due to the high intervention rate in Italy [163] and because only primiparae were recruited, a choice has been made to include women who experienced a I or II degree tear or an episiotomy. These criteria could impact on women's feelings of fulfilment [152,158,161].
The researcher declared to the participants that she is a midwife before the focus group discussions. It is acknowledge that parents may have difficulties to report negative experience

about midwifery care that they received, that could impact on the fulfilment of expectations [152,154,161,169,182]. Whether this element could be a limitation in the research, will only be identified after data analysis.

4.4 Implications for Midwifery practice and Future Research

This study should identify Italian women's expectations on labour and delivery, with their partners' perceptives as well, for the first time, adding credibility to the research and future publications.

This study could highlight differences in mothers' and fathers' birth expectations and feelings of fulfilment, providing midwives with recommendations to support them accordingly, by adapting care provision surrounding childbirth. Midwives in order to promote a family centred care approach, must support fathers to-be during labour and birth as they do for women.

Since fulfilment of expectations could predict experience satisfaction [151–153] and since a positive experience of labour and birth is what the World Health Organisation recommends for every women, midwives have the responsibility to give to couples the opportunity to share their expectations, in order to shape midwifery care around them.

Midwives are ideally place and recognized as the most appropriate health care professionals to empower women and their families, to be aware of their innate competencies in order to support them to have a positive experience of birth [164].

Possible future research could investigate if parents are satisfied with their overall experience of birth. Furthermore, it would be interesting to explore midwives' perceptives on what they think mothers and fathers expect from their birth, in order to compare parents' and professionals' views. Moreover it would be important to include a larger sample size, in order to involve parents from different Hospitals.

References

[1] Peristat Monitoring and Evaluating Perinatal Health in Europe n.d.
[2] Lewis G. Saving Mothers' Lives: The Continuing Benefits for Maternal Health From the United Kingdom (UK) Confidential Enquires Into Maternal Deaths. Seminars in Perinatology 2012;36:19–26. https://doi.org/10.1053/j.semperi.2011.09.005.
[3] Harvey M. Research methods for nurses and midwives. Place of Publication Not Identified: Sage Publications; 2015.
[4] Speziale HS, Carpenter DR. Qualitative research in nursing: advancing the humanistic imperative. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2011.
[5] Harvey M, Land L. Research methods for nurses and midwives. Theory and Practice. Place of Publication Not Identified: Sage Publications; 2015.
[6] Paruk F, Moodley J. Severe obstetric morbidity: Current Opinion in Obstetrics and Gynecology 2001;13:563–8. https://doi.org/10.1097/00001703-200112000-00003.
[7] Canada, Canadian Perinatal Surveillance System, editors. Special report on maternal mortality and severe morbidity in Canada: enhanced surveillance: the path to prevention. Ottawa: Health Canada; 2004.
[8] Madsen P, Dillon RL, Tinsley CH. Airline Safety Improvement Through Experience with Near-Misses: A Cautionary Tale: Airline Safety Improvement Through Experience with Near-Misses. Risk Analysis 2016;36:1054–66. https://doi.org/10.1111/risa.12503.
[9] Geller SE, Rosenberg D, Cox SM, Kilpatrick S. Defining a conceptual framework for near-miss maternal morbidity. J Am Med Womens Assoc (1972) 2002;57:135–9.
[10] Pattinson R, Hall M. Near misses: a useful adjunct to maternal death enquiries. British Medical Bulletin 2003;67:231–43. https://doi.org/10.1093/bmb/ldg007.
[11] Say L, Pattinson RC, Gülmezoglu AM. WHO systematic review of maternal morbidity and mortality: the prevalence of severe acute maternal morbidity (near miss). Reprod Health 2004;1:3. https://doi.org/10.1186/1742-4755-1-3.
[12] Filippi V, Alihonou E, Mukantaganda S, Graham WJ, Ronsmans C. Near misses: maternal morbidity and mortality. The Lancet 1998;351:145–6. https://doi.org/10.1016/S0140-6736(05)78106-X.
[13] Fitzpatrick C, Halligan A, McKenna P, Coughlan BM, Darling MR, Phelan D. Near miss maternal mortality (NMM). Ir Med J 1992;85:37.
[14] Say L, Souza JP, Pattinson RC. Maternal near miss – towards a standard tool for monitoring quality of maternal health care. Best Practice & Research Clinical Obstetrics & Gynaecology 2009;23:287–96. https://doi.org/10.1016/j.bpobgyn.2009.01.007.
[15] Oliveira-Neto A, Parpinelli MA, Cecatti JG, Souza JP, Sousa MH. Sequential Organ Failure Assessment Score for Evaluating Organ Failure and Outcome of Severe Maternal Morbidity in Obstetric Intensive Care. The Scientific World Journal 2012;2012:1–8. https://doi.org/10.1100/2012/172145.
[16] Pattinson R, Say L, Souza JP, van den Broek N, Rooney C. WHO maternal death and near-miss classifications. Bull World Health Org 2009;87:734–734. https://doi.org/10.2471/BLT.09.071001.
[17] Knight M, INOSS. The International Network of Obstetric Survey Systems (INOSS): benefits of multi-country studies of severe and uncommon maternal morbidities. Acta Obstet Gynecol Scand 2014;93:127–31. https://doi.org/10.1111/aogs.12316.
[18] Knight M, Lindquist A. The UK Obstetric Surveillance System: Impact on patient safety. Best Practice & Research Clinical Obstetrics & Gynaecology 2013;27:621–30. https://doi.org/10.1016/j.bpobgyn.2013.03.002.
[19] Zwart J, Richters J, Öry F, de Vries J, Bloemenkamp K, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide

population-based study of 371 000 pregnancies. BJOG: An International Journal of Obstetrics & Gynaecology 2008;115:842–50. https://doi.org/10.1111/j.1471-0528.2008.01713.x.
[20] Driessen M, Bouvier-Colle M-H, Dupont C, Khoshnood B, Rudigoz R-C, Deneux-Tharaux C. Postpartum Hemorrhage Resulting From Uterine Atony After Vaginal Delivery: Factors Associated With Severity. Obstetrics & Gynecology 2011;117:21–31. https://doi.org/10.1097/AOG.0b013e318202c845.
[21] Donati S, Senatore S, Ronconi A, the Regional Maternal Mortality Working Group. Obstetric near-miss cases among women admitted to intensive care units in Italy: Obstetric near-miss in Italy. Acta Obstetricia et Gynecologica Scandinavica 2012;91:452–7. https://doi.org/10.1111/j.1600-0412.2012.01352.x.
[22] Dell'Oro S, Maraschini A, Lega I, D'Aloja P, Andreozzi S, Donati S. Primo Rapporto ItOSS. Sorveglianza della Mortalita Materna 2019.
[23] Tunçalp Ö, Souza J. Maternal near-miss audits to improve quality of care. BJOG: Int J Obstet Gy 2014;121:102–4. https://doi.org/10.1111/1471-0528.12868.
[24] World Health Organization, editor. Beyond the numbers: reviewing maternal deaths and complications to make pregnancy safer. Geneva: Dept. of Reproductive Health and Research, World Health Organization; 2004.
[25] Graham WJ. Criterion-based clinical audit in obstetrics: bridging the quality gap? Best Practice & Research Clinical Obstetrics & Gynaecology 2009;23:375–88. https://doi.org/10.1016/j.bpobgyn.2009.01.017.
[26] Lewis G. The cultural environment behind successful maternal death and morbidity reviews. BJOG: Int J Obstet Gy 2014;121:24–31. https://doi.org/10.1111/1471-0528.12801.
[27] Knight M, Lewis G, Acosta C, Kurinczuk J. Maternal near-miss case reviews: the UK approach. BJOG: Int J Obstet Gy 2014;121:112–6. https://doi.org/10.1111/1471-0528.12802.
[28] Pattinson RC, Buchmann E, Mantel G, Schoon M, Rees H. Can enquiries into severe acute maternal morbidity act as a surrogate for maternal death enquiries? BJOG: An International Journal of Obstetrics & Gynaecology 2003;110:889–93. https://doi.org/10.1111/j.1471-0528.2003.03044.x.
[29] Browne JL, van Nievelt SW, Srofenyoh EK, Grobbee DE, Klipstein-Grobusch K. Criteria-Based Audit of Quality of Care to Women with Severe Pre-Eclampsia and Eclampsia in a Referral Hospital in Accra, Ghana. PLoS ONE 2015;10:e0125749. https://doi.org/10.1371/journal.pone.0125749.
[30] Bhattacharyya S, Srivastava A, Knight M. Developing a framework to review near-miss maternal morbidity in India: a structured review and key stakeholder analysis. BMC Health Serv Res 2014;14:553. https://doi.org/10.1186/s12913-014-0553-x.
[31] Bacci A, Hodorogea S, Khachatryan H, Babojonova S, Irsa S, Jansone M, et al. What is the quality of the maternal near-miss case reviews in WHO European Region? Cross-sectional study in Armenia, Georgia, Latvia, Republic of Moldova and Uzbekistan. BMJ Open 2018;8:e017696. https://doi.org/10.1136/bmjopen-2017-017696.
[32] Okong P, Byamugisha J, Mirembe F, Byaruhanga R, Bergstrom S. Audit of severe maternal morbidity in Uganda – implications for quality of obstetric care. Acta Obstet Gynecol Scand 2006;85:797–804. https://doi.org/10.1080/00016340600593331.
[33] Lazzerini M, Richardson S, Ciardelli V, Erenbourg A. Effectiveness of the facility-based maternal near-miss case reviews in improving maternal and newborn quality of care in low-income and middle-income countries: a systematic review. BMJ Open 2018;8:e019787. https://doi.org/10.1136/bmjopen-2017-019787.
[34] Hutchinson C, Lange I, Kanhonou L, Filippi V, Borchert M. Exploring the sustainability of obstetric near-miss case reviews: a qualitative study in the South of Benin. Midwifery 2010;26:537–43. https://doi.org/10.1016/j.midw.2010.05.016.
[35] World Health Organization. Evaluating the quality of care for severe pregnancy complications. The WHO near-miss approach for maternal health. Geneva: World Health Organisation: 2011.

[36] Jabir M, Abdul-Salam I, Suheil DM, Al-Hilli W, Abul-Hassan S, Al-Zuheiri A, et al. Maternal near miss and quality of maternal health care in Baghdad, Iraq. BMC Pregnancy Childbirth 2013;13:11. https://doi.org/10.1186/1471-2393-13-11.
[37] Souza JP, Gülmezoglu AM, Vogel J, Carroli G, Lumbiganon P, Qureshi Z, et al. Moving beyond essential interventions for reduction of maternal mortality (the WHO Multicountry Survey on Maternal and Newborn Health): a cross-sectional study. The Lancet 2013;381:1747–55. https://doi.org/10.1016/S0140-6736(13)60686-8.
[38] van den Akker T, Beltman J, Leyten J, Mwagomba B, Meguid T, Stekelenburg J, et al. The WHO Maternal Near Miss Approach: Consequences at Malawian District Level. PLoS ONE 2013;8:e54805. https://doi.org/10.1371/journal.pone.0054805.
[39] Nelissen E, Mduma E, Broerse J, Ersdal H, Evjen-Olsen B, van Roosmalen J, et al. Applicability of the WHO Maternal Near Miss Criteria in a Low-Resource Setting. PLoS ONE 2013;8:e61248. https://doi.org/10.1371/journal.pone.0061248.
[40] Ngan Kee WD. Confidential Enquiries into Maternal Deaths : 50 years of closing the loop. British Journal of Anaesthesia 2005;94:413–6. https://doi.org/10.1093/bja/aei069.
[41] RCOG. Confidential Enquiry into Maternal and Child Health. Why Mothers Die 2000–2002: The Sixth Report of the Confidential Enquiries into Maternal Death in the United Kingdom. London: 2004.
[42] Knight M, Acosta C, Brocklehurst P, Cheshire A, Fitzpatrick K, Hinton L, et al. Beyond maternal death: improving the quality of maternal care through national studies of 'near-miss' maternal morbidity. Programme Grants Appl Res 2016;4:1–180. https://doi.org/10.3310/pgfar04090.
[43] Andreucci CB, Cecatti JG, Pacagnella RC, Silveira C, Parpinelli MA, Ferreira EC, et al. Does Severe Maternal Morbidity Affect Female Sexual Activity and Function? Evidence from a Brazilian Cohort Study. PLoS ONE 2015;10:e0143581. https://doi.org/10.1371/journal.pone.0143581.
[44] Fenech G, Thomson G. Tormented by ghosts from their past': A meta-synthesis to explore the psychosocial implications of a traumatic birth on maternal well-being. Midwifery 2014;30:185–93. https://doi.org/10.1016/j.midw.2013.12.004.
[45] Thompson JF, Heal LJ, Roberts CL, Ellwood DA. Women's breastfeeding experiences following a significant primary postpartum haemorrhage: A multicentre cohort study. Int Breastfeed J 2010;5:5. https://doi.org/10.1186/1746-4358-5-5.
[46] Kozhimannil KB, Jou J, Attanasio LB, Joarnt LK, McGovern P. Medically Complex Pregnancies and Early Breastfeeding Behaviors: A Retrospective Analysis. PLoS ONE 2014;9:e104820. https://doi.org/10.1371/journal.pone.0104820.
[47] Storeng KT, Murray SF, Akoum MS, Ouattara F, Filippi V. Beyond body counts: A qualitative study of lives and loss in Burkina Faso after 'near-miss' obstetric complications. Social Science & Medicine 2010;71:1749–56. https://doi.org/10.1016/j.socscimed.2010.03.056.
[48] Assarag B, Dujardin B, Essolbi A, Cherkaoui I, De Brouwere V. Consequences of severe obstetric complications on women's health in Morocco: please, listen to me! Trop Med Int Health 2015;20:1406–14. https://doi.org/10.1111/tmi.12586.
[49] Filippi V, Goufodji S, Sismanidis C, Kanhonou L, Fottrell E, Ronsmans C, et al. Effects of severe obstetric complications on women's health and infant mortality in Benin: **Effects of severe obstetric complications**. Tropical Medicine & International Health 2010;15:733–42. https://doi.org/10.1111/j.1365-3156.2010.02534.x.
[50] Hinton L, Locock L, Knight M. Support for mothers and their families after life-threatening illness in pregnancy and childbirth: a qualitative study in primary care. Br J Gen Pract 2015;65:e563–9. https://doi.org/10.3399/bjgp15X686461.
[51] Godoy SR de, Gualda DMR, Bergamasco RB, Tsunechiro MA. "Near miss": repercussões e percepção da assistência recebida por mulheres sobreviventes egressas de uma unidade de

terapia intensiva. Acta Paul Enferm 2009;22:162–8. https://doi.org/10.1590/S0103-21002009000200008.
[52] Tunçalp Ö, Hindin MJ, Adu-Bonsaffoh K, Adanu R. Listening to Women's Voices: The Quality of Care of Women Experiencing Severe Maternal Morbidity, in Accra, Ghana. PLoS ONE 2012;7:e44536. https://doi.org/10.1371/journal.pone.0044536.
[53] Souza JP, Cecatti JG, Parpinelli MA, Krupa F, Osis MJD. An Emerging "Maternal Near-Miss Syndrome": Narratives of Women Who Almost Died During Pregnancy and Childbirth. Birth 2009;36:149–58. https://doi.org/10.1111/j.1523-536X.2009.00313.x.
[54] Schaap T, Bloemenkamp K, Deneux-Tharaux C, Knight M, Langhoff-Roos J, Sullivan E, et al. Defining definitions: a Delphi study to develop a core outcome set for conditions of severe maternal morbidity. BJOG: Int J Obstet Gy 2019;126:394–401. https://doi.org/10.1111/1471-0528.14833.
[55] Ministero della Salute, Dipartimento della qualità, Direzione generale della programmazione sanitaria, dei livelli di assistenza e dei principi etici di sistema. Raccomandazione per la prevenzione della morte materna correlata al travaglio e/o parto 2007.
[56] World Health Organization, Reproductive Health and Research, World Health Organization, Special Programme of Research D and Research Training in Human Reproduction (World Health Organization). WHO recommendations for prevention and treatment of maternal peripartum infections. 2015.
[57] Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. The Lancet Global Health 2014;2:e323–33. https://doi.org/10.1016/S2214-109X(14)70227-X.
[58] Senior K. In the dark about sepsis. The Lancet Infectious Diseases 2012;12:751–2. https://doi.org/10.1016/S1473-3099(12)70233-5.
[59] Schutte J, Steegers E, Schuitemaker N, Santema J, de Boer K, Pel M, et al. Rise in maternal mortality in the Netherlands: Rise in maternal mortality in the Netherlands. BJOG: An International Journal of Obstetrics & Gynaecology 2010;117:399–406. https://doi.org/10.1111/j.1471-0528.2009.02382.x.
[60] Acosta CD, Knight M, Lee HC, Kurinczuk JJ, Gould JB, Lyndon A. The Continuum of Maternal Sepsis Severity: Incidence and Risk Factors in a Population-Based Cohort Study. PLoS ONE 2013;8:e67175. https://doi.org/10.1371/journal.pone.0067175.
[61] Acosta CD, Kurinczuk JJ, Lucas DN, Tuffnell DJ, Sellers S, Knight M, et al. Severe Maternal Sepsis in the UK, 2011–2012: A National Case-Control Study. PLoS Med 2014;11:e1001672. https://doi.org/10.1371/journal.pmed.1001672.
[62] Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med 2017;43:304–77. https://doi.org/10.1007/s00134-017-4683-6.
[63] Knight M, Kenyon S, Brocklehurst P, Neilson J, Shakespeare J, Kurinczuk JJ (Eds.) on behalf of MBRRACEUK. Saving Lives, Improving Mothers' Care - Lessons learned to inform future maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009–12. Oxford: National Perinatal Epidemiology Unit, University of Oxford: 2014.
[64] Mohamed-Ahmed O, Nair M, Acosta C, Kurinczuk J, Knight M. Progression from severe sepsis in pregnancy to death: a UK population-based case-control analysis. BJOG: Int J Obstet Gy 2015;122:1506–15. https://doi.org/10.1111/1471-0528.13551.
[65] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:801. https://doi.org/10.1001/jama.2016.0287.
[66] Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the

Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:775. https://doi.org/10.1001/jama.2016.0289.
[67] World Health Organization. Statement on Maternal Sepsis. Geneva: World Health Organisation: 2017.
[68] Royal Berkshire - NHS Foundation Trust. Maternal, Sepsis prevention, recognition and management 2016.
[69] Bonet M, Souza JP, Abalos E, Fawole B, Knight M, Kouanda S, et al. The global maternal sepsis study and awareness campaign (GLOSS): study protocol. Reprod Health 2018;15:16. https://doi.org/10.1186/s12978-017-0437-8.
[70] Oud L. Pregnancy-Associated Severe Sepsis: Contemporary State and Future Challenges. Infect Dis Ther 2014;3:175–89. https://doi.org/10.1007/s40121-014-0037-7.
[71] Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. BJOG: An International Journal of Obstetrics & Gynaecology 2011;118:1–203. https://doi.org/10.1111/j.1471-0528.2010.02847.x.
[72] Acosta CD, Knight M. Sepsis and maternal mortality: Current Opinion in Obstetrics and Gynecology 2013;25:109–16. https://doi.org/10.1097/GCO.0b013e32835e0e82.
[73] Kramer HMC, Schutte JM, Zwart JJ, Schuitemaker NWE, Steegers EAP, van Roosmalen J. Maternal mortality and severe morbidity from sepsis in the Netherlands. Acta Obstet Gynecol Scand 2009;88:647–53. https://doi.org/10.1080/00016340902926734.
[74] Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, et al. Saving mothers' lives: reviewing maternal deaths to make motherhood safer: 2006–2008. The eighth report of the confidential enquiries into maternal deaths in the United Kingdom. BJOG; 2011.
[75] Knight M, Kenyon S, Brocklehurst P, Neilson JP, Shakespeare J, Kurinczuk JJ. Saving lives, improving mothers' care: lessons learned to inform future maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-2012. 2014.
[76] Knight M, Nair M, Tuffnell D, Shakespeare J, Kenyon S, Kurinczuk JJ (Eds.) on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2013–15. Oxford: National Perinatal Epidemiology Unit, University of Oxford: 2017.
[77] Donati S, Maraschini A, Lega I, D'Aloja P, Buoncristiano M, Manno V, et al. Maternal mortality in Italy: Results and perspectives of record-linkage analysis. Acta Obstet Gynecol Scand 2018;97:1317–24. https://doi.org/10.1111/aogs.13415.
[78] Serena Donati, Alice Maraschini, Stefania Dell'Oro, Ilaria Lega, Paola D'Aloja1, and the Regional Maternal Mortality Working Group. The way to move beyond the numbers: the lesson learnt from the Italian Obstetric Surveillance System. Ann Ist Super Sanità 2019;55:363–70. https://doi.org/DOI: 10.4415/ANN_19_04_10.
[79] Chantry AA, Berrut S, Donati S, Gissler M, Goldacre R, Knight M, et al. Monitoring severe acute maternal morbidity across Europe: A feasibility study. Paediatr Perinat Epidemiol 2020;34:416–26. https://doi.org/10.1111/ppe.12557.
[80] Acosta C, Bhattacharya S, Tuffnell D, Kurinczuk J, Knight M. Maternal sepsis: a Scottish population-based case-control study: Maternal sepsis: population-based case-control study. BJOG: An International Journal of Obstetrics & Gynaecology 2012;119:474–83. https://doi.org/10.1111/j.1471-0528.2011.03239.x.
[81] Chebbo A, Tan S, Kassis C, Tamura L, Carlson RW. Maternal Sepsis and Septic Shock. Critical Care Clinics 2016;32:119–35. https://doi.org/10.1016/j.ccc.2015.08.010.
[82] Buppasiri P, Lumbiganon P, Thinkhamrop J, Thinkhamrop B. Antibiotic prophylaxis for third- and fourth-degree perineal tear during vaginal birth. Cochrane Database of Systematic Reviews 2014. https://doi.org/10.1002/14651858.CD005125.pub4.
[83] Elton R, Chaudhari S. Sepsis in obstetrics. BJA Education 2015;15:259–64. https://doi.org/10.1093/bjaceaccp/mku062.

[84] Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early Goal-Directed Therapy in the Treatment of Severe Sepsis and Septic Shock. N Engl J Med 2001;345:1368–77. https://doi.org/10.1056/NEJMoa010307.
[85] Rivers EP, Katranji M, Jaehne KA, Brown S, Abou Dagher G, Cannon C, et al. Early interventions in severe sepsis and septic shock: a review of the evidence one decade later. Minerva Anestesiol 2012;78:712–24.
[86] Rusconi AM, Bossi I, Lampard JG, Szava-Kovats M, Bellone A, Lang E. Early goal-directed therapy vs usual care in the treatment of severe sepsis and septic shock: a systematic review and meta-analysis. Intern Emerg Med 2015;10:731–43. https://doi.org/10.1007/s11739-015-1248-y.
[87] Royal College of Obstetricians and Gynaecologists. Bacterial Sepsis in Pregnancy. 2012.
[88] Yoon BH, Romero R, Park JS, Kim CJ, Kim SH, Choi J-H, et al. Fetal exposure to an intra-amniotic inflammation and the development of cerebral palsy at the age of three years. American Journal of Obstetrics and Gynecology 2000;182:675–81. https://doi.org/10.1067/mob.2000.104207.
[89] van Dillen J, Mesman J, Zwart J, Bloemenkamp K, van Roosmalen J. Introducing maternal morbidity audit in the Netherlands: Audit of severe acute maternal morbidity in the Netherlands. BJOG: An International Journal of Obstetrics & Gynaecology 2010;117:416–21. https://doi.org/10.1111/j.1471-0528.2009.02480.x.
[90] World Health Organization. WHO recommendations for prevention and treatment of preeclampsia and eclampsia. Implications and Actions. 2013.
[91] Shennan AH, Redman C, Cooper C, Milne F. Are most maternal deaths from pre-eclampsia avoidable? The Lancet 2012;379:1686–7. https://doi.org/10.1016/S0140-6736(11)60785-X.
[92] Sibai BM. Diagnosis, Prevention, and Management of Eclampsia: Obstetrics & Gynecology 2005;105:402–10. https://doi.org/10.1097/01.AOG.0000152351.13671.99.
[93] Royal College of Obstetricians and Gynaecologists. Management of severe pre-eclampsia/eclampsia. 2006.
[94] Douglas KA, Redman CWG. Eclampsia in the United Kingdom. BMJ 1994;309:1395–400. https://doi.org/10.1136/bmj.309.6966.1395.
[95] Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews 2010. https://doi.org/10.1002/14651858.CD000025.pub2.
[96] Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. The Lancet 1995;345:1455–63.
[97] Knight M. Eclampsia in the United Kingdom 2005. BJOG: An International Journal of Obstetrics & Gynaecology 2007;114:1072–8. https://doi.org/10.1111/j.1471-0528.2007.01423.x.
[98] Schaap T, Knight M, Zwart J, Kurinczuk J, Brocklehurst P, van Roosmalen J, et al. Eclampsia, a comparison within the International Network of Obstetric Survey Systems. BJOG: Int J Obstet Gy 2014;121:1521–8. https://doi.org/10.1111/1471-0528.12712.
[99] Schaap TP, van den Akker T, Zwart JJ, van Roosmalen J, Bloemenkamp KWM. A national surveillance approach to monitor incidence of eclampsia: The Netherlands Obstetric Surveillance System. Acta Obstet Gynecol Scand 2019;98:342–50. https://doi.org/10.1111/aogs.13493.
[100] Senatore S, Donati S, Andreozzi S. (Ed.). Studio della cause di mortalità e morbosità materna e messa a punto di modelli di sorveglianza della mortalità materna. Istituto Superiore di Sanità; 2012.
[101] Hastie R, Brownfoot FC, Cluver CA, Walker SP, Hesselman S, Tong S, et al. Predictive Value of the Signs and Symptoms Preceding Eclampsia: A Systematic Review. Obstetrics & Gynecology 2019;134:677–84. https://doi.org/10.1097/AOG.0000000000003476.

[102] Sibai B. Diagnosis and Management of Gestational Hypertension and Preeclampsia. Obstetrics & Gynecology 2003;102:181–92. https://doi.org/10.1016/S0029-7844(03)00475-7.
[103] Fitzpatrick K, Tuffnell D, Kurinczuk J, Knight M. Incidence, risk factors, management and outcomes of amniotic-fluid embolism: a population-based cohort and nested case-control study. BJOG: Int J Obstet Gy 2016;123:100–9. https://doi.org/10.1111/1471-0528.13300.
[104] Pacheco LD, Saade G, Hankins GDV, Clark SL. Amniotic fluid embolism: diagnosis and management. American Journal of Obstetrics and Gynecology 2016;215:B16–24. https://doi.org/10.1016/j.ajog.2016.03.012.
[105] Clark SL, Romero R, Dildy GA, Callaghan WM, Smiley RM, Bracey AW, et al. Proposed diagnostic criteria for the case definition of amniotic fluid embolism in research studies. American Journal of Obstetrics and Gynecology 2016;215:408–12. https://doi.org/10.1016/j.ajog.2016.06.037.
[106] Sultan P, Seligman K, Carvalho B. Amniotic fluid embolism: update and review. Current Opinion in Anaesthesiology 2016;29:288–96. https://doi.org/10.1097/ACO.0000000000000328.
[107] Fitzpatrick KE, van den Akker T, Bloemenkamp KWM, Deneux-Tharaux C, Kristufkova A, Li Z, et al. Risk factors, management, and outcomes of amniotic fluid embolism: A multicountry, population-based cohort and nested case-control study. PLoS Med 2019;16:e1002962. https://doi.org/10.1371/journal.pmed.1002962.
[108] Knight M, Berg C, Brocklehurst P, Kramer M, Lewis G, Oats J, et al. Amniotic fluid embolism incidence, risk factors and outcomes: a review and recommendations. BMC Pregnancy Childbirth 2012;12:7. https://doi.org/10.1186/1471-2393-12-7.
[109] Overview of the Nationwide Inpatient Sample (NIS). n.d.
[110] National hospital morbidity database (NHMD). n.d.
[111] Kramer M, Rouleau J, Liu S, Bartholomew S, Joseph K, for the Maternal Health Study Group of the Canadian Perinatal Surveillance System. Amniotic fluid embolism: incidence, risk factors, and impact on perinatal outcome: Amniotic fluid embolism. BJOG: An International Journal of Obstetrics & Gynaecology 2012;119:874–9. https://doi.org/10.1111/j.1471-0528.2012.03323.x.
[112] Bonnet M-P, Zlotnik D, Saucedo M, Chassard D, Bouvier-Colle M-H, Deneux-Tharaux C. Maternal Death Due to Amniotic Fluid Embolism: A National Study in France. Anesthesia & Analgesia 2018;126:175–82. https://doi.org/10.1213/ANE.0000000000002511.
[113] Clark SL, Hankins GDV, Dudley DA, Dildy GA, Porter TF. Amniotic fluid embolism: Analysis of the national registry. American Journal of Obstetrics and Gynecology 1995;172:1158–69. https://doi.org/10.1016/0002-9378(95)91474-9.
[114] Yentis S. Amniotic fluid embolism. Can J Anesth/J Can Anesth 2001;48:829–829. https://doi.org/10.1007/BF03016710.
[115] Dean LS, Rogers RP, Harley RA, Hood DD. Case Scenario: Amniotic Fluid Embolism. Anesthesiology 2012;116:186–92. https://doi.org/10.1097/ALN.0b013e31823d2d99.
[116] Benson MD. A hypothesis regarding complement activation and amniotic fluid embolism. Medical Hypotheses 2007;68:1019–25. https://doi.org/10.1016/j.mehy.2006.09.052.
[117] Kaur K, Bhardwaj M, Kumar P, Singhal S, Singh T, Hooda S. Amniotic fluid embolism. J Anaesthesiol Clin Pharmacol 2016;32:153. https://doi.org/10.4103/0970-9185.173356.
[118] Lier MCI, Malik RF, Ket JCF, Lambalk CB, Brosens IA, Mijatovic V. Spontaneous hemoperitoneum in pregnancy (SHiP) and endometriosis — A systematic review of the recent literature. European Journal of Obstetrics & Gynecology and Reproductive Biology 2017;219:57–65. https://doi.org/10.1016/j.ejogrb.2017.10.012.
[119] Brosens IA, Lier MC, Mijatovic V, Habiba M, Benagiano G. Severe spontaneous hemoperitoneum in pregnancy may be linked to in vitro fertilization in patients with endometriosis: a systematic review. Fertility and Sterility 2016;106:692–703. https://doi.org/10.1016/j.fertnstert.2016.05.025.

[120] Brosens IA, Fusi L, Brosens JJ. Endometriosis is a risk factor for spontaneous hemoperitoneum during pregnancy. Fertility and Sterility 2009;92:1243–5. https://doi.org/10.1016/j.fertnstert.2009.03.091.
[121] Glavind MT, Forman A, Arendt LH, Nielsen K, Henriksen TB. Endometriosis and pregnancy complications: a Danish cohort study. Fertility and Sterility 2017;107:160–6. https://doi.org/10.1016/j.fertnstert.2016.09.020.
[122] Vigano P, Corti L, Berlanda N. Beyond infertility: obstetrical and postpartum complications associated with endometriosis and adenomyosis. Fertility and Sterility 2015;104:802–12. https://doi.org/10.1016/j.fertnstert.2015.08.030.
[123] Lier MCI, Brosens IA, Mijatovic V, Habiba M, Benagiano G. Decidual Bleeding as a Cause of Spontaneous Hemoperitoneum in Pregnancy and Risk of Preterm Birth. Gynecol Obstet Invest 2017;82:313–21. https://doi.org/10.1159/000468933.
[124] Pollock W, Peek MJ, Wang A, Li Z, Ellwood D, Homer CSE, et al. Eclampsia in Australia and New Zealand: A prospective population-based study. Aust N Z J Obstet Gynaecol 2020;60:533–40. https://doi.org/10.1111/ajo.13100.
[125] Bell MJ. A Historical Overview of Preeclampsia-Eclampsia. Journal of Obstetric, Gynecologic & Neonatal Nursing 2010;39:510–8. https://doi.org/10.1111/j.1552-6909.2010.01172.x.
[126] Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. The Lancet 2005;365:785–99. https://doi.org/10.1016/S0140-6736(05)17987-2.
[127] Cooray SD, Edmonds SM, Tong S, Samarasekera SP, Whitehead CL. Characterization of Symptoms Immediately Preceding Eclampsia: Obstetrics & Gynecology 2011;118:995–9. https://doi.org/10.1097/AOG.0b013e3182324570.
[128] Sibai BM, Abdella TN, Spinnato JA, Anderson GD. Eclampsia. American Journal of Obstetrics and Gynecology 1986;154:581–6. https://doi.org/10.1016/0002-9378(86)90605-8.
[129] Berhan Y, Berhan A. Should magnesium sulfate be administered to women with mild pre-eclampsia? A systematic review of published reports on eclampsia: Systematic review of reports on eclampsia. J Obstet Gynaecol Res 2015;41:831–42. https://doi.org/10.1111/jog.12697.
[130] Walsh CA, Baxi LV. Mean arterial pressure and prediction of pre-eclampsia. BMJ 2008;336:1079–80. https://doi.org/10.1136/bmj.39555.518750.80.
[131] Nair M, Kurinczuk JJ, Knight M. Ethnic Variations in Severe Maternal Morbidity in the UK– A Case Control Study. PLoS ONE 2014;9:e95086. https://doi.org/10.1371/journal.pone.0095086.
[132] Cromi A, Marconi N, Casarin J, Cominotti S, Pinelli C, Riccardi M, et al. Maternal intra- and postpartum near-miss following assisted reproductive technology: a retrospective study. BJOG: Int J Obstet Gy 2018;125:1569–78. https://doi.org/10.1111/1471-0528.15308.
[133] Martin AS, Monsour M, Kissin DM, Jamieson DJ, Callaghan WM, Boulet SL. Trends in Severe Maternal Morbidity After Assisted Reproductive Technology in the United States, 2008–2012. Obstetrics & Gynecology 2016;127:59–66. https://doi.org/10.1097/AOG.0000000000001197.
[134] Sibai BM, Hauth J, Caritis S, Lindheimer MD, MacPherson C, Klebanoff M, et al. Hypertensive disorders in twin versus singleton gestations. American Journal of Obstetrics and Gynecology 2000;182:938–42. https://doi.org/10.1016/S0002-9378(00)70350-4.
[135] Jackson RA, Gibson KA, Wu YW, Croughan MS. Perinatal Outcomes in Singletons Following In Vitro Fertilization: A Meta-Analysis: Obstetrics & Gynecology 2004;103:551–63. https://doi.org/10.1097/01.AOG.0000114989.84822.51.
[136] Italian Ministry of Health. RELAZIONE DEL MINISTRO DELLA SALUTE AL PARLAMENTO SULLO STATO DI ATTUAZIONE DELLA LEGGE CONTENENTE NORME IN MATERIA DI PROCREAZIONE MEDICALMENTE ASSISTITA (LEGGE 19 FEBBRAIO 2004, N. 40, ARTICOLO 15). 2018.

[137] Zwart JJ, Richters A, Öry F, de Vries JIP, Bloemenkamp KWM, van Roosmalen J. Eclampsia in the Netherlands: Obstetrics & Gynecology 2008;112:820–7. https://doi.org/10.1097/AOG.0b013e3181875eb3.
[138] Tolcher MC, Chu DM, Hollier LM, Mastrobattista JM, Racusin DA, Ramin SM, et al. Impact of USPSTF recommendations for aspirin for prevention of recurrent preeclampsia. American Journal of Obstetrics and Gynecology 2017;217:365.e1-365.e8. https://doi.org/10.1016/j.ajog.2017.04.035.
[139] Poon LC, Wright D, Rolnik DL, Syngelaki A, Delgado JL, Tsokaki T, et al. Aspirin for Evidence-Based Preeclampsia Prevention trial: effect of aspirin in prevention of preterm preeclampsia in subgroups of women according to their characteristics and medical and obstetrical history. American Journal of Obstetrics and Gynecology 2017;217:585.e1-585.e5. https://doi.org/10.1016/j.ajog.2017.07.038.
[140] American College of Obstetrician and Gynecologists (ACOG). Low-dose aspirin use during pregnancy. ACOG Committee Opinion N 743 2018;132:e44-52.
[141] Magpie Trial Follow-Up Study Collaborative Group. The Magpie Trial: a randomised trial comparing magnesium sulphate with placebo for pre-eclampsia. Outcome for women at 2 years. BJOG: An International Journal of Obstetrics & Gynaecology 2006;114:300–9. https://doi.org/10.1111/j.1471-0528.2006.01166.x.
[142] Jaskolka D, Retnakaran R, Zinman B, Kramer C. Fetal sex and maternal risk of pre-eclampsia/eclampsia: a systematic review and meta-analysis. BJOG: Int J Obstet Gy 2017;124:553–60. https://doi.org/10.1111/1471-0528.14163.
[143] Vincent J-L, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, et al. Sepsis in European intensive care units: Results of the SOAP study*: Critical Care Medicine 2006;34:344–53. https://doi.org/10.1097/01.CCM.0000194725.48928.3A.
[144] Basili, Messia, Montorio, Tamburini. Certificato di assistenza al parto (CeDAP) Analisi dell'evento nascita - Anno 2015 2018.
[145] Acosta CD, Harrison DA, Rowan K, Lucas DN, Kurinczuk JJ, Knight M. Maternal morbidity and mortality from severe sepsis: a national cohort study. BMJ Open 2016;6:e012323. https://doi.org/10.1136/bmjopen-2016-012323.
[146] Bakhtawar S, Sheikh S, Qureshi R, Hoodbhoy Z, Payne B, Azam I, et al. Risk factors for postpartum sepsis: a nested case-control study. BMC Pregnancy Childbirth 2020;20:297. https://doi.org/10.1186/s12884-020-02991-z.
[147] Chief Nursing Officers of England, Northen Ireland, Scotland and Wales. Midwifery 2020: Delivering Expectation, 2010 2010.
[148] World Health Organization. WHO recommendations: intrapartum care for a positive childbirth experience. 2018.
[149] Royal College of Midwives. Reaching out: Involving Fathers in Maternity Care 2011.
[150] Schytt E, Bergström M. First-time fathers' expectations and experiences of childbirth in relation to age. Midwifery 2014;30:82–8. https://doi.org/10.1016/j.midw.2013.01.015.
[151] Rijnders M. Perinatal Factors Related to Negative or Positive Recall of Birth Experience in Women 3 Years Postpartum in the Netherlands 2008.
[152] Hildingsson I. Women's birth expectations, are they fulfilled? Findings from a longitudinal Swedish cohort study. Women and Birth 2015;28:e7–13. https://doi.org/10.1016/j.wombi.2015.01.011.
[153] Mei JY, Afshar Y, Gregory KD, Kilpatrick SJ, Esakoff TF. Birth Plans: What Matters for Birth Experience Satisfaction. Birth 2016;43:144–50. https://doi.org/10.1111/birt.12226.
[154] Fair CD, Morrison TE. The relationship between prenatal control, expectations, experienced control, and birth satisfaction among primiparous women. Midwifery 2012;28:39–44. https://doi.org/10.1016/j.midw.2010.10.013.

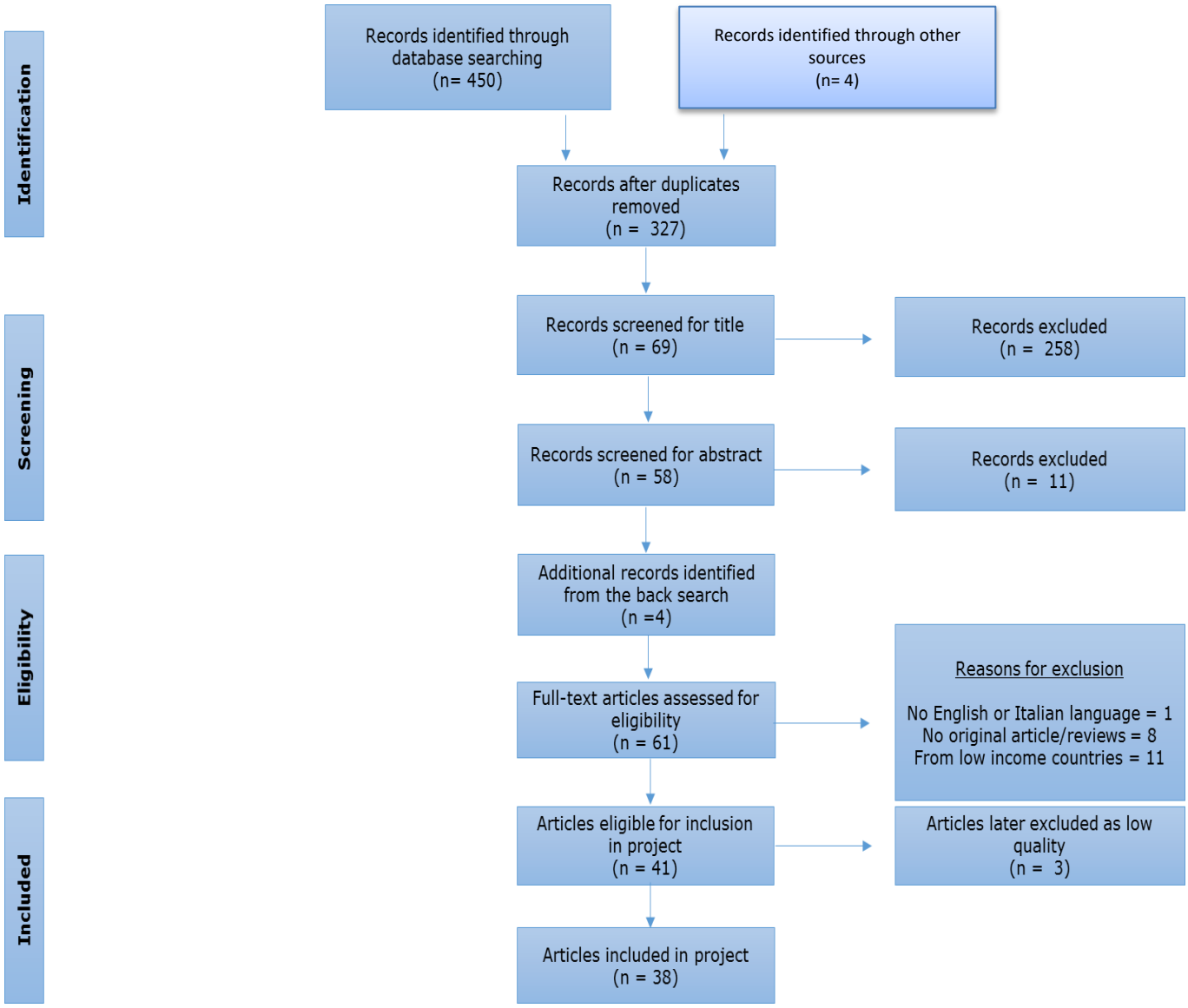
[155] DeLuca RS, Lobel M. Diminished Control and Unmet Expectations: Testing a Model of Adjustment to Unplanned Cesarean Delivery: Adjustment to Cesarean Delivery. Analyses of Social Issues and Public Policy 2014;14:183–204. https://doi.org/10.1111/asap.12040.
[156] Iles J, Pote H. Postnatal posttraumatic stress: A grounded theory model of first-time mothers' experiences. Journal of Reproductive and Infant Psychology 2015;33:238–55. https://doi.org/10.1080/02646838.2015.1030732.
[157] D'Cruz L, Lee C. Childbirth expectations: an Australian study of young childless women. Journal of Reproductive and Infant Psychology 2014;32:199–211. https://doi.org/10.1080/02646838.2013.875134.
[158] van Bussel J, Spitz B, Demyttenaere K. Childbirth expectations and experiences and associations with mothers' attitudes to pregnancy, the child and motherhood. Journal of Reproductive and Infant Psychology 2010;28:143–60. https://doi.org/10.1080/02646830903295026.
[159] Haines H, Rubertsson C, Pallant JF, Hildingsson I. Womens' attitudes and beliefs of childbirth and association with birth preference: A comparison of a Swedish and an Australian sample in mid-pregnancy. Midwifery 2012;28:e850–6. https://doi.org/10.1016/j.midw.2011.09.011.
[160] Christiaens W, Verhaeghe M, Bracke P. Childbirth expectations and experiences in Belgian and Dutch models of maternity care. Journal of Reproductive and Infant Psychology 2008;26:309–22. https://doi.org/10.1080/02646830802350872.
[161] Cipolletta S, Sperotto A. From the hospital organisation to the childbirth practice: Italian women's experiences. Journal of Reproductive and Infant Psychology 2012;30:326–36. https://doi.org/10.1080/02646838.2012.707777.
[162] Rota A, Antolini L, Colciago E, Nespoli A, Borrelli SE, Fumagalli S. Timing of hospital admission in labour: latent versus active phase, mode of birth and intrapartum interventions. A correlational study. Women and Birth 2017. https://doi.org/10.1016/j.wombi.2017.10.001.
[163] Euro-Peristat Project. European Perinatal Health Report. Core indicators of the health and care of pregnant women and babies in Europe in 2015. 2018.
[164] International Confederation of Midwives. Core Document International Definition of the Midwife 2017.
[165] Sanders RA, Crozier K. How do informal information sources influence women's decision-making for birth? A meta-synthesis of qualitative studies. BMC Pregnancy and Childbirth 2018;18. https://doi.org/10.1186/s12884-017-1648-2.
[166] Young K, Miller YD. Keeping it Natural: Does Persuasive Magazine Content Have an Effect on Young Women's Intentions for Birth? Women & Health 2015;55:447–66. https://doi.org/10.1080/03630242.2015.1022690.
[167] Soriano-Vidal FJ, Vila-Candel R, Soriano-Martín PJ, Tejedor-Tornero A, Castro-Sánchez E. The effect of prenatal education classes on the birth expectations of Spanish women. Midwifery 2018;60:41–7. https://doi.org/10.1016/j.midw.2018.02.002.
[168] Preis H, Chen R, Eisner M, Pardo J, Peled Y, Wiznitzer A, et al. Testing a biopsychosocial model of the basic birth beliefs. Birth 2018;45:79–87. https://doi.org/10.1111/birt.12313.
[169] Takács L, Seidlerová JM, Šulová L, Hoskovcová SH. Social psychological predictors of satisfaction with intrapartum and postpartum care – what matters to women in Czech maternity hospitals? Open Medicine 2015;10. https://doi.org/10.1515/med-2015-0022.
[170] Bar-On S, Benyamini Y, Ebrahimoff M, Many A. Mother knows best? Comparing primiparous parturients' expectations and predictions with actual birth outcomes. Journal of Perinatal Medicine 2014;42. https://doi.org/10.1515/jpm-2013-0236.
[171] Raphael-Leff, J. Psychological processes of childbearing. London, United Kingdom: Ann Freud Centre. 2005.
[172] Brodrick A. Exploring women's pre-birth expectations of labour and the role of the midwife. Evidence Based Midwifery 2008.

[173] Fleming SE, Donovan-Batson C, Burduli E, Barbosa-Leiker C, Hollins Martin CJ, Martin CR. Birth Satisfaction Scale/Birth Satisfaction Scale-Revised (BSS/BSS-R): A large scale United States planned home birth and birth centre survey. Midwifery 2016;41:9–15. https://doi.org/10.1016/j.midw.2016.07.008.
[174] Bayes S, Fenwick J, Hauck Y. A Qualitative Analysis of Women's Short Accounts of Labour and Birth in a Western Australian Public Tertiary Hospital. Journal of Midwifery & Women's Health 2008;53:53–61. https://doi.org/10.1016/j.jmwh.2007.07.021.
[175] Goldbort J. Women's Lived Experience of Their Unexpected Birthing Process. MCN 2009;34.
[176] Moore MF. Multicultural Differences in Women's Expectations of Birth. ABNF J 2016;27:39–43.
[177] Morrow, R., Rodriguez, A. and King, N. . Colaizzi's descriptive phenomenological method. The Psychologist 2015;28:643–4.
[178] Hollander MH, van Hastenberg E, van Dillen J, van Pampus MG, de Miranda E, Stramrood CAI. Preventing traumatic childbirth experiences: 2192 women's perceptions and views. Archives of Women's Mental Health 2017;20:515–23. https://doi.org/10.1007/s00737-017-0729-6.
[179] Glaser BG, Strauss AL. The discovery of grounded theory: strategies for qualitative research. 4. paperback printing. New Brunswick: Aldine; 2009.
[180] Fenwick J, Bayes S, Johansson M. A qualitative investigation into the pregnancy experiences and childbirth expectations of Australian fathers-to-be. Sexual & Reproductive Healthcare 2012;3:3–9. https://doi.org/10.1016/j.srhc.2011.11.001.
[181] Young E. Maternal expectations: do they match experience? Community Pract 2008;81:27–30.
[182] Mattern E, Lohmann S, Ayerle GM. Experiences and wishes of women regarding systemic aspects of midwifery care in Germany: a qualitative study with focus groups. BMC Pregnancy and Childbirth 2017;17. https://doi.org/10.1186/s12884-017-1552-9.
[183] Gadamer, Hans Georg. Philosophical hermeneutics. David E. Linge, Ed. & Trans. Berkeley, CA: University of California Press.: 1976.
[184] Paterson, Higgs. Using hermeneutics as a qualitative research approach in professional practice. The Qualitative Report 2005:339–57.
[185] Borrelli SE, Spiby H, Walsh D. The kaleidoscopic midwife: A conceptual metaphor illustrating first-time mothers' perspectives of a good midwife during childbirth. A grounded theory study. Midwifery 2016;39:103–11. https://doi.org/10.1016/j.midw.2016.05.008.
[186] World Health Organization. Standards for improving quality of maternal and newborn care in health facilities. 2016.
[187] Bélanger-Lévesque M-N, Pasquier M, Roy-Matton N, Blouin S, Pasquier J-C. Maternal and paternal satisfaction in the delivery room: a cross-sectional comparative study. BMJ Open 2014;4:e004013. https://doi.org/10.1136/bmjopen-2013-004013.
[188] Lewis L, Hauck YL, Ronchi F, Crichton C, Waller L. Gaining insight into how women conceptualize satisfaction: Western Australian women's perception of their maternity care experiences. BMC Pregnancy and Childbirth 2016;16. https://doi.org/10.1186/s12884-015-0759-x.
[189] Johnson RB, Onwuegbuzie AJ, Turner LA. Toward a Definition of Mixed Methods Research. Journal of Mixed Methods Research 2007;1:112–33. https://doi.org/10.1177/1558689806298224.
[190] Chin R, Daiches A, Hall P. A qualitative exploration of first-time fathers' experiences of becoming a father. Community Pract 2011;84:19–23.
[191] Porrett L, Barkla S, Knights J, de Costa C, Harmen S. An Exploration of the Perceptions of Male Partners Involved in the Birthing Experience at a Regional Australian Hospital. Journal

of Midwifery & Women's Health 2013;58:92–7. https://doi.org/10.1111/j.1542-2011.2012.00238.x.
[192] Walsh D, Downe S. Appraising the quality of qualitative research. Midwifery 2006;22:108–19. https://doi.org/10.1016/j.midw.2005.05.004.
[193] M Reiners G. Understanding the Differences between Husserl's (Descriptive) and Heidegger's (Interpretive) Phenomenological Research. J Nurs Care 2012;01. https://doi.org/10.4172/2167-1168.1000119.
[194] Stewart, Shandasani. Focus groups. Theory and practice. London: Sage Publications. London: Sage Pubblication: 1990.
[195] Carlsen B, Glenton C. What about N? A methodological study of sample-size reporting in focus group studies. BMC Med Res Methodol 2011;11:26. https://doi.org/10.1186/1471-2288-11-26.
[196] Cleary M, Horsfall J, Hayter M. Data collection and sampling in qualitative research: does size matter? J Adv Nurs 2014;70:473–5. https://doi.org/10.1111/jan.12163.
[197] Rees,C. Introduction to Research for Midwives. Great Britain: Elsevier; 2011.
[198] Parahoo, K. Nursing Research. Principles, Process and Issues. 2nd Edition. Basingstoke.: Palgrave Macmillan.; 2006.
[199] Shenton, Andrew K. Strategies for ensuring trustworthiness in qualitative research projects. Education for Information 2004:63–75.
[200] Johansson M, Fenwick J, Premberg å. A meta-synthesis of fathers′ experiences of their partner′s labour and the birth of their baby. Midwifery 2015;31:9–18. https://doi.org/10.1016/j.midw.2014.05.005.
[201] Longworth HL, Kingdon CK. Fathers in the birth room: What are they expecting and experiencing? A phenomenological study. Midwifery 2010. https://doi.org/10.1016/j.midw.2010.06.013.

Appendix 1

PRISMA Flow Diagram (The PRISMA Group, 2009)



Appendix 2

Participants Information Sheet

Titolo del progetto: aspettative genitoriali sul travaglio e parto: studio qualitativo con approccio fenomenologico descrittivo

Introduzione

Sono una studentessa del Dottorato di Ricerca in Sanitá Pubblica presso l'Universitá di Milano-Biccocca e vorrei invitarvi a prendere parte ad un progetto di ricerca.

All'interno di questo foglio informativo troverete tutte le informazioni che riguardano lo studio, vi chiedo pochi minuti per leggerle.

Scopo dello studio

Lo studio ha lo scopo di comprendere quali sono le aspettative materne e paterne sul travaglio e sul parto e se queste aspettative sono state realmente soddisfatte.

Lo studio si rivolge alle madri e ai padri che sono alla prima esperienza di gravidanza e che rientrano in un percorso di fisiologia (in cui la madre non assume medicinali e non ha effettuato visite o esami specialistici durante la gravidanza).

Perché sono stata/o coinvolta/o?

I percorsi di accompagnamento alla nascita sono il luogo in cui i genitori si incontrano ed entrano spesso in contatto con la struttura che hanno scelto per il parto. Per questo motivo verrá richiesta a voi la disponibilitá di partecipare allo studio.

Devo per forza accettare?

No, nessuno é obbligato a partecipare allo studio. Nel caso accetterete di partecipare a questa ricerca, potrete conservare questo foglio informativo. Prima di iniziare lo studio vi verrá chiesto di firmare un consenso informato, i vostri dati saranno mantenuti anonimi e potrete abbandonare lo studio in ogni momento.

Come si svolgerá lo studio?

Per la prima parte dello studio verranno organizzati dei gruppi, uno in cui si riuniranno le donne e un altro a cui parteciperanno gli uomini. La ricercatrice fará delle domande per rispondere allo scopo della ricerca e vi verrá chiesto di discuterne nel gruppo. La discussione potrebbe durare circa 60 minuti e verrá registrata.

La ricercatrice vi chiederá quali sono le vostre aspettative sul travaglio ed il parto, cosa é importante per voi in quel momento.
Potremo organizzare i gruppi in un luogo e ad un orario comodo per tutti.
La seconda parte dello studio prevede di intervistare singolarmente madri e padri sei settimane dopo la nascita del bambina/o, per comprendere come é stata la loro esperienza.
I partecipanti potranno decidere il luogo e l'orario dell'intervista, la ricercatrice é disponibile a raggiungere i genitori anche al loro domicilio.

Ci sono dei vantaggi partecipando a questo progetto?
È improbabile che ci siano dei vantaggi diretti per i partecipanti, anche se condividere i propri pensieri, le proprie opinioni e parlare della propria esperienza, é un momento solitamente piacevole e arricchente. Le informazioni che darete saranno preziose per comprendere cosa davvero vogliono i genitori dalla loro esperienza di parto e cosa possono fare i professionisti sanitari per migliorare l'assistenza ostetrica offerta.

Ci sono degli svantaggi partecipando a questo progetto?
L'argomento che si affronta é delicato e, nel caso si abbia necessitá di supporto, la ricercatrice sará disponibile ad offrirlo.

I miei dati e ció che riporto durante le interviste saranno informazioni confidenziali?
Certo, l'identitá dei partecipanti verrá mantenuta anonima grazie all'utilizzo di pseudonimi, le discussioni registrate verranno riportate all'interno di un software informatico e i documenti protetti da password segreta.

Cosa succede dopo la discussion in gruppo e l'intervista?
La ricercatrice dovrá analizzare i dati raccolti e, nel caso siate interessati, potrá inviarvi un documento in cui vi verranno descritti i risultati della ricerca.

Cosa devo fare se voglio partecipare allo studio?
Potrete contattare direttamente la ricercatrice per telefono (chiamata, messaggio, whatsapp) o via mail, i contatti sono disponibili di seguito.
Oppure potrete inserire il vostro numero di telefono o il vostro indirizzo mail in un foglio dedicato, disponibile nella sala in cui si svolgono gli incontri di accompagnamento alla nascita. Verrete poi contattati dalla ricercatrice.

Celullare: 346 5613065

Email: e.colciago2@campus.unimib.it

Email2: elisabetta.colciago@gmail.com

Non voglio partecipare. Puó spiegare brevemente perché non se la sente? Grazie.

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Appendix 3

Consent form

Titolo del progetto: aspettative genitoriali sul travaglio e parto: studio qualitativo con approccio fenomenologico descrittivo

1. Confermo di aver letto e compreso le informazioni riguardanti lo svolgimento del progetto. Ho ricevuto chiarimenti, se richiesti.

2. Ho compreso che la mia partecipazione allo studio é volontaria e che posso decidere in qualsiasi momento di non prendervi parte.

3. Fornisco il consenso all'utilizzo dei miei dati personali. I dati personali verranno protetti nel rispetto del Decreto Legislativo 30 giugno 2003, n. 196 - Codice in materia di protezione dei dati personali.

4. Le informazioni raccolte possono essere utilizzate solo a scopi di ricerca.

5. Consento alla registrazione delle informazioni trasmesse durante il focus group e l'intervista.

Nome del Partecipante	Data	Firma
_____	_____	
_____		

Nome della Ricercatrice	Data	Firma
_____	_____	
_____		

Appendix 4

Topic guide for focus groups

The purpose of a focus group is that participants not only respond to the questions asked by the researcher, but that they also discuss issues raised by fellow participants.

The researcher conducted the focus groups using this topic guide, which consists of key open questions and probes, in order to encourage participants to share their expectations of labour and birth. The focus group was structured as follows.

Introduction

I introduced myself and the colleagues who took notes and audio-recorded the discussion, I informed the participants that I am a midwife and I clarified my role in the study.

I thank women/fathers-to-be for participating.

I provided an opportunity for women to use the toilet before commencing the focus group.

I reiterated assurances of confidentiality and anonymity.

I confirmed women's/men's consent to participate.

I explaind to women/men that a focus group is a group discussion, that their views and opinions were important. There were no right or wrong or desirable or undesirable answers. Participants could disagree with each other, and they could change their mind.

I explained that I would like them to feel comfortable saying what they really thought and how they really felt.

I explained that I only intervened when necessary or if I needed to explore further.

I reminded participants that they had the right to withdraw at any time.

Present the purpose

I introduced the aim of the study and the aim of the focus group.

Participants' introduction

I asked participants to introduce themselves.

Rapport building

I asked if the participants felt comfortable and how easy it was for them to reach the venue.

As women were recruited from antenatal classes, I asked if they were enjoying them.

Questions

Question 1: how do you feel when thinking about labour and birth?

Prompts: do you often think and talk about your labour and birth? Who do you talk with about this moment?

Question 2: when you think about your labour, what are your expectations?

Prompts: who would you expect to be with you? Could you explain that? How do you expect the midwife will be? Is there anything you don't want?

Question 3: when you think about the moment of birth, how do you expect it will be?

Prompts: What do you expect from the midwife?

Question 4: Is there something you and your partner have different ideas about? Could you discuss your expectations about labour and birth with your midwife/doctor?

Prompts: Could you explain that?

Question 5: how relevant was your midwife/doctor in shaping your expectations?

Prompts: did you seek information somewhere else? What do you think about these types of information?

Question 6: Is there anything else that you would like to add about your expectations on labour and birth?

Members checking: did you mean this …? From what you said, I understood this, is it correct?

Closing the discussion

Debrief with the group. I offered individual support if needed. The researcher ensured that participants understood what happened next and that they had her contact details in case they need it.

I said thank to participants for their time.

Appendix 5

Topic guide for interviews

The purpose of semi-structured in-depth interviews is to gain a deeper understanding about the phenomenon, to stimulate discussion and enable participants to respond as comprehensively as possible. The interview, characterised by open questions, will be planned in order to address all topics, but the order of questions could change. This will help to follow the interviewee discussion and enables flexibility in the semi-structured interviews.

Before meeting with parents, the interviewer will re-read the transcripts of the focus groups. At the time of the interview, references will be made to the topics previously discussed with the participant, stimulating the comparison between expectations and experiences.

Introduction

The researcher thank women/fathers for participating.

I reiterated assurances of confidentiality and anonymity.

I confirmed women's/men's consent to participate.

I explained to women/men that an interview is a method to gain rich information about theirs views and thoughts, that their opinions are what was important, that there were no right or wrong or desirable or undesirable answers.

I explained that I only intervened when necessary or if I neded to explore further.

Present the purpose

The researcher presented the aim of the study and the aim of the interview.

Rapport building

I asked if the participants feel comfortable and how easy it was for them to reach the venue. In case the interview takes place at the participant's home, I would thank the interviewee to welcome her.

As women were recruited from antenatal classes, the researcher could ask if they organized the post-natal meeting and how it was.

Questions

Question 1: How do you feel when thinking back about labour and birth?

Prompts: did you have the chance to reflect about your labour and birth? Is this the first time you talk about it?

Question 2: we discussed about your expectations during the focus group and we red them now, could you compare them with the actual experience you had?

Prompts: who was with you during that time? Could you please tell me about the care that you received? Could you tell me how do you think your partner was feeling?

Question 3: thinking about the birth, is there something you want to talk about that you did not expect?

Prompts: could you explain it?

Question 4: Is there anything else that you would like to add about your experience?

Member checking: did you mean this …? From what you said, I understood this, is it correct?

Closing the interview

Debrief with the interviewee. Offer support if needed. The researcher ensured that participant understood what happened next.

The researcher said thank to the participant for her/his time.