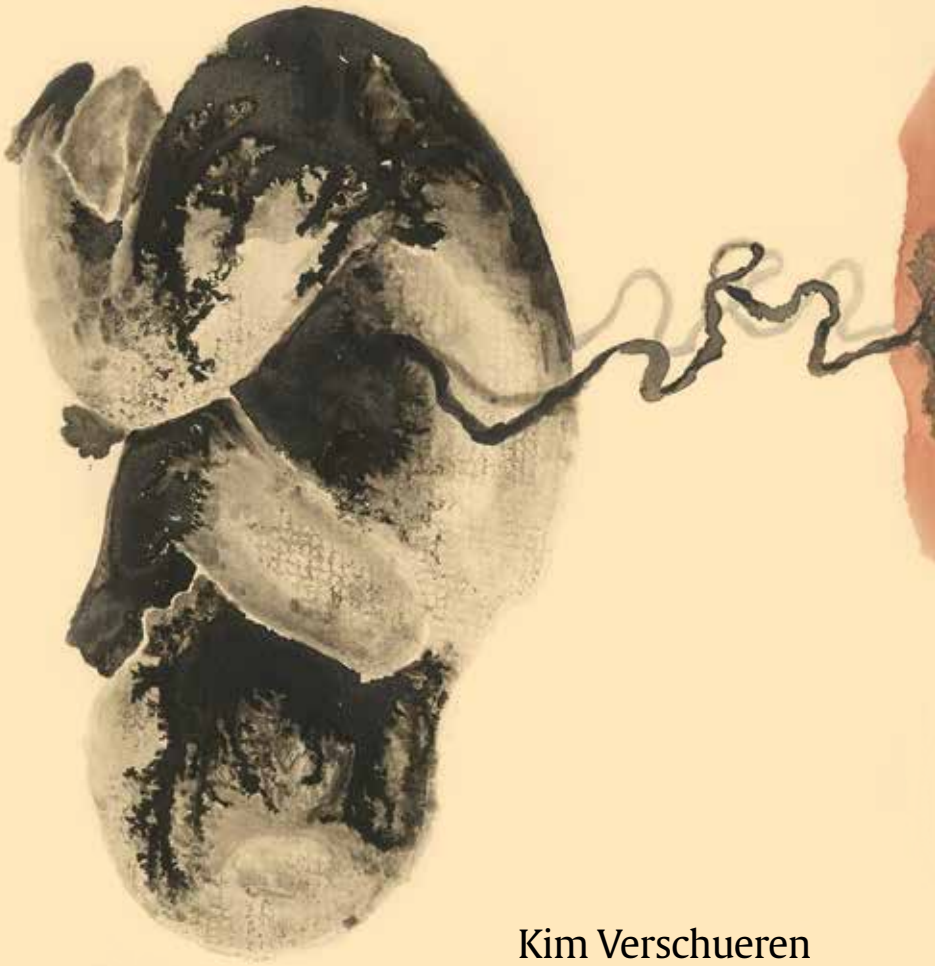
Safe Motherhood

Maternal mortality, near-miss and stillbirths in Suriname

Time to respond



Kim Verschueren

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Maternal mortality, near-miss and stillbirths in Suriname: Time to respond
Kim Johanna Catharina Verschueren
Doctoral Dissertation, University of Utrecht, The Netherlands

Maternal mortality, near-miss and stillbirths in Suriname

Time to respond

Maternale sterfte, near-miss en foetale sterfte in Suriname:
Tijd voor respons
(met een samenvatting in het Nederlands)

Proefschrift

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door

Kim J.C. Verschueren

geboren op 15 september 1993
op St. Maarten

PROMOTIECOMMISSIE

Promotor	Prof. dr. K.W.M. Bloemenkamp
Copromotoren	Dr. J.L. Browne
	Dr. M.J. Rijken
Beoordelingscommissie	Prof. dr. M.J.N.L. Benders
	Prof. dr. D.E. Grobbee
	Prof. dr. M. Knight
	Prof. dr. A.M. McCaw-Binns
	Dr. S. Vreden

Contents

Dedicated to Ms X & baby Y

PERSONAL JUSTIFICATION

During one of my first internships as a medical student, I met Ms X, a mother of three girls and pregnant with her fourth child. She moved from the interior of Suriname to the suburbs of the capital, Paramaribo, a couple of years ago for a better job and better educational opportunities for her children. Her pregnancy was without complications, like her previous three pregnancies. Her contractions had started, and in the late evening she arrived at the hospital. I was excited to assist her and remember the midwife saying, "Perfect for you; fourth babies are always fast and easy". I sat next to Ms X, who was by herself, for several hours after which she gave birth to a healthy boy. However, just minutes later, she started bleeding heavily. We delivered the placenta and provided all available medical treatment – with little effect. The gynaecologist was called and on his way. We ordered and transfused blood, but she was already agitated due to the shock; her hands were cold and her pulse was weak. I was unexperienced at the time; but the expression on the face of the midwife said it all: it was too late. I held Ms X's hand and apologized. She left behind four children.

She went into the reports as a maternal death due to postpartum haemorrhage. Her story remained untold, while it had the potential to tell us what we could have done to save her, and other women in similar situations. The questions I dared not to ask aloud remained unanswered: "Why did she die? Could we have prevented it? Would she have died if she gave birth in St. Maarten or in the Netherlands …?"

Just a few weeks later I had a brief encounter with baby boy Y. The mother was a 15-year old girl from an indigenous village in the interior. After being in labour for hours, with poor progression and without a birth companion, she delivered her baby. Despite vigorous rubs, the upside-down hold and several smacks, the baby showed no sign of life. In a great panic, the baby was given to me for resuscitation, unsuccessfully. The teenage girl asked why her baby died, but received no answer and she felt it was her fault. She was not allowed to see her baby; because that 'would be better for her' and was told that, 'she should try to forget about it and have another child'. Baby Y, did not receive a name and was neglected before and

after birth. He did not make it to any report, was not formally registered and he remains invisible. The teenage mom risks long-term, devastating psychological consequences.

'Why did Mrs X die?' is actually a World Health Organization film (1988)[1] about key issues associated with safe motherhood.[1] The fundamental issues described in this film remain the same decade after decade, which can be characterized by two words: substantial and unacceptable.

In our professional careers, we all have experiences that strongly affect us and are part of our professional journey. Yet, preventable deaths are intolerable and the silenced voices of mothers and babies are a call for action. After my first internship (2015), I was lucky to meet a very devoted Surinamese gynaecologist, Lachmi Kodan. We discovered our shared passion and determination to break the silence. The stories of these women and babies had to be told to discover where, why and how they died and what could be done to prevent such incidences from happening again. By counting the number of maternal deaths, near deaths and stillbirths, collecting information on where and why these (near) deaths occurred and by trying to understand underlying contributing and avoidable factors, health-care providers and policymakers can improve the quality of care and the health system and help to eliminate preventable deaths.[1] Although Lachmi and I initially started without any intention to complete a PhD thesis, we feel very honoured that through our theses, we may share the stories of many women and babies, answer very important questions and advocate for improved care for mothers and babies in Suriname and other countries.

General introduction

1

The world is not changing if you don't shoulder the burden of responsibility

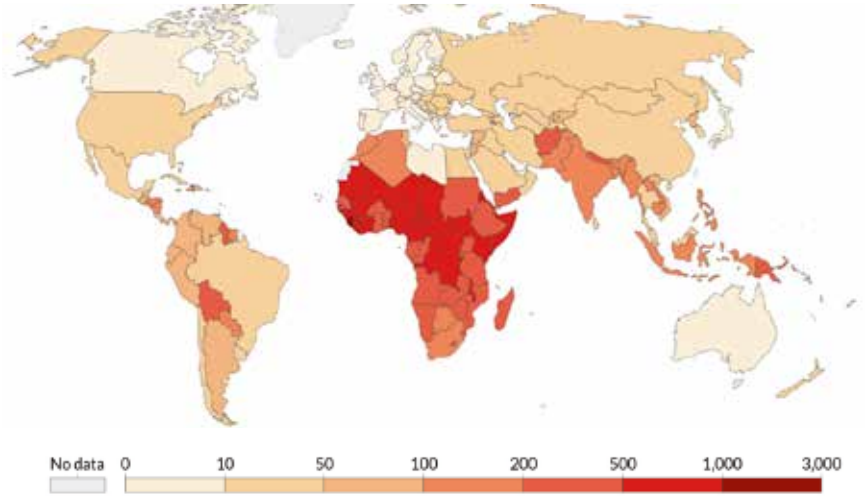
~ Ai Wei Wei

INTRODUCTION

Maternal mortality in context

Reducing maternal mortality is one of the major challenges to health systems worldwide – especially in low- and middle-income countries (LMIC), where 95% of global maternal deaths occur.[2] Global maternal mortality was reduced by 45% between 1990 and 2015, from 385 to 216 maternal deaths per 100.000 live births.[3] Strategies focused mostly on increasing skilled birth attendants, promoting facility-based deliveries and universal access to reproductive and maternal care. Despite the implementation of these successful strategies, maternal mortality has not declined as rapidly as intended by the Millennium Development Goals (MDGs): 75% reduction of maternal mortality ratio (MMR) between 1990 and 2015.[3] The MDGs' successor, the Sustainable Development Goals (SDGs), continued the agenda with the target to reduce the global MMR to less than 70 per 100.000 live births and a two-thirds reduction in MMR per country by 2030.[4]

Figure 1. Estimated maternal mortality ratios (per 100.000 live births), 2015[5]



A maternal death is the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes.

Three-delay model and obstetric transition

The conceptual 'three-delay' model and 'obstetric transition' framework are useful to understand the dynamic process of maternal mortality reduction strategies in different parts of the world.[6-8]

Thaddeus & Maine (1991)[6] first described the concept of 'delays' between the onset of a complication and maternal death to look beyond medical causes ('Too Far to Walk'[6]). The delays are sequential:

- Phase I: delay in deciding to seek care by the woman or her family;
- Phase II: delay in reaching an adequate health care facility; and
- Phase III: delay in receiving proper care at that facility.

Most maternal deaths cannot be attributed to a single delay. More commonly, a combination of factors ultimately leads to the woman's death.[7] Sociocultural and economic accessibility of care are known determinants of seeking and reaching care. However, it is equally important to consider the perceived benefit/need of care and the quality of care, especially in middle-income countries with a majority of births in facilities ('Still Too Far to Walk').[7]

The transition models describe global shifts in disease and/or demographic patterns.[8-10] Omran (1971)[9] first described the epidemiologic transition, with a global shift from a pattern of a high prevalence of communicable diseases (low- and middle-income countries) to a pattern characterized by a high prevalence of non-communicable diseases (high-income countries). Popkin (1993)[10] proposed the nutritional transition, which depicts the transformation from human diets to the global epidemic of obesity.

Souza et al. (2014)[8] proposed the obstetric transition framework, which describes the transition from a stage with high MMR and fertility rates to low MMR and fertility rates.[9] The obstetric transition stages help to identify specific challenges and targeted strategies to reduce maternal mortality. There are five stages of obstetric transition, with stage distinct improvement approaches:

- Stage I is characterized by a high MMR (>1000 per 100.000 live births) and high fertility rate. Women experience a situation close to 'natural history', with very little to no health care services to reduce the risk of maternal mortality. This is

often the result of political and economic factors impeding access and delivery of basic services.

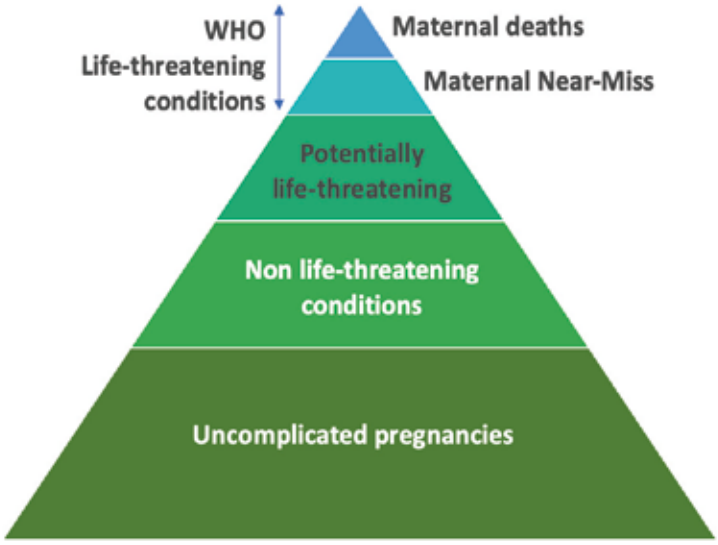
- In stage II the MMR is lower (999-300 per 100.000 live births) and women mostly die due to direct (obstetric) causes of maternal mortality and communicable diseases. A higher proportion of women receive maternal care, yet the infrastructure and the health care system are weak. This is the result of a lack of access (i.e. first and second delays) and poor quality of care with severe shortages of staff and resources.
- In Stage III the MMR lowers to 299-50 per 100.000 live births and fertility rates drop. This stage is considered a tipping point as women generally reach hospitals, and quality of care becomes the key determinant of health outcomes (i.e. third delay). While direct causes still cause the majority of deaths, there is an increase in indirect causes and non-communicable diseases.
- In Stage IV, the MMR is <50 per 100.000 live births. Indirect causes are the primary cause of maternal mortality, and non-communicable disease, as well as overmedicalization emerge as the greatest threat to the quality and improved health outcomes.
- Stage V, MMR <5 per 100.000 live births, is mostly aspirational with no avoidable maternal deaths.

Though maternal mortality seems to be associated with the income level of a country, the increase in national income does not guarantee a decrease in maternal mortality.[11] Differences in maternal mortality ratios within countries are great, especially in middle-income countries, and can often be attributed to social inequity within the country.[11] Latin America is the world region with the highest income inequality and is also the region with the largest health disparities.[12,13]

Maternal near-miss

Maternal mortality is only the tip of the iceberg (Figure 2[14,15]). For each woman who dies, many more suffer from life-threatening conditions. These women narrowly escape death either by chance or because of the care they received, but often have life-lasting disabilities.[14]

Figure 2. A representation of the maternal mortality continuum[14,15]



The advantage of studying maternal near-miss (MNM), over maternal deaths, is that it occurs more frequently and is less threatening to audit by health care providers. In high-income countries with only few maternal deaths per year, or settings with an absolute low number of maternal deaths (Suriname for example), studying near-miss has been used as a proxy to measure the quality of obstetric care.[16] Clinical audit is a useful approach to review cases, identify deficiencies in the provision of care, and ultimately improve the quality of obstetric care.[17] The global challenge in studying MNM is the definition – when to consider a woman to have 'narrowly escaped death' (Figure 2), and, how to systematically identify these women (paragraph 2).[14-16,18-20]

Complications during pregnancy and childbirth are associated with long-lasting adverse physical and psychosocial effects for mother, families and their offspring.[21,22] Maternal near-miss is also strongly associated with perinatal mortality (stillbirths and early neonatal deaths), and other adverse perinatal outcomes (i.e. birth asphyxia, preterm birth, low birth weight, Neonatal Intensive Care Unit admission).[23-27] Therefore, efforts made to reduce maternal mortality and near-miss will likely also reduce the occurrence of adverse perinatal outcomes.

Stillbirths

Stillbirths form a sensitive marker of the health system's strength. An estimated 2.6 million stillbirth occurred globally in 2015 (18 per 1000 births), most in LMIC and half from preventable causes.[28] Stillbirths are a neglected issue, excluded from the MDGs and SDGs and invisible in most national policies.[3,4] One important reason these babies are undocumented is the lack of registration of stillborn babies by vital statistics in many countries.[28,29] Compared to maternal and neonatal mortality, fewer studies have been conducted, and the reduction of stillbirths has been even slower.[30,31] The *Lancet Series 'Ending Preventable Stillbirth'* called for action and established the aim to reduce stillbirths to no more than 10 per 1000 total births in every country by 2035.[29] Most countries in the world, including Suriname, have not endorsed this target within their national health plan.[30-33] Improved registration and surveillance of stillbirths, classification of causes and audit may contribute to identifying the gaps in quality of care which need to be targeted to eliminate preventable stillbirths, and due to the intricate relationship with maternal conditions also reduce severe maternal outcomes.[30,31]

Classification of death and near-miss causes

Classification of diseases and underlying causes is crucial to enable global and local comparison and develop targeted strategies. The World Health Organization (WHO) developed the International Classification of Diseases - Maternal Mortality (ICD-MM, 2012) and Perinatal Mortality (ICD-PM, 2016).[34,35] Classification challenges include difficulty in determining the cause in a long chain of events, and how to deal with the many 'unknown causes' due to a lack of (post-mortem) investigations, especially in LMIC.[36,37] In maternal near-miss classification there is the challenge that the definition 'life-threatening' differs per settings. The WHO developed the near-miss tool (WHO-MNM, 2011)[14], using only organ-dysfunction criteria. However, both high- and low-income countries report underreporting and call for local adaptations of the criteria.[19,20] Current classification tools may not be perfect, yet recommendations for improvement will only unveil through its application.

Quality of care and criterion-based audit

The WHO defines quality of care as 'the extent to which health care services provided improve desired health outcomes. In order to achieve this, health care must be safe, effective, timely, efficient, equitable and people-centred.[38] To assess (improvements in) quality of care, it must be measured, preferably in a standardized form.[38,39] Criterion-based audit (CBA) is a useful method for evaluating quality of care and involves structured peer-review, whereby clinicians examine the practice (patients' medical record) against agreed standard of good-quality care.[40,41] Though not extensive, the WHO developed a set of global indicators for the evaluation of quality of obstetric care.[39,42] To define 'quality of care' and standards for CBA, national guidelines and international recommendations can be used next to the WHO global indicators.

PDSA-cycle

A powerful four-step approach to continually improve and adapt processes was developed by William Edwards Deming: The Plan-Do-Study-Act (PDSA) cycle.[43] The impact of the cycle is dependent on all components, 'no stronger than its weakest link'.[43] The PDSA-cycle can also be applied in the attempt to reduce maternal mortality, near-miss and stillbirths.[44-47] Examples of its application are within the Maternal Death Surveillance and Response (MDSR)[44,45], CBA[40,41], and within nationwide surveillance studies.[46,47] The repeatedly implemented PDSA-cycle in spirals of increasing knowledge bring each cycle closer than the previous to the ultimate goal. We will apply this useful approach during the studies presented in this thesis.

Suriname

Setting

Suriname is a multi-ethnic, upper-middle-income country on the northeast coast of South America. It covers an area of 163.820 km^2, consists of tropical rainforest for 90% and most of the population (80%) lives in the narrow coastal plain to the country's north.[48] With an estimated population of 576.000 people (2019), it is one of the least populous countries in the Americas.[48,49]

Diversity and ethnic distribution

The ethnical distribution among women in Suriname is: Hindustani (28%), Maroon (23%), Creole (17%), Javanese (13%), Mixed (12%), Indigenous (4%) and Other (3%) (in 2018).[48,49] Diversity in Suriname is a reflection of the country's history.[49-52] Indigenous people, also known as Amerindians, are the original inhabitants of the country. Maroon and Creoles are African-descendants who were enslaved and brought to Suriname by Europeans in the seventeenth and eighteenth century. Maroon people, in contrast to Creoles, escaped into the interior of the country. Creoles gained their freedom in 1863 when slavery was abolished in Suriname and often have mixed African – European (Dutch and British) ancestry. Asian-descendants: Hindustani (from East-India), Javanese (from Indonesia, then a Dutch-ruled colony) and Chinese people, came to Suriname in the late nineteenth century as contract workers. Mixed people are the result of interchanging identities between almost all ethnicities. Other ethnicities include mostly Brazilians, Caucasians (descendants of Dutch colonists) and few Lebanese.[50]

Equity and economy

Inequities in health, education and economic status have been described among people living in rural regions, among the poor and among the Indigenous and Maroon people in Suriname.[33,51,52] While the Multiannual Development Plan proposed several large investment projects, the economic recession since 2015 has severely affected these plans.[53] Additionally, the COVID-19 pandemic will result in an even worse recession with massive health, social and economic shock.[54]

Especially Latin American and Caribbean countries (and Suriname) are vulnerable to the consequences of COVID-19 due to weak social protection, fragmented health systems and the region's distinctively high and persistent inequality (even though most are classified as middle-income).[54] 'Building back better' will demand equality, protection of fundamental rights, universal welfare and economic resilience.[44]

Health care system

There are five hospitals, four of which are located in Paramaribo (Academic Hospital, 's Lands Hospital, Diakonessenhuis, St. Vincentius) and one in the district of Nickerie (Streekziekenhuis Nickerie) at the western border. Primary health care facilities are government-subsidized and include Regional Health Services (51 primary health clinics) in the coastal area and the Medical Mission (54 primary health clinics) in the interior districts.[48] Additionally, there are private primary health care clinics (approximately 200) in the coastal area.[48] The Bureau of Public Health (BOG, Dutch acronym Bureau Openbare Gezondheidsdienst) is responsible for all public health programs, including maternal deaths surveillance.[33]

Maternal health in Suriname

Approximately 10.000 live births take place per year, of which 92% in health care facilities (86% in hospitals and 6% in primary health care centres), 4% at home and 4% are unknown.[48] In 2018, 98% gave birth with a skilled birth attendant, and 85% received at least one antenatal care visit.[48] In 2014 legislation regarding basic health care insurance for all was enacted.[55] However, providing universal access to health care for mothers and their newborns remains a challenge, and disparities in access are often related to geographic location and insurance coverage.[48,49,51] Due to restrictions of public health insurance companies, in 2010 a third (30%) of women were confronted with additional payments for antenatal services such as ultrasounds and catastrophic out-of-pocket costs for additional services as hospitalization of newborns.[48,49,56]

The Safe Motherhood and Newborn Health Action Plans of 2014[32] and 2019[33] emphasized the lack of uniformity in ante-, intra-, and postpartum and emergency obstetric care protocols, which limited the monitoring of the quality of services. Abortion services are illegal and actual numbers are not registered.[51] The use of modern contraceptives is 40% in sexually active women of reproductive age (25% in sexually active adolescents and 35% in women aged 20-25).[48] Contraception use has hardly increased over the past 12 years, with some types of contraceptives not or only partly covered (i.e. IUD, implants, sterilization).[48]

Maternal mortality in Suriname

The Central Bureau of Vital Registry was established in 1917 and registers 98% of all live births in Suriname.[56] Stillbirths are not registered. A confidential enquiry into maternal deaths (identifying any shortfalls in the care provided and devising recommendations to improve future care) was conducted in Suriname by Mungra et al. between 1991-1993.[57] Mungra et al. (1999) reported a maternal mortality ratio of 226 per 100.000 live births, which was six times higher than reported by vital registry.[58] By 2000, the BOG initiated active surveillance of maternal deaths. In 2015 BOG reported a maternal mortality ratio of 130 per 100.000 live births, which implies a reduction in maternal deaths of 42% in 23 years.[33,51] Surveillance however, was not entirely reliable due to the fact that (1) coincidental and accidental causes were not excluded, and some late maternal deaths (more than 42 days after childbirth) were included, which may have led to an overestimation of the maternal mortality rate; (2) no reproductive age mortality survey was conducted, which may have led to underreporting of women who died in early pregnancy, or on non-obstetric wards; and (3) no maternal death review was performed to determine the underlying cause and lessons learned. The underlying causes were established based on the death certificate (which lacks a pregnancy box) and completed by the treating physician, often not familiar with ICD-MM.[33,51] In 2015, at the start of the studies presented in this thesis, there was no maternal death review committee and data on maternal mortality, maternal near-miss and stillbirths was lacking.

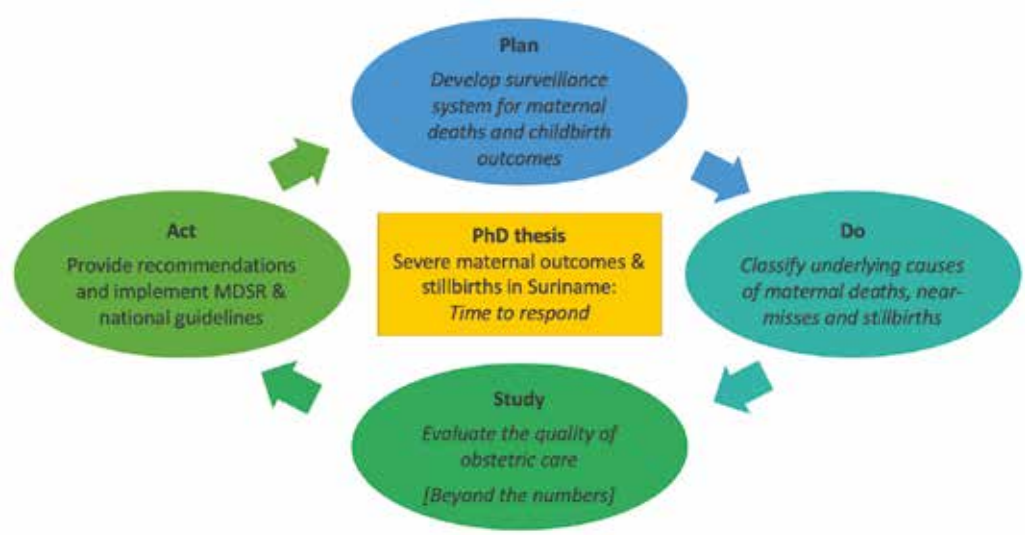
Thesis general aim

The general aim of this thesis is to provide recommendations to improve the quality of obstetric care in Suriname and reduce severe maternal and perinatal outcomes. We will apply the four-step Plan-Do-Study-Act (PDSA) cycle to the studies in this thesis on maternal mortality, maternal near-miss and stillbirth studies (figure 3). After robust surveillance, ascertainment and review of cases, lessons will be learned on how to improve surveillance, target childbirth disparities, enhance the use of international classification systems for underlying causes and, finally, improve the quality of maternal health care by the implementation of interventions, such as Maternal Death Surveillance and Response and national obstetric guidelines. Lastly, we aim to provide recommendations for the way forward (re-do PDSA-cycle).

Thesis research question

How can a reduction of severe maternal outcomes (maternal mortality and near-miss) and stillbirths be achieved in Suriname, and how can global maternal health care providers and policy makers contribute to this in Suriname and other middle-income countries?

Figure 3. Severe maternal outcomes & stillbirths in Suriname using the PDSA-cycle



Specific research questions and thesis structure

Part I: Surveillance

Provide an overview of maternal mortality and childbirth outcomes in Suriname

What is the national maternal mortality ratio and the degree of underreporting? Why do women in Suriname die during pregnancy, childbirth and in the puerperium? Do childbirth health care disparities exist in Suriname, and if so, which women are most at risk? What are the recommendations to improve maternal death surveillance and reduce underreporting? What are the recommendations to improve national perinatal data acquisition? What are the most important recommendations to reduce maternal mortality and adverse perinatal outcomes in Suriname?

Part II: Global classification systems

Assess underlying causes and evaluate global classification tools

What is the difference in underlying causes of maternal deaths when comparing classification between local experts and international experts? What is the maternal near-miss ratio and how applicable are the WHO maternal near-miss (organ-based) criteria? What is the stillbirth rate and what are the underlying causes of stillbirths? How can the applicability and feasibility of the global classification tools (ICD-MM, WHO-MNM and ICD-PM) be improved?

Part III: Beyond the numbers

In-depth review (audit) of maternal deaths and maternal near-miss

Why do women die or nearly die due to severe obstetric complications maternal sepsis, eclampsia and major obstetric haemorrhage in Suriname? How can future (near) deaths due to maternal sepsis, eclampsia and major obstetric haemorrhage be prevented in Suriname?

Part IV: Response

Formulate recommendations to implement necessary interventions

What is the most important enabler of obstetric guideline development? How can implementation of Maternal Death Surveillance and Response (MDSR) be enhanced?

Table 1. Outline of this thesis

	Chapter 1 General introduction
Part I *Surveillance*	**Chapter 2** Maternal death audits in Suriname **Chapter 3** Childbirth outcomes and ethnic disparities
Part II *Global Classification Systems*	**Chapter 4** ICD-MM challenges, application by three countries **Chapter 5** Maternal near miss and comparison of different tools **Chapter 6** ICD-PM application to stillbirths
Part III *Beyond the numbers*	**Chapter 7** Eclampsia and the importance of different management factors **Chapter 8** Postpartum haemorrhage magnitude, risk factors and audit **Chapter 9** The 'golden hour' in maternal sepsis
Part IV *Response*	**Chapter 10** "Bottom-up" development of obstetric guidelines **Chapter 11** Maternal Death Surveillance and Response
	Chapter 12 General discussion
	Chapter 13 Summary / Samenvatting

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Part I

Surveillance

San tu sma sabi moro betre lek sa wan sabi

[Two heads are better than one]

Maternal mortality audit in Suriname between 2010 and 2014, a reproductive age mortality survey

2

Lachmi R. Kodan*
Kim J.C. Verschueren*
Jos J.M. van Roosmalen
Humphrey H. H. Kanhai
Kitty W. M. Bloemenkamp
* *Contributed equally*

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ABSTRACT

Background: The fifth Millennium Development Goal (MDG-5) aimed to improve maternal health, targeting a maternal mortality ratio (MMR) reduction of 75% between 1990 and 2015. The objective of this study was to identify all maternal deaths in Suriname, determine the extent of underreporting, audit the maternal deaths and assess underlying causes and substandard care factors.

Methods: A reproductive age mortality survey was conducted in Suriname (South-American upper-middle income country) between 2010 and 2014 to identify all maternal deaths in the country. MMR was compared to vital statistics and a previous confidential enquiry from 1991 to 1993 with a MMR 226. A maternal mortality committee audited the maternal deaths and identified underlying causes and substandard care factors.

Results: In the study period 65 maternal deaths were identified in 50,051 live births, indicating a MMR of 130 per 100. 000 live births and implicating a 42% reduction of maternal deaths in the past 25 years. Vital registration indicated a MMR of 96, which marks underreporting of 26%. Maternal deaths mostly occurred in the urban hospitals (84%) and the causes were classified as direct (63%), indirect (32%) or unspecified (5%). Major underlying causes were obstetric and non-obstetric sepsis (27%) and haemorrhage (20%). Substandard care factors (95%) were mostly health professional related (80%) due to delay in diagnosis (59%), delay or wrong treatment (78%) or inadequate monitoring (59%). Substandard care factors most likely led to death in 47% of the cases.

Conclusion: Despite the reduction in maternal mortality, Suriname did not reach MDG-5 in 2015. Steps to reach the Sustainable Development Goal in 2030 (MMR ≤ 70 per 100.000 live births) and eliminate preventable deaths include improving data surveillance, installing a maternal death review committee, and implementing national guidelines for prevention and management of major complications of pregnancy, childbirth and puerperium.

BACKGROUND

Reducing maternal mortality is one of the major challenges to health systems worldwide. United Nations' (UN) Millennium Development Goal 5 (MDG-5) called for a 75% reduction of the maternal mortality ratio (MMR) between 1990 and 2015.[1] The global MMR fell from 385 deaths per 100.000 live births in 1990 to 216 in 2015, corresponding to a decline of 44%.[1] A vision of ending all preventable maternal deaths has emerged in 2015, being one of the Sustainable Development Goals (SDGs); it aims to reduce the global MMR to less than 70 deaths per 100.000 live births by 2030. Achievement of this tar- get will require robust information systems with high- quality data, specifically on causes of death, as it is of great importance in informing decision-makers and ultimately reducing maternal mortality.[1]

UN's Maternal Mortality Estimation Inter-Agency Group reports that Suriname is one of the few countries with an increase in MMR from 127 in 1990 to 155 in 2015.[2,3] However, a confidential enquiry by Mungra et al. reported an MMR of 226 per 100.000 live births in 1991-1993, suggesting a 31% decrease instead of the 25% increase as suggested by the UN.[4,5] However, it is unclear whether, and if so, to what extent, vital registration has become more reliable over the years.

Maternal health outcomes are strongly associated with higher capital levels, suggesting that an increase in Gross National Income (GNI) per capita should correspond with a reduction in maternal mortality.[6] Suriname was upgraded from lower-middle income country to upper-middle income country in 2013 as the GNI in- creased from $1430 in 1990 to $9370 in 2013.[7] Yet, progress made on different basic health indicators (e.g. under five mortality, health insurance coverage and maternal mortality) in the country is relatively marginal.[8]

According to WHO-estimates, Suriname (MMR 155) belongs to the four worst performing countries in Latin America and the Caribbean (Haiti - MMR 359, Guyana - MMR 229 and Bolivia - MMR 206).[1-3] These are, in contrast to Suriname, low and lower-middle income countries. Suriname's poor performance concerning

maternal mortality is unexplained, as the country performs fairly well on maternal health indicators, e.g. skilled professionals attended 96% of the deliveries in the coastal area and 77% in the rural interior and antenatal care visits occurred at least once in 91% of the pregnant women and at least four times in 67%.[8]

Therefore, the aim of the study is first to identify all maternal deaths in Suriname from 2010 to 2014, second to determine whether maternal deaths were accurately registered and classified, third to assess the reduction of maternal deaths in 25 years, fourth to perform an in- depth audit of the deaths and finally to determine the level of substandard care.

METHODS

Study design: A reproductive age mortality survey (RAMoS) was con- ducted, using different methods to identify maternal deaths nationwide in Suriname between January 1st 2010 and December 31st 2014.

Study setting: Suriname is a multi-ethnical South American country with a population of 541,638 served by four referral hospitals in the capital, Paramaribo, and one hospital near the western coast, Nickerie. In addition to general practitioners, Regional Health Services (RGD) and Medical Mission (MZ) are responsible for primary healthcare. RGD comprises of 43 facilities serving the whole coastal area and the Medical Mission has 56 health posts throughout the interior. Figure 1 demonstrates the urban area I (Paramaribo) and II (Nickerie), rural coastal area III and rural interior IV. Annually approximately 10,000 live births take place, of which hospitals cover an estimated 82% and primary health institutions 10%, 4% of deliveries are at home and the remaining 4% is unknown.[9] Social insurance, which is for the near poor and poor population, covers an estimated 45% of the general population. The ethnic distribution among the female population is Hindustani (28%), Maroon (24%), Creole (18%), Javanese (14%), Mixed (14%) and other (2%).[10]

Classification & definitions: According to the ICD-MM a pregnancy-related death is the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause.[11] A maternal death is the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes. Direct obstetric deaths are those resulting from obstetric complications, while indirect obstetric deaths are those resulting from either a previous existing disease or a disease that developed during pregnancy and which is not due to direct obstetric causes, but which is aggravated by physiologic effects of pregnancy. In unspecified maternal deaths the underlying cause is unknown or cannot be determined. Late maternal deaths are direct or indirect deaths, more than 42 days, but less than 1 year after termination of pregnancy. MMR is the number of direct, indirect and unspecified maternal deaths per 100,000 live births.[11,12]

Figure 1. Map of Suriname: urban (I-II), rural coastal (III) and rural interior (IV)

Data collection: Vital registration Maternal deaths in Suriname are identified mainly by the collection of death certificates and sporadic informing in the hospitals. No independent surveillance systems are adapted to investigate deaths in women of reproductive age. Notification of death is compulsory by law. However, burial can take place with- out the official death certificate, when there is 'an act of death' (an unofficial note signed by a medical doctor). The death certificate is filled in afterwards and often received with a delay (>3 months) and in 15% not received at all. In addition the death certificate lacks a pregnancy checkbox.[13] Identified maternal deaths are not reviewed and thus not classified. Due to a lack of classification, most accidental/incidental deaths and late maternal deaths are also included in the official maternal mortality statistics.

Reproductive age mortality survey (RAMoS): The RAMoS consisted of different steps. First, case records of maternal deaths from 2010 to 2014 identified by vital registration were collected. Second, all medical records of deceased women aged 10 to 50 years in our study period were collected from the archives of all hospitals and the primary health care institutions (Medical Mission and Regional Health Services). Third, The Central Bureau of Civil Affairs provided a list of all deceased women in the country between 2010 and 2014 with an offspring in the pre- ceding year. Fourth, an inventory was performed in the largest mortuary (receiving also deaths occurring outside health care institutions). Fifth, obstetric health care professionals in all facilities were asked their knowledge on local maternal deaths in the past 5 years. Medical records were collected and examined extensively and in case of an incomplete file involved health care professionals were interviewed. Verbal autopsy with family member(s) was performed when maternal deaths occurred outside of the hospital. This was conducted according to the WHO-instrument on verbal autopsy.[14] All available information was gathered (i.e. laboratory and pathology reports, in delivery-books and autopsy information). An elaborate clinical case summary of every pregnancy- related death was made according to the FIGO-LOGIC MDR: Clinical summary form tool.[15] Information on patients, health care providers and hospitals was kept strictly confidential.

An expert committee, consisting of different obstetricians, an internal medicine specialist or anaesthesiologist and midwives, audited all pregnancy-related deaths with two authors (LK and KV) presenting and moderating the sessions. When no consensus was achieved, external ex- pert opinion (JR and HK) was sought. The committee reviewed the cases and agreed to a mode of death, under- lying cause, contributing factors and classified each death using WHO guidelines on applications of ICD-MM.[12] Substandard care factors were analysed according to an adapted version of the FIGO-LOGIC MDR Grid analysis of clinical case management form.[15] Due to lack of guidelines substandard care was defined as a deviation from 'standard practice' according to local clinicians.

Data analysis: Data were manually entered into IBM SPSS version 21.0 (Armonk, New York, USA) for analysis. All maternal deaths were individually analysed and cross-linked with registered maternal deaths by civil registration. Causes, contributing factors and substandard care factors were recoded into categorical variables.

Figure 2. Flowchart of pregnancy related deaths in Suriname

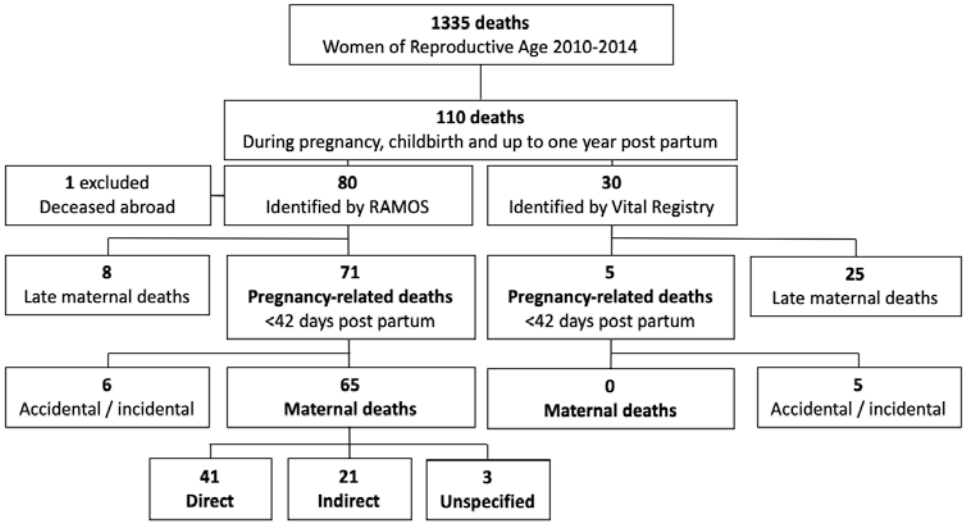


Table 1. Maternal deaths found by RAMOS in comparison to vital registration

	Area I Urban Paramaribo Wanica	**Area II** Urban Nickerie	**Area III** Rural coastal Coronie Saramacca Para Commewijne Marowijne	**Area IV** Rural interior Brokopondo Sipaliwini
General population, n=534.189	66 %	6 %	18 %	10 %
Live births, n= 50.051				
Residency	67 %	4 %	18 %	11 %
Location of delivery [1]	77 %	5 %	5 %	5 %
Maternal deaths, n=65				
Location of residence	40 (62)	4 (6)	10 (15)	11 (17)
Location of death	56 (86)	2 (3)	3 (5)	4 (6)
Hospital, n=55	53	2	N/A	N/A
Primary health care, n=5	-	-	3	2
Home, n=5	3	-		2
MMR per 100.000 live births	145	80	120	160

Legend

[1] Unknown location of live births in 8% (of which half of live births at home)

Table 2. Demographics of Surinamese population and of maternal deaths

	2010	**2011**	**2012**	**2013**	**2014**	**Total**
Live births	9712	9703	10217	10012	10407	**50051**
RAMOS						
MMR per 100.000 live births	154	144	69	130	154	**130**
Maternal deaths	15	14	7	13	16	**65**
Vital registration						
MMR per 100.000 live births	82	113	49	130	154	**106**
Maternal deaths	8	11	5	13	16	**53**
Underreporting	0	1	0	1	3	**5**
Misclassification of causes (%)	50	60	60	75	70	**65**
Misidentification (%)	47	28	30	8	18	**26**
Correction factor	1.88	1.40	1.40	1.08	1.23	**1.35**

RESULTS

Of the 1335 deceased women of reproductive age between 2010 and 2014, 71 were pregnancy-related and 65 were maternal deaths (figure 2). The 65 maternal deaths were identified among 50.051 live births, resulting in a MMR of 130 with an annual range from 69 to 154 per 100.000 live births (table 1).

Underreporting occurred by misidentification in 26% (n=17) and by misclassification in 65% (n=31) (table 1). The predictive value for the current vital registration to identify maternal deaths is 74% (48/48+17). The maternal deaths not identified by vital registration (n=17) occurred in the hospitals in 88% (n=15) or at home in 12% (n=2). The causes of these hospital-deaths were infectious diseases in 87% (n=13), admitted and deceased on non-obstetric wards. These death certificates did not indicate or suggest that the woman was or had been pregnant. Maternal deaths, which were identified by vital registration but were classified incorrectly, consisted of deaths without the cause mentioned on the death certificate (n=9), non-obstetric diseases (n=13), deaths complicated with more than one diagnosis (n=8) and cases in which the mode of death was reported on the death certificate rather than the underlying cause (n=17). Apart from the 48 true maternal deaths identified by vital registration, another five maternal deaths were incorrectly classified as maternal deaths (these were accidental or incidental causes or late maternal deaths).

Characteristics of maternal deaths

The women in Suriname who died during pregnancy, childbirth or puerperium lived in a rural coastal area or in the rural interior in respectively 18 and 11% (figure 1 and table 2). Maternal deaths, however, occurred in these areas in respectively 5 and 6%. Maternal deaths in urban hospitals (89%) occurred on the ICU (60%), ward (30%) or emergency or operating room (10%). Characteristics of maternal deaths are shown in table 3. Social insurance, indicating the (near) poor, covered 69% (n = 45) of the deceased women. Socially insured women were maroons or creoles in 75% (n = 34) of the cases. Anaemia (Hb $\leq$ 6.0 mmol/L) complicated 45% of the cases. Post-mortem investigation was performed in 3% (n = 2) of maternal deaths.

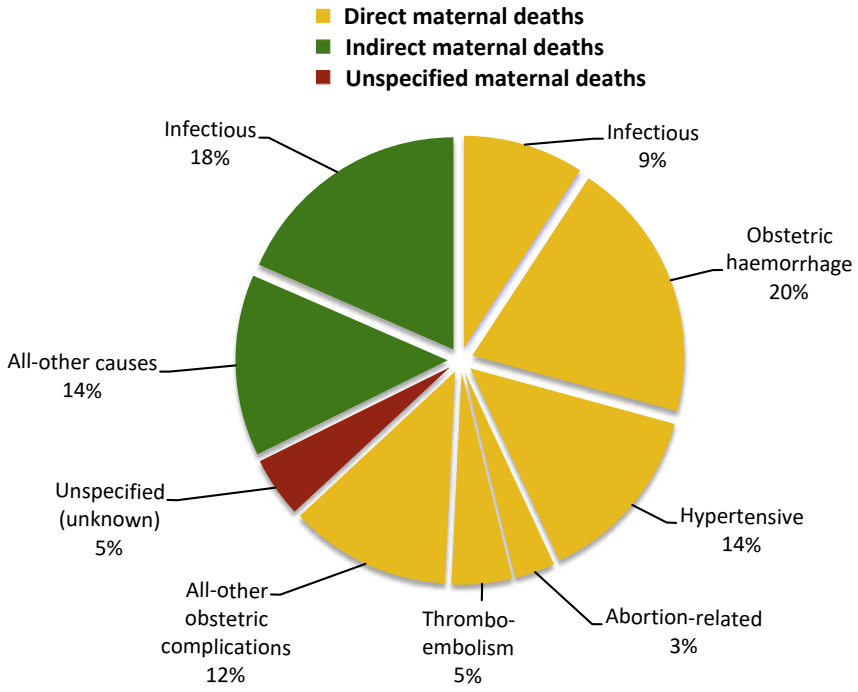
Table 3. Maternal characteristics of all maternal deaths

	n = 65 (%)
Age	
<20	11 (17)
20-35	42 (64)
36-50	12 (18)
Mean, range of age	29, 16-45
Ethnicity	
Hindu	12 (18)
Creole	13 (20)
Maroon	24 (37)
Javanese	8 (12)
Indigenous	3 (5)
Mixed	5 (8)
Insurance (n=63)	
Social insurance (poor)	45 (69)
State Health	10 (15)
Private	8 (12)
Antenatal care (n=58)	
None	12 (23)
< 4	8 (15)
≥ 4	33 (62)
Parity at time of death (n=62)	
0	5 (8)
1	14 (23)
2	17 (27)
≥ 3	26 (42)
Pregnancy state	
Abortive (< 16 weeks)	5 (8)
Antepartum	15 (23)
Intrapartum	4 (6)
Post partum	41 (63)
Mode of delivery (n=41)	
Spontaneous, vaginal	25 (61)
Instrumental delivery	3 (7)
Caesarean section	13 (32)
Perinatal death (n=57)	
Yes	36 (64)
Intrauterine foetal death	8 (14)
Early neonatal (within 7 days)	8 (14)

Classification and causes of maternal deaths

Of the 65 maternal deaths, 41 (63%) were due to direct causes, 21 (32%) due to indirect causes and three (5%) maternal deaths were classified as unspecified because the cause of death was unknown (figure 3). The two leading causes of maternal mortality were obstetric and non- obstetric sepsis (n = 18, 27%) and obstetric haemorrhage (n=13, 20%). Obstetric haemorrhage was mainly due to postpartum haemorrhage (n=11, 85%) caused by uterine atony (29%), retained placenta (23%), ruptured uterus (15%), vaginal or cervical tear (8%), and unspecified causes (10%). Underlying cause of all antepartum haemorrhage was placental abruption (n=2, 15%). Hypertensive disorders and its complications (e.g. cerebral bleeding, HELLP, eclampsia) accounted for 14% of maternal deaths. However, hypertensive disorders, such as pregnancy induced hypertension and pre-eclampsia, were diagnosed in 30% of all maternal deaths. Though not the underlying cause of death, they were commonly classified as a contributing factor.

Figure 3. Classification of underlying causes of the maternal deaths (n=65)



The remaining other causes of direct maternal deaths (n=8, 12%) were four probable amniotic fluid embolisms, one obstructed labour, one suicide by intoxication at 24 weeks, one case of acute fatty liver of pregnancy with consequently hepatic encephalopathy and multi- organ failure. The underlying cause of one case remained unknown as the woman died without any reported symptoms within a few hours after caesarean section for foetal indication. Sepsis occurred either due to direct obstetric complications (9%) of which one third had puerperal sepsis while being HIV positive or due to medical conditions aggravated by the pregnancy (e.g. non-obstetric septicaemia, pneumonia, gastro-enteritis, AIDS) and therefore were classified as indirect maternal deaths (18%). The other non-sepsis indirect maternal deaths (n=9) concerned two cases of endocarditis resulting in heart failure, one pulmonary bleeding caused by idiopathic thrombocytopenia, one case of end-stage renal failure due to diabetes and one woman, with pre-existent hypertension, died due to a cerebrovascular accident.

Table 4. Substandard care factors analysed in maternal deaths (n=59)

	n= (%)
Substandard care present	56 (95)
Professional factors	
Quality	47 (80)
Availability	11 (19)
Attitude / work-ethic	13 (22)
Medical service factors	
Wrong or delay in diagnosis	35 (59)
No/wrong treatment	46 (78)
Poor monitoring	35 (59)
Communication	19 (32)
Unavailability medical supplies	
Lack of diagnostic equipment	8 (14)
ICU-bed needed (n=45)	11 (24)
Blood necessary (n=31)	10 (32)
Lack of medication, oxygen-therapy, crash-cart	12 (20)
Patient factors	
Poor compliance to treatment	13 (22)
Refusing treatment	4 (7)
Delay in transportation	9 (15)

Substandard care factors were found in 95% (n=56/ 59) of the cases (table 4). More than 5 substandard care factors were present in 55% of cases. In 80% of the cases care provided by health professionals was below the standard due to delay in diagnosis (59%), inadequate treatment (78%) or poor monitoring (59%). Blood transfusion was unavailable in 10 of 31 cases (32%) when this was required. An ICU bed was not available when requested in 11 (24%) of 45 cases. The committee agreed that in 47% of the maternal deaths substandard care factors certainly (21%) or most likely (26%) led to death.

DISCUSSION

The MMR in Suriname is 130 per 100,000 live births between 2010 and 2014. Mungra et al. reported a MMR of 226 between 1991 and 1993, which indicates a 42% reduction in maternal deaths and an improvement in underreporting from 64% to 26%.[4,5] A comparison of the MMR and underreporting is difficult, as to our best knowledge there are few countries that have performed a RAMoS of confidential enquiry.[16-19]

Though our study suggests that, over the years, there is a growing reliability on identification of maternal deaths, the underreporting rate in Suriname (26%) is still higher than reported in Jamaica (20%), Argentina (9.5%) and Mexico (13%).[16-19] The underreporting due to misidentification of maternal deaths in Suriname can be explained by numerous facts: first, physicians are not obliged to report maternal deaths. Second, part of the death certificate (including the cause of death) is not always available as it is not obliged to be completed before the burial takes place. Third, the death certificate does not include a pregnancy checkbox and finally no active enquiry or RAMoS is per- formed. The effectiveness of a pregnancy check box on death certificates has proven to be effective in identifying pregnancy-associated mortality.[20,21] Misclassification of deaths by vital registration in Suriname can be explained by different factors. First, maternal death causes are designated by the ICD-code on the death certificate (patient records frequently unavailable), while the ICD- MM coding alone is considered inadequate.[22] Second, post-mortem investigations are rare. Third, verbal autopsies and maternal death reviews are not

performed to identify causes. These last strategies are best in identifying causes and evaluating quality of care in order to improve.[11,14,15,22]

Social insurance as a marker indicating poverty was found in the majority of maternal deaths (69%), while less than half of the general population had social insurance. A difference in ethnicity is seen between the general female population (Hindustani 28%; Maroon 24%; Mixed 14%) and the maternal deaths (Hindustani 18%; Maroon 37%; Mixed 8%).

Similar to two decades ago, obstetric haemorrhage is the most common direct cause of death, which is lower than reported in low-income countries (27%) and higher than in high-income countries (16%).[3] Hypertensive disorders are known to be an important cause of maternal deaths in Latin America and the Caribbean (22%).[1-3] While eclampsia was the underlying cause in just 14% of the deaths in Suriname, it was an important contributing factor (30%) to deaths with another underlying cause. The authors advise health authorities to implement nation- wide protocols for the prevention and management of hypertensive disorders and post-partum haemorrhage. Illegal abortion is the cause of death in only one case (1.5%), which is in great contrast to the 12% abortion-related deaths in Latin America and the Caribbean.[3,17,19]

Although illegal in Suriname, most abortions are self-induced with misoprostol and women present with an incomplete abortion after which safe surgical evacuation is performed in the hospital by a gynaecologist or gynaecologist in training. However, since termination of pregnancy is not registered, underreporting could have occurred. Indirect maternal deaths (32%), in particular non-obstetric sepsis (18%), accounted for a greater part of the maternal deaths in our study compared to the 27% of other Latin American and Caribbean countries.[3] Therefore, we recommend that these maternal deaths from should be analysed in detail to gain more knowledge of underlying causes, circumstances and preventive measurements.

The most striking finding of our survey is that the majority of maternal deaths occurred in hospital (85%) with the most important substandard care factor being delay in diagnosis (59%) and delay in treatment by health care providers, and less

frequently due to patient delay (15%). This finding necessitates actions such as training and retaining skilled staff and implementation of evidence- based guidelines. Another important finding is that most of the deaths occurred postpartum, indicating that improvements can be made in the care provided in the period after birth. Patients should be provided with more information. We advise more frequent and qualitative better postnatal checks and if necessary, home-visits should be performed. Lastly, a great number of maternal deaths occurred on the wards (30%) and the monitoring of patients is found to be inadequate in 59% of these cases. Implementation of an early warning system for timely interventions in order to reduce serious adverse events has been proven effective and is recommended.[23]

Limitations of this study are indwelled in its retrospective nature. Though we performed a robust enquiry, maternal deaths could have been missed, especially if they occurred outside of health care facilities or during early pregnancy. In addition, not all case files were available, records were often incomplete and post-mortem investigations were generally not performed. This affected the quality of the classification of causes and evaluation of substandard care during the maternal death reviews. Fi- nally, but most importantly, due to lack of national data on characteristics of the pregnant population, pregnancy and delivery, we were not able to perform multivariate analysis and assess risk factors.

CONCLUSION

Suriname has a high MMR compared to other Latin American countries and the Caribbean with similar or lower income economies. We highly recommend (1) to improve national data surveillance, (2) install a maternal mortality committee to review all maternal deaths, (3) implement an early warning score and national guide- lines on postpartum haemorrhage and eclampsia and (4) improve postnatal care strategies. Lastly, as maternal mortality is merely the tip of the iceberg, severe morbidity research should be conducted to assess and prevent severe obstetric complications and make progress to reach the SDG of a MMR <70 in 2030.

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Childbirth outcomes and ethnic disparities in Suriname: a nationwide registry-based study in a middle-income country

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Kim J. C. Verschueren
Zita D. Prüst
Raëz R. Paidin
Lachmi R. Kodan
Kitty W. M. Bloemenkamp
Marcus J. Rijken
Joyce L. Browne

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ABSTRACT

Background: Our study aims to evaluate the current perinatal registry, analyze national childbirth outcomes and study ethnic disparities in middle-income country Suriname, South America.

Methods: A nationwide birth registry study was conducted in Suriname. Data were collected for 2016 and 2017 from the childbirth books of all five hospital maternity wards, covering 86% of all births in the country. Multinomial regression analyses were used to assess ethnic disparities in outcomes of maternal deaths, stillbirths, teenage pregnancy, caesarean delivery, low birth weight and preterm birth with Hindustani women as reference group.

Results: 18.290 women gave birth to 18.118 (98%) live born children in the five hospitals. Hospital-based maternal mortality ratio was 112 per 100.000 live births. Hospital-based late stillbirth rate was 16 per 1000 births. Stillbirth rate was highest among Maroon (African-descendent) women (25 per 1000 births, aOR = 2.0 (95%CI 1.3–2.8) and lowest among Javanese women (6 stillbirths per 1000 births, aOR = 0.5, 95%CI 0.2–1.2). Preterm birth and low birthweight occurred in 14 and 15% of all births. Teenage pregnancy accounted for 14% of all births and was higher in Maroon women (18%) compared to Hindustani women (10%, aOR = 2.1, 95%CI 1.8–2.4). The national caesarean section rate was 24% and was lower in Maroon (17%) than in Hindustani (32%) women (aOR = 0.5 (95%CI 0.5–0.6)). Caesarean section rates varied between the hospitals from 17 to 36%.

Conclusion: This is the first nationwide comprehensive overview of maternal and perinatal health in a middle income country. Disaggregated perinatal health data in Suriname shows substantial inequities in outcomes by ethnicity which need to be targetted by health professionals, researchers and policy makers.

BACKGROUND

Maternal and perinatal vital registration systems are essential to monitor outcomes of pregnant women and their offspring, identify inequities in service provision and health outcomes and facilitate quality control in perinatal care.[1,2] Following lessons learned from the Millennium Development Goals (MDGs), the Sustainable Development Goals (SDGs) call for statistics "disaggregated by income, gender, age, race, ethnicity, migratory status, disability, geographic location and other characteristics relevant in national contexts" to monitor progress and identified inequities in health outcomes.[2-4]

The Global Strategy for Women's, Children's and Adolescents' Health, 2016–2030 is a roadmap for ending all preventable maternal and newborn deaths (including stillbirths) and is central to the achievement of the SDGs.[5] This strategy urgently calls for the extension and strengthening of health information systems to generate high quality data and evidence to measure progress and be in able to reach the target of a global maternal mortality ratio (MMR) under 70 per 100.000 live births and stillbirth rate (SBR) under 12 stillbirths per 1000 births.[2,6]

National childbirth registries have been established in several high income countries.[7-9] Low and middle-income countries (LMIC) are increasingly investing in robust national information on maternal and perinatal health indicators for SDG monitoring. However, given the complexity of establishing a well-functioning registry system, data collection in these countries is often not uniform, lack important indicators and data are frequently missing.[1] In many (currently, 34) Latin American and Caribbean countries, the Perinatal Information System (SIP), a digital clinical record and local management software standard has been implemented.[10] Suriname, an upper middle-income country, is one of the countries where SIP will be re-launched after a previous attempt in 2014, which failed for unknown reasons.[11]

Ethnic disparities in birth outcomes have modestly been studied compared to other social determinants of health, such as wealth, education, age and place of residence. Several studies in high-income countries have shown that women of African descent experience a two to six times higher risk for severe maternal outcomes

compared to Caucasian women (often linked to socio-economic factors).[12-16] Suriname is particularly of interest as it has multiple ethnic groups without one great majority.[17] To promote an efficient and adequate implementation process of the new perinatal data system in Suriname and subsequently evaluate its effect, this study provides a baseline assessment of perinatal data from all hospitals in the country. Our study aims to evaluate the current perinatal registry, analyze national maternal and perinatal characteristics and study ethnic disparities in childbirth outcomes in Suriname.

Table 1. Overview of maternal and perinatal data registration per hospital

	Hospital				
	I	II	III	IV	V
Childbirth registry	On paper	On paper	On paper	On paper	On paper
Digitalizing of paper parturition books	Special secretary for this task	General secretary, with other responsibilities	General secretary, with other responsibilities	No one; students used for this study	Responsible midwife doing the delivery
Software used	SPSS	Excel	Access	Excel	Excel
Common reported variables	Maternal age, ethnicity, gravidity, parity, gestational age, singleton or twin, data and time of delivery, presentation, mode of delivery, indication for caesarean section, APGAR score after 1 and 5 minutes, sex, birth weight, length, head circumference, stillbirth, weight placenta, length of umbilical cord, rupture type, blood loss				
Other variables reported per hospital					
HIV	Yes	No	No	Yes	Yes
Hepatitis B	No	No	No	Yes	No
Syphilis	No	No	No	Yes	No
1st ANC visit	Yes	No	No	Yes	No
No. ANC visits	No	No	Yes	No	No
1st ultrasound	Yes	No	No	No	No
Haemoglobin	Yes	No	No	Yes	Yes
Blood type	Yes	Yes	No	Yes	Yes
Induction	Yes	No	No	No	No
Augmentation	Yes	No	No	No	No
Active 3rd stage	No	Yes	Yes	Yes	Yes

METHODS

Study design: A two-year registry-based nationwide study of all hospital births was conducted, using the childbirth books of the five maternity wards between January 1st, 2016 and December 31st, 2017.

Study context and ethnicities: Suriname is a multi-ethnical, upper middle-income country on the northeast coast of South-America. With an estimated population of 598,000 people, it is one of the least populous countries in the Americas.[18,19] Ethnical distribution among the general Surinamese population in 2013 was: Hindustani (27%), Maroon (22%), Creole (16%), Javanese (14%), Mixed (13%), Indigenous (4%), Chinese (1%) and Other (3%) [19,20]. Diversity in Suriname is a reflection of the country's history. Indigenous people, also known as Amerindians, are the original inhabitants of the country. Maroon and Creoles are African-descendants who were enslaved and brought to Suriname in the seventeenth 17th and eighteenth century. Maroon people, in contrast to Creoles, escaped into the interior of the country. Creoles gained their freedom in 1863 when slavery was abolished in Suriname and often have mixed African - European (Dutch and British) ancestry. Asian-descendants: Hindustani (from East-India), Javanese (from Indonesia, then a Dutch-ruled colony) and Chinese people, came to Suriname in the late nineteenth century as contract workers. Mixed people are the result of interchanging identities between almost all ethnicities. Other ethnicities include mostly Brazilians, Caucasians (descendants of Dutch colonists) and few Lebanese.[17]

Study setting: The study was conducted in all hospitals in Suriname: four hospitals located in the capital Paramaribo and one hospital in Nickerie (West coast). Institutions perform approximately 92% of all births in Suriname with approximately 86% in hospitals and 6% in primary health care centres. Information regarding the primary health care births, home births (4%) and births of unknown location (4%) were not available.[19,20] The Multiple Indicator Cluster Survey (MICS) of 2018, estimated that 13% of women did not receive antenatal care, 56% received their first antenatal care visit within the first 3 months of pregnancy, 62–80%

received at least four antenatal care visits and 95–98% of births were attended by skilled birth attendants.[20] Maternal mortality has dropped 43%, from 226 to 130 per 100.000 live births, between 1990 and 2015, as demonstrated by two Reproductive Age Mortality Surveys.[21,22]

Participants and data collection: All hospital births with babies born by at least 22 weeks of gestation or with a birth weight of at least 500 g, were eligible for inclusion.[23] Paper childbirth books provide manually written data on every birth in all hospitals. Birth attendants are responsible for the information to be registered in the books. Hospital personnel digitalised this data in Microsoft Excel and IBM SPSS with instructions and prespecified definitions. All variables were entered in the secured database anonymously. Three of the authors (KV, ZP, RP) cross-checked the digital data with the paper childbirth book data. Medical files were assessed for stillbirths and maternal deaths to validate the death.

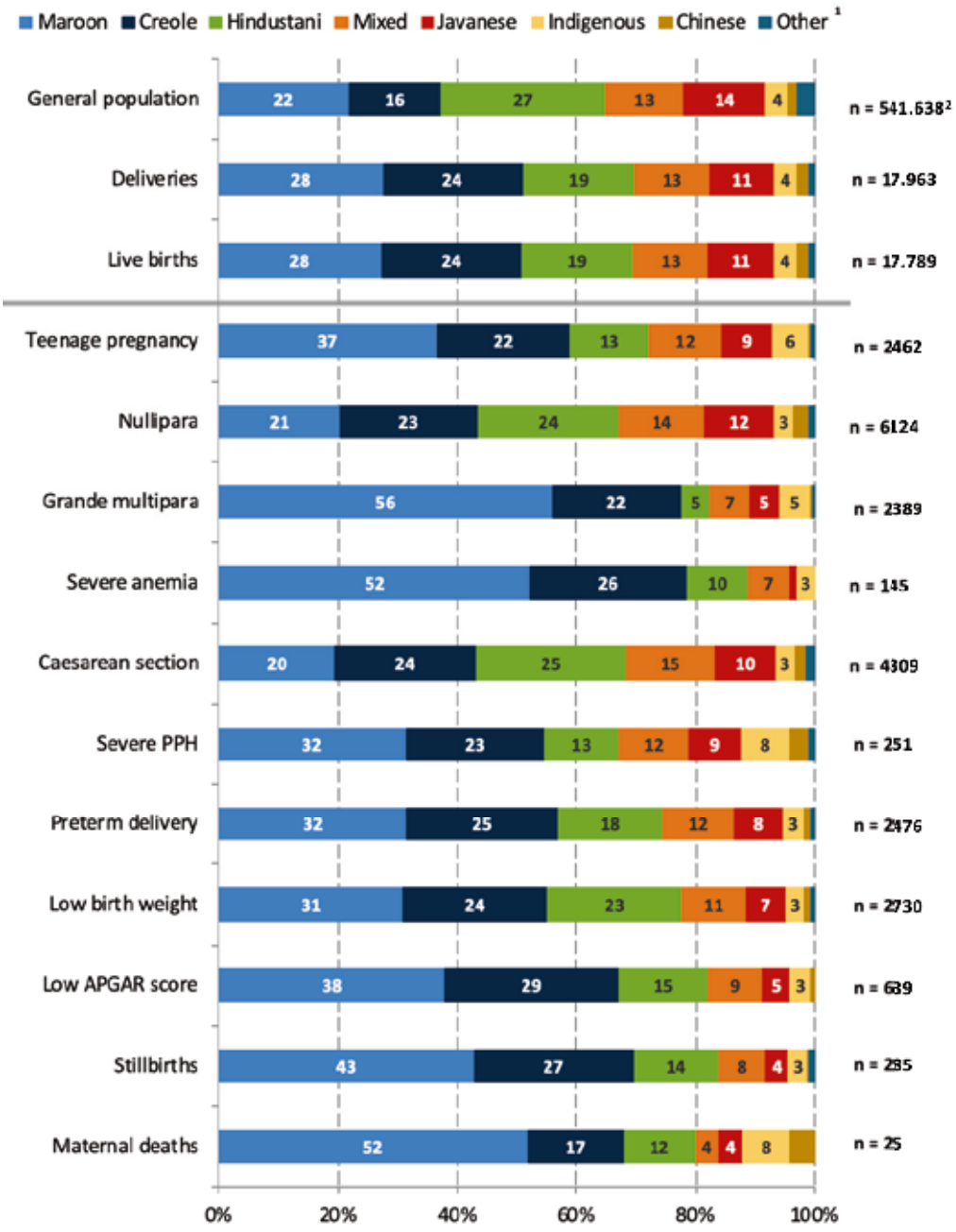
Variables: The digitalization, software used and reported variables per hospital can be found in table 1 and an elaborated version in Supplementary file 1. Ethnicity was self-reported similar to the MICS.[20] Teenage pregnancy was defined as childbirth below the age of 20 years.[24] Severe anaemia was defined according to the WHO definition: a hemoglobin level below 70 g/L (4.3 mmol/L) was considered severe and below 100 g/L (6.2 mmol/L) was moderate.[25] Sickle cell anaemia is assessed during antenatal care in each woman in Suriname, but not reported in the childbirth book and could therefore not be studied. Outcome variables were coded into categories, based on the Dutch Perinatal data registry data.[26] Preterm birth was defined as childbirth before 37 weeks of gestation.[26] Low birth weight was defined as a newborn with a birth weight below 2500 g.[26] APGAR score was considered low when the 5 min APGAR score was below 7.[26] Postpartum haemorrhage (PPH) was defined as blood loss of at least 500 mL and severe PPH at least 1000 mL.[27] Stillbirth was defined as a foetus born with no signs of life. Late stillbirth was defined, according to the International Classification of Diseases – Perinatal Mortality (ICD-PM), as stillbirth after 28 weeks of gestation or, if gestational age was unknown,

birth weight of 1000 g or more.[28] Stillbirth rate (SBR) was calculated as the number of late stillbirths per 1000 births beyond 28 weeks of gestation (or > 1000 g).[28] Maternal death was defined according to the International Classification of Diseases – Maternal Mortality (ICD-MM), as death of a woman while pregnant or within 42 days of termination of pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes.[29] The national MMR was calculated as the number of maternal deaths per 100.000 live births beyond 22 weeks of gestation (or > 500 g).[29] Data on social economic status such as income and level of education, and data on obesity and smoking were not available.

Statistical methods: Descriptive statistics were used for baseline characteristics analysis using frequencies and percentages for categorical data. Differences between groups were tested with chi-square test for significance ($p < 0.05$). Missing data on ethnicity was negligible (< 5%) and no data imputation was performed. To assess the relation between ethnic groups and health outcomes, multinomial logistic regression was performed. Hindustani ethnicity was used as reference group as they represent the largest proportion of the general population. Odds ratios (OR) were obtained, which were interpreted as relative risks in the case that the probability of the disease was less than 10%.[30] Possible confounders were selected by constructing causal diagrams and adjusted odds ratios (aOR) were obtained.[31] IBM SPSS version 25 was used for statistical analyses.

Ethical approval: This research was performed according to the Declaration of Helsinki and has been approved by the ethical review board of the Surinamese Committee on Research Involving Human Subjects (#VG11–18).

Figure 1. Ethnic distribution in percentages among the pregnant population



Legend

[1] Other ethnicity (n=137) includes Brazilian (n=101, 74%), Caucasian (n=25, 18%), Caribbean or regional origin (n=11, 8%); [2] Office of Statistics Suriname. The eight population and household count in Suriname, 2013.

Table 2. Maternal characteristics of all hospital births in Suriname in 2016-2017

	Total n = (%)
Total deliveries	18290
Hospitals	
I	4380 (23.9)
II	5070 (27.7)
III	5089 (27.8)
IV	3034 (16.6)
V	717 (3.9)
Age (years)	
< 20	2518 (13.8)
20 - 35	13646 (74.8)
≥ 36	2087 (11.4)
Missings n=39	
Ethnicity	
Maroon	4950 (27.6)
Creole	4217 (23.5)
Hindustani	3395 (18.9)
Mixed	2254 (12.5)
Javanese	1948 (10.9)
Indigenous	681 (3.8)
Chinese	381 (2.1)
Other[1]	137 (0.8)
Missings n=327	
Parity	
0	6243 (34.3)
1-3	9553 (52.4)
≥ 4	2428 (13.3)
Missings n=66	
Gestational age (GA)	
< 28 weeks	217 (1.2)
28 – 36 weeks	2312 (12.8)
≥ 37 weeks	15569 (86.0)
Missings n=192	
Anaemia	
Moderate	2571 (39.9)
Severe	153 (2.4)
Missings n=11.851	
Multiple pregnancy	
Twin	208 (1.1)
Triplet	3 (-)

Table 2. Continued

	Total n = (%)
Total deliveries	18290
Mode of delivery	
Spontaneous	13650 (74.6)
Instrumental	231 (1.3)
Caesarean section	4409 (24.1)
Presentation	
Cephalic	17671 (96.6)
Breech	560 (3.1)
Transverse	59 (0.3)
Post partum haemorrhage	
500 – 999 mL	1031 (6.3)
≥ 1000 mL	256 (1.6)
Missings n=1942	
Total babies born	18504
Live births	18118 (97.9)
Stillbirths, >22 weeks	386 (2.1)
Sex	
Girls	8915 (48.2)
Missings n=17	
Birth weight	
< 2500 grams	2774 (15.1)
2500 – 4000 grams	15069 (81.9)
≥ 4000 grams	558 (3.0)
Missings n=103	
Apgar-score 5 minutes	
Below 7	648 (3.9)
Missings n=1704	
Late stillbirth	
n=	285
SBR per 1000 hospital births [2]	15.6
Maternal deaths	
n=	25[3]
National MMR per 100.000 LB [4]	127
n=	20
Hospital-based MMR per 100.000 LB [4]	110

Legend [1] Ethnicity other: Brazilian (n=101, 0.5%), Caucasian (n=25, 0.1%), Caribbean (n=11); [2] SBR: stillbirth rate = per 1000 births ≥ 28 weeks or ≥ 1000 grams; [3] Two maternal death occurred at home, one during transport, two in primary health care services. Four deaths occurred antepartum, three of which in the hospitals; [4] MMR: maternal mortality rate, maternal deaths per 100.000 live births (LB)

RESULTS

There were 18.290 hospital births, 9202 in 2016 and 9088 in 2017. A total of 18.504 babies were born, 97.9% (n = 18.118) were live births. The approach to maternal and perinatal data registration by the different hospitals is shown in table 1. Supplementary file 2 illustrates maternal and neonatal characteristics and outcomes per hospital. The largest differences between the hospitals are teenage pregnancy rates (range from 7.3 to 17.9%), ethnical distribution, grand multiparous births (range from 4.6 to 18.5%), low birth weight rates (range from 11.3 to 20.8%), caesarean section rates (range from 17.4 to 36.2%) and stillbirth rates (range from 7.3 to 25.6 per 1000 births).

Table 2 presents maternal and perinatal characteristics. Median age for nulliparous women to give birth was 22 (IQR 19–27) years. Teenage pregnancies occurred in 13.8% (n = 2518) of births. The majority of women giving birth were African descendants: Maroon (27.6%) and Creole (23.5%) women (figure 1). Preterm birth occurred in 14.0% (n = 2529) and birthweight was below 2500 g in 15.1% (n = 2774). Caesarean section was performed in 24.1% of all births. In primiparous women the caesarean section rate was 27.0% (n = 1683). Repeat caesareans (n = 1321) contributed to 30% of all caesarean sections. Post partum haemorrhage of 500 mL or more occurred in 7.9% of births (n = 1287/16348). In caesarean sections the incidence of post partum haemorrhage was 17.9% (n = 501/2838, missings n = 1571) and in vaginal births 5.8% (n = 786/13510, missings n = 371). Twenty maternal deaths occurred in the hospitals, resulting in a hospital-based maternal mortality ratio (MMR) of 112 per 100.000 live births. Among all babies with a gestational age of > 22 weeks or more (or if unknown, > 500 g), 386 stillbirths (2.1%) occurred. Of these, 285 were late stillbirths (gestational age > 28 or if unknown > 1000 g), resulting in a hospital-based stillbirth rate of 15.6 per 1000 births.

Table 3 and figure 1 show ethnic disparities in maternal and perinatal characteristics.

Table 3. Ethnic disparities in maternal and perinatal characteristics and outcomes in Suriname, 2016 – 2017

	Total n = (%)	Maroon n = (%)	Creole n = (%)	Hindustani n = (%)	Mix n = (%)	Javanese n = (%)	Indigenous n = (%)	Chinese n = (%)	Other [1] n = (%)	p-value
Deliveries	18290	4950 (27.6)	4217 (23.5)	3395 (18.9)	2254 (12.5)	1948 (10.8)	681 (3.8)	381 (2.1)	137 (0.8)	
Maternal age										
< 20 years	2462 (13.7)	904 (18.3)	552 (13.1)	322 (9.5)	303 (13.5)	211 (10.9)	146 (21.4)	11 (2.9)	13 (9.5)	
20 – 35 years	13420 (74.9)	3383 (68.4)	3164 (75.1)	2774 (82.0)	1704 (75.8)	1504 (77.4)	465 (68.3)	326 (85.6)	101 (73.7)	**<0.05**
≥ 36 years	2043 (11.4)	654 (13.2)	496 (11.8)	286 (8.5)	241 (10.7)	229 (11.8)	70 (10.3)	44 (11.5)	23 (16.8)	
Parity										
0	6124 (34.2)	1253 (25.4)	1411 (33.6)	1456 (43.0)	883 (39.3)	704 (36.2)	212 (31.3)	148 (38.8)	57 (41.6)	
1-3	9387 (52.5)	2346 (47.5)	2267 (54.0)	1812 (53.6)	1204 (53.6)	1122 (57.7)	338 (49.9)	228 (59.8)	71 (51.8)	**<0.05**
≥ 4	2389 (13.3)	1338 (27.1)	519 (12.4)	115 (3.4)	159 (7.1)	117 (6.0)	127 (18.8)	5 (1.3)	9 (6.6)	
Gestational age										
< 28 weeks	210 (1.2)	72 (1.5)	64 (1.5)	35 (1.0)	21 (0.9)	10 (0.5)	7 (1.0)	1 (0.3)	-	
28 – 37 weeks	2266 (12.7)	711 (14.6)	561 (13.4)	405 (12.0)	274 (12.3)	192 (9.9)	82 (12.2)	29 (7.7)	13 (9.7)	**<0.05**
Term	15299 (86.1)	4104 (84.0)	3548 (85.1)	2933 (87.0)	1933 (86.8)	1728 (89.5)	583 (86.8)	349 (92.1)	121 (90.3)	
Anaemia antepartum										
Moderate	2258 (36.4)	808 (51.8)	667 (43.8)	372 (33.5)	146 (20.9)	147 (19.0)	71 (37.6)	36 (13.9)	11 (11.7)	**<0.05**
Severe	145 (2.3)	76 (4.9)	38 (2.5)	15 (1.4)	10 (1.4)	2 (0.3)	4 (2.1)	-	-	
Mode of delivery										
Spontaneous	13428 (74.8)	4074 (82.3)	3174 (75.3)	2223 (65.5)	1575 (69.9)	1482 (76.1)	531 (78.0)	301 (79.0)	69 (50.4)	**<0.05**
Vacuum	225 (1.3)	31 (0.6)	28 (0.7)	84 (2.5)	34 (1.5)	31 (1.6)	12 (1.8)	4 (1.0)	1 (0.7)	
Caesarean	4309 (24.0)	845 (17.1)	1015 (24.1)	1088 (32.1)	645 (28.7)	435 (22.3)	138 (20.3)	76 (19.9)	67 (48.9)	
Presentation										
Cephalic	17359 (96.7)	4787 (96.7)	4093 (97.1)	3252 (95.8)	2193 (97.3)	1873 (96.1)	661 (97.1)	367 (96.3)	134 (97.8)	**0.03**
Haemorrhage										
500 – 999 mL	1012 (6.3)	288 (6.3)	239 (6.3)	140 (4.8)	144 (7.3)	121 (6.9)	50 (8.1)	21 (6.2)	9 (9.0)	**<0.05**
≥ 1000 mL	251 (1.6)	79 (1.7)	58 (1.5)	32 (1.1)	29 (1.5)	22 (1.3)	21 (3.4)	8 (2.4)	2 (2.0)	

Table 3. Continued

	Total n = (%)	Maroon n = (%)	Creole n = (%)	Hindustani n = (%)	Mix n = (%)	Javanese n = (%)	Indigenous n = (%)	Chinese n = (%)	Other [1] n = (%)	p-value
Total babies born	18504	5035 (27.7)	4268 (23.5)	3422 (18.8)	2277 (12.5)	1965 (10.8)	687 (3.8)	382 (2.1)	139 (0.8)	
Live Births	17789 (97.9)[2]	4877 (96.9)	4157 (97.4)	3370 (98.5)	2240 (98.4)	1951 (99.3)	674 (98.1)	381 (99.7)	139 (98.6)	**<0.05**
Stillbirths (≥22w)	386 (2.1)	158 (3.1)	111 (2.6)	52 (1.5)	37 (1.6)	14 (0.7)	13 (1.9)	1 (0.3)	0 (0)	
Sex										
Girl	8767 (48.3)	2485 (49.4)	2083 (48.9)	1637 (47.9)	1064 (46.8)	926 (47.1)	321 (46.9)	181 (47.4)	70 (50.4)	0.39
Birth weight										
< 2500 g	2730 (15.1)	847 (16.9)	662 (15.6)	614 (18.0)	294 (13.0)	183 (9.4)	87 (12.6)	32 (8.4)	11 (8.0)	
2500 – 4000 g	14805 (81.9)	4047 (80.8)	3449 (81.4)	2710 (79.6)	1887 (83.2)	1690 (86.4)	568 (83.4)	334 (87.9)	120 (86.1)	**<0.05**
≥ 4000 g	542 (3.0)	115 (2.3)	127 (3.0)	81 (2.4)	88 (3.9)	83 (4.2)	26 (3.8)	14 (3.7)	8 (5.8)	
APGAR 5 minutes										
< 7	639 (3.8)	243 (5.3)	187 (4.8)	95 (3.0)	58 (2.8)	31 (1.7)	21 (3.5)	4 (1.1)	-	**<0.05**
Late stillbirth										
n=	285	122	77	40	23	11	9	1	2	**<0.05**
SBR/1000 deliveries [3]	15.6	25.0	18.6	11.9	10.3	5.7	13.4	-	14.6	
Maternal deaths (MDs)										
National MDs, n=	25	13	4	3	1	1	2	1	-	
National-MMR[4]	127	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
Hospital MDs, n=	20	9	4	3	1	1	1	1	-	0.59
Hospital-MMR[4]	112	184	96	89	45	51	147	262	-	

Legend

[1] Ethnicity other: Brazilian (n=101, 73.7%), Caucasian (n=25, 18.2%), Afro-Caribbean (n=11). Missing ethnicities, n=327 (1.8%); [2] Missing ethnicities n=328 with no significant differences within the variables; [3] SBR: stillbirth rate = per 1000 deliveries ≥ 28 weeks or ≥ 1000 grams; [4] MMR: maternal mortality rate, maternal deaths per 100.000 live births (LB), of 20 hospital maternal deaths two occurred antepartum

Table 4. Childbirth outcomes in different ethnicities, with Hindustani as reference

Outcome	cOR (95% CI)	aOR (95% CI))
Teenage pregnancy		
Maroon	**2.1 (1.9 - 2.5)**	**2.1 (1.8 - 2.4)[1]**
Creole	**1.4 (1.2 - 1.7)**	**1.4 (1.2 - 1.6)[1]**
Mixed	**1.5 (1.3 - 1.8)**	**1.5 (1.3 - 1.8)[1]**
Javanese	1.2 (1.0 - 1.4)	1.2 (1.0 - 1.4)[1]
Indigenous	**2.7 (2.1 - 3.3)**	**2.6 (2.1 - 3.2)[1]**
Chinese	**0.3 (0.2 - 0.5)**	**0.3 (0.2 - 0.6)[1]**
Other	1.0 (0.6 - 1.8)	1.1 (0.6 - 1.9)[1]
Primiparous women		
Maroon	**0.5 (0.4 - 0.5)**	**0.5 (0.4 - 0.5)[1]**
Creole	**0.7 (0.6 - 0.7)**	**0.7 (0.6 - 0.8)[1]**
Mixed	**0.9 (0.8 - 1.0)**	**0.8 (0.8 - 0.9)[1]**
Javanese	**0.8 (0.7 - 0.8)**	**0.7 (0.7 - 0.8)[1]**
Indigenous	**0.6 (0.5 - 0.7)**	**0.6 (0.5 - 0.7)[1]**
Chinese	0.8 (0.7 - 1.1)	0.8 (0.6 - 1.0)[1]
Other	1.0 (0.7 - 1.3)	1.0 (0.6 - 1.3)[1]
Grand multiparous women		
Maroon	**10.6 (8.7 - 12.8)**	**14.7 (11.9 - 18.1)[1]**
Creole	**4.0 (3.3 - 4.9)**	**4.1 (3.3 - 5.1)[1]**
Mixed	**2.2 (1.7 - 2.8)**	**2.2 (1.7 - 2.9)[1]**
Javanese	**1.8 (1.4 - 2.4)**	**1.7 (1.3 - 2.3)[1]**
Indigenous	**6.6 (5.0 - 8.6)**	**9.9 (7.4 - 13.4)[1]**
Chinese	**0.4 (0.2 - 0.9)**	**0.3 (0.1 - 0.8)[1]**
Other	2.0 (1.0 - 4.0)	1.6 (0.7 - 3.4)[1]
Severe anaemia		
Maroon	**3.7 (2.1 - 6.5)**	**2.4 (1.4 - 4.3)[1]**
Creole	**1.9 (1.0 - 3.4)**	1.7 (0.9 - 3.0)[1]
Mixed	1.1 (0.5 - 2.4)	1.8 (0.8 - 4.2)[1]
Javanese	**0.2 (0.1 - 0.8)**	0.3 (0.1 - 1.3)[1]
Indigenous	1.6 (0.5 - 4.8)	1.1 (0.4 - 3.5)[1]
Caesarean section		
Maroon	**0.4 (0.4 - 0.5)**	**0.7 (0.6 - 0.8)[2]**
Creole	**0.7 (0.6 - 0.7)**	**0.8 (0.7 - 0.9)[2]**
Mixed	0.9 (0.7 - 1.0)	**0.9 (0.8 - 1.0)[2]**
Javanese	**0.6 (0.5 - 0.7)**	**0.6 (0.5 - 0.7)[2]**
Indigenous	**0.5 (0.4 - 0.7)**	**0.8 (0.6 - 0.9)[2]**
Chinese	**0.5 (0.4 - 0.7)**	**0.4 (0.3 - 0.5)[2]**
Other	**2.0 (1.4 - 2.7)**	**1.7 (1.2 - 2.4)[2]**
Post partum haemorrhage		
Maroon	**1.6 (1.1 - 2.4)**	**1.5 (1.0 - 2.4)[3]**
Creole	1.4 (0.9 - 2.2)	**1.4 (0.9 - 2.2)[3]**
Mixed	1.4 (0.8 - 2.3)	1.2 (0.7 - 1.9)[3]
Javanese	1.2 (0.7 - 2.0)	1.1 (0.7 - 2.0)[3]
Indigenous	**3.2 (1.8 - 5.5)**	**3.0 (1.7 - 5.3)[3]**
Chinese	**2.2 (1.0 - 4.8)**	2.1 (0.9 - 4.6)[3]
Other	1.9 (0.4 - 7.8)	1.4 (0.3 - 6.0)[3]

Table 4. Continued

Outcome	cOR (95% CI)	aOR (95% CI))
Preterm birth		
Maroon	**1.3 (1.1 - 1.4)**	**1.2 (1.1 - 1.4)[1]**
Creole	**1.2 (1.0 - 1.3)**	1.1 (1.0 - 1.3)[1]
Mixed	1.0 (0.8 - 1.3)	1.0 (0.9 - 1.2)[1]
Javanese	**0.8 (0.7 - 0.9)**	**0.8 (0.7 - 0.9)[1]**
Indigenous	1.0 (0.8 - 1.3)	1.0 (0.8 - 1.3)[1]
Chinese	**0.6 (0.4 - 0.8)**	**0.6 (0.4 - 0.9)[1]**
Other	0.8 (0.5 - 1.4)	0.8 (0.4 - 1.4)[1]
Low birth weight		
Maroon	0.9 (0.8 - 1.0)	**0.7 (0.6 - 0.8)[2]**
Creole	**0.8 (0.7 - 0.9)**	**0.6 (0.5 - 0.7)[2]**
Mixed	**0.7 (0.6 - 0.8)**	**0.6 (0.5 - 0.7)[2]**
Javanese	**0.5 (0.4 - 0.5)**	**0.4 (0.3 - 0.5)[2]**
Indigenous	**0.7 (0.5 - 0.8)**	**0.5 (0.4 - 0.7)[2]**
Chinese	**0.4 (0.3 - 0.6)**	**0.5 (0.3 - 0.8)[2]**
Other	**0.4 (0.2 - 0.8)**	0.6 (0.3 - 1.1)[2]
Low APGAR score		
Maroon	**1.8 (1.4 - 2.3)**	**1.6 (1.2 - 2.0)[2]**
Creole	**1.6 (1.3 - 2.1)**	**1.4 (1.0 - 2.0)[2]**
Mixed	0.9 (0.7 - 1.3)	1.0 (0.7 - 1.6)[2]
Javanese	**0.6 (0.4 - 0.9)**	0.7 (0.4 - 1.2)[2]
Indigenous	1.2 (0.7 - 1.9)	1.1 (0.6 - 2.0)[2]
Chinese	0.4 (0.1 - 1.0)	0.5 (0.1 - 1.7)[2]
Late stillbirth		
Maroon	**2.1 (1.5 - 3.0)**	**1.7 (1.1 - 2.5)[3]**
Creole	**1.5 (1.1 - 2.3)**	1.4 (0.9 - 2.1)[3]
Mixed	0.9 (0.6 - 1.6)	1.0 (0.6 - 1.8)[3]
Javanese	**0.5 (0.2 - 0.9)**	**0.4 (0.2 - 0.9)[3]**
Indigenous	1.1 (0.5 - 2.3)	1.1 (0.5 - 2.5)[3]
Chinese	0.2 (0.0 - 1.6)	0.3 (0.0 - 2.4)[3]
Maternal death		
Maroon	3.4 (0.8 - 15.7)	3.3 (0.7 - 16.1)[4]
Creole	1.2 (0.2 - 7.2)	1.2 (0.2 - 7.1)[4]
Mixed	N/A	N/A
Javanese	1.7 (0.2 - 12.4)	1.8 (0.2 - 12.5)[4]
Indigenous	2.5 (0.2 - 27.5)	2.5 (0.2 - 28.5)[4]
Chinese	4.5 (0.4 - 49.4)	4.7 (0.4 - 53.4)[4]

Legend: Bold = significant results. Adjusted for [1]maternal age and hospital; [2] maternal age, parity, hospital, birth weight, gestational age; [3]maternal age, parity, hospital, caesarean section, birth weight, gestational age; [4] maternal age, parity and hospital; Due to low numbers severe anaemia not available for Chinese/Other, low Apgar score and late stillbirth not available for Other and maternal death not available for Mixed and Other.

Table 4 presents associations between ethnic group and outcomes, adjusted for confounders and with Hindustani women as reference group. Teenage pregnancy was twice higher among Maroon women (18.3%, n = 904) compared to Hindustani women (9.5%, n = 322), (aOR = 2.1, 95%CI 1.8–2.4). Compared to Hindustani women, Maroon women had a higher risk for severe anaemia (4.9%, aOR = 2.4, 95%CI 1.4–4.3). Maroon and Indigenous women were most often grand multiparous women (27.1%, aOR = 14.4 (95%CI 11.9–18.1) and 19%, aOR = 9.9 (95%CI 7.4–13.4)) compared to Hindustani (3.4%). Women of other ethnicities had a significantly lower risk of giving birth to low birth weight infants compared to Hindustani women (aOR range of 0.4–0.7). The caesarean section rate was lower in Maroon women (17.1%) compared to Hindustani women (32.1%) (aOR = 0.7 (95%CI 0.6–0.8)). Post-partum haemorrhage occurred most frequently in Indigenous women (8.1%, aOR = 3.0, 95%CI 1.7–5.3). MMR was highest in Maroon women with 184 (n = 9/4877) per 100.000 live births. In Hindustani, Javanese and mixed women MMRs were 89 (n = 3/3370), 51 (n = 1/1951) and 45 (n = 1/2240). Stillbirth rates were significantly higher for African-descendent Maroon women (25.0 per 1000 births, aOR = 1.7, 95%CI 1.1–2.5) and significantly lower for Javanese women (5.7 per 1000 births, aOR = 0.4 95%CI 0.2–0.9) compared to Hindustani women (11.9 per 1000 births).

DISCUSSION

This study provides a national overview of maternal and perinatal health in multi-ethnic, middle-income country Suriname, where no formal national perinatal registry is in place yet. Disaggregation of the perinatal data showed substantial inequities in maternal and perinatal health for specific ethnic groups.

Although Suriname is classified as an upper middle-income country, it is among countries in the Latin America and the Caribbean region with the highest maternal mortality ratio and stillbirth rate. The maternal mortality ratio of 127 maternal deaths per 100.000 live births is comparable to previous studies conducted in Suriname the past years.[22,32] Suboptimal quality of care plays an important role in the high maternal mortality ratio in Suriname and led to different quality improvement projects such as maternal death and morbidity audits, obstetric

guidelines and obstetric skills team training.[22,32,33] The stillbirth rate, 15.6 stillbirths per 1000 births, is second highest of the region, preceded only by Haiti (SBR 24.9), and followed by Paraguay (13.4) and Bolivia (12.9).[34] Timing and underlying causes of stillbirths are unknown and audit and in-depth case review is necessary to understand why these babies die.

Inequity in maternal and perinatal health within countries are as great as or greater than those between countries.[34,35] In the SDGs, equity in health, i.e. available and affordable high-quality health services to all, is emphasised as a priority, and this was further stressed in the 2019 Report of the Commission of the Pan American Health Organization (PAHO) on Equity and Health Inequalities in the Americas.[45] Disaggregating perinatal health data can identify and target inequity within the health system. Ethnicity or race is a non-modifiable risk factor to adverse maternal and perinatal outcomes, and an important social determinant of health.[4,35] The causal pathway of ethnical disparities is influenced partly by biological factors, such as genetic predisposition, but mostly by environmental and socio-economic mediators, such as wealth, culture, nutrition and socio-economic situation – often a reflection of underlying structural and historical drivers.[34] While place of residence (urban vs. rural) is an important proxy of environmental and socio-economic factors as well as access to health care, place of residence has a smaller role in Suriname, where most pregnant women (temporarily) reside in urban areas and give birth in hospitals.[20]

Biological factors of ethnical disparities seem to contribute quite strongly to infants born small for gestational age. In our study in Suriname, Hindustani women generally have more favorable socio-economic status than women of other ethnical backgrounds, yet their babies are significantly smaller.[17] An explanation for this finding is lacking, as Hindustani women are not prone to severe anaemia, as seen in this study, and are generally known to have a high dietary diversity.[36] A WHO study confirms that significant differences in foetal weight are seen between 10 ten countries, with the lowest median birth weight among Indian women, also after adjustment for maternal characteristics, gestational age and foetal sex.[37]In

contrast, INTERGROWTH-21 found that when mothers' nutritional and health needs are met and there are few environmental constraints on growth, only 3.5% of the total variability of growth was due to differences between populations.[38] It is therefore controversial to locally adjust growth charts to increase predictive performance, as they can potentially deprive smaller babies of their needs for intensified health care given that most have impaired foetal growth due to malnutrition or other environmental factors.

Giving birth during adolescence is not only a risk for adverse outcomes, but also has a negative impact on the future well-being of the mother and infant, leading to stigmatism and socio-economic consequences with school drop-out, lower employment opportunities, and a higher risk of poverty and intergenerational transmission of inequities.[4,39] High numbers of pregnancies among teenagers were seen in Maroon (18.3%) and Indigenous women (21.4%). This results in a threefold higher adolescent birth rate for Maroons and Indigenous girls (79 and 88 per 1000 girls 15–19 years) compared to Hindustani girls (27 per 1000 girls 15–19 years). In a recently conducted nationwide survey, the adolescent birth rates for Maroon and Indigenous girls are reported even higher (124 and 99 per 1000 girls 15–19 years).[20] While the national teenage pregnancy rate (13.8%) in Suriname is somewhat lower than in many Latin American countries (16–22%), ethnic disparities within the country are significant.[40,41] Tailored health care services for teenagers should be made available, including prevention of teenage pregnancy with free contraception, especially geared towards the groups most at risk.[24,42]
Ethnic disparities for caesarean section rates have been observed in many low- and middle income countries.[43] This is similar to findings in Suriname, where Maroon women have the lowest caesarean section rate despite increased risks of adverse pregnancy outcomes. Hospital differences in caesarean section rates may partially reflect ethnic distributions between the hospitals.

Multiple studies in high-income countries with Caucasian majorities such as the United Kingdom, the United States, the Netherlands and different Latin American

countries, demonstrated an increased risk of maternal deaths, maternal morbidity and stillbirths in ethnic minority women, such as women from African, Asian or Indigenous descent, compared to Caucasian women.[12-15,44,45] African-descendant Maroon women in Suriname are at two- to four-fold higher risk of stillbirth (25 stillbirths per 1000 births) compared to Asian-descendant women (12 and 6 stillbirths per 1000 births in Hindustani and Javanese women). Despite low numbers of maternal death, similar trends are found with MMRs of 184 in Maroon women compared to 89 per 100.000 live births in Hindustani women, though not statistically significant due to absolute low numbers of deaths.

Women from ethnic minorities, women of low socio-economic status, adolescents, migrant women and women living with HIV are particularly likely to not only have increased adverse pregnancy outcomes, but also more likely to experience disrespectful or even neglect during pregnancy and childbirth.[46] Respecful maternity care, i.e. effective communication and equal engagement of health care workers to all women, is essential in reducing disparities in pregnancy care and outcomes.[47] Dialogue, research into disparities of health care and health outcomes and advocacy of safe motherhood is an important public health and human rights issue.

Limitations: A number of limitations need to be considered. First, this study only covers hospital births. Although these comprise majority of all live births in the country, women who delivered in the more deprived interior settings (mostly maroons and indigenous women), may be underrepresented. As a result, the national teenage pregnancy rate or stillbirth rate could be higher than reported in this study. Second, important explanatory or risk factors such as body mass index, smoking, level of education, level of income, residency, number of antenatal care visits and medical and obstetric history were not available. Other important indicators for quality of care, such as early neonatal mortality, timing of stillbirths and indications of caesarean sections for classification according to Robson criteria were not provided by the childbirth books.[48,49] It is recommended that these factors are included in perinatal registries in the future.

Recommendations: While achievement of health equity requires overarching structural changes that promote social, economic and political equality, there are specific strategies policymakers could prioritise to achieve equity in reproductive, maternal and perinatal health.[34] In connection to our discussion, recommendations can be made in the following direction:

(1) develop a nationwide perinatal registry that includes primary health care centres and allows for disaggregated analysis by groups at risk of inequities in health outcomes;
(2) ensure that quality obstetric care along the continuum from preconception and antenatal to postpartum, including safe abortion services, is accessible to all equitably;
(3) monitor the quality of care, including auditing of maternal and perinatal mortality, stillbirths, severe maternal morbidity and caesarean sections;
(4) provide free contraception and adolescent programs for sexual and reproductive health;
(5) strenghten community based outreach and improve health literacy of women; and
(6) address the structural drivers and conditions of daily life which determine equity and a dignified life.

CONCLUSION

This first nationwide comprehensive overview of maternal and perinatal health status in Suriname, a middle-income country in South America shows substantial inequities in maternal and perinatal health by ethnicity. African-descendent Maroon women experienced the highest risk of adverse outcomes (maternal mortality, stillbirth, increased preterm birth, low apgar score). Hindustani women have lower risk on adverse outcomes, yet give birth to smaller babies and give birth by caesarean section most frequently. Disaggregating perinatal health data can identify and help target inequity within the health system.

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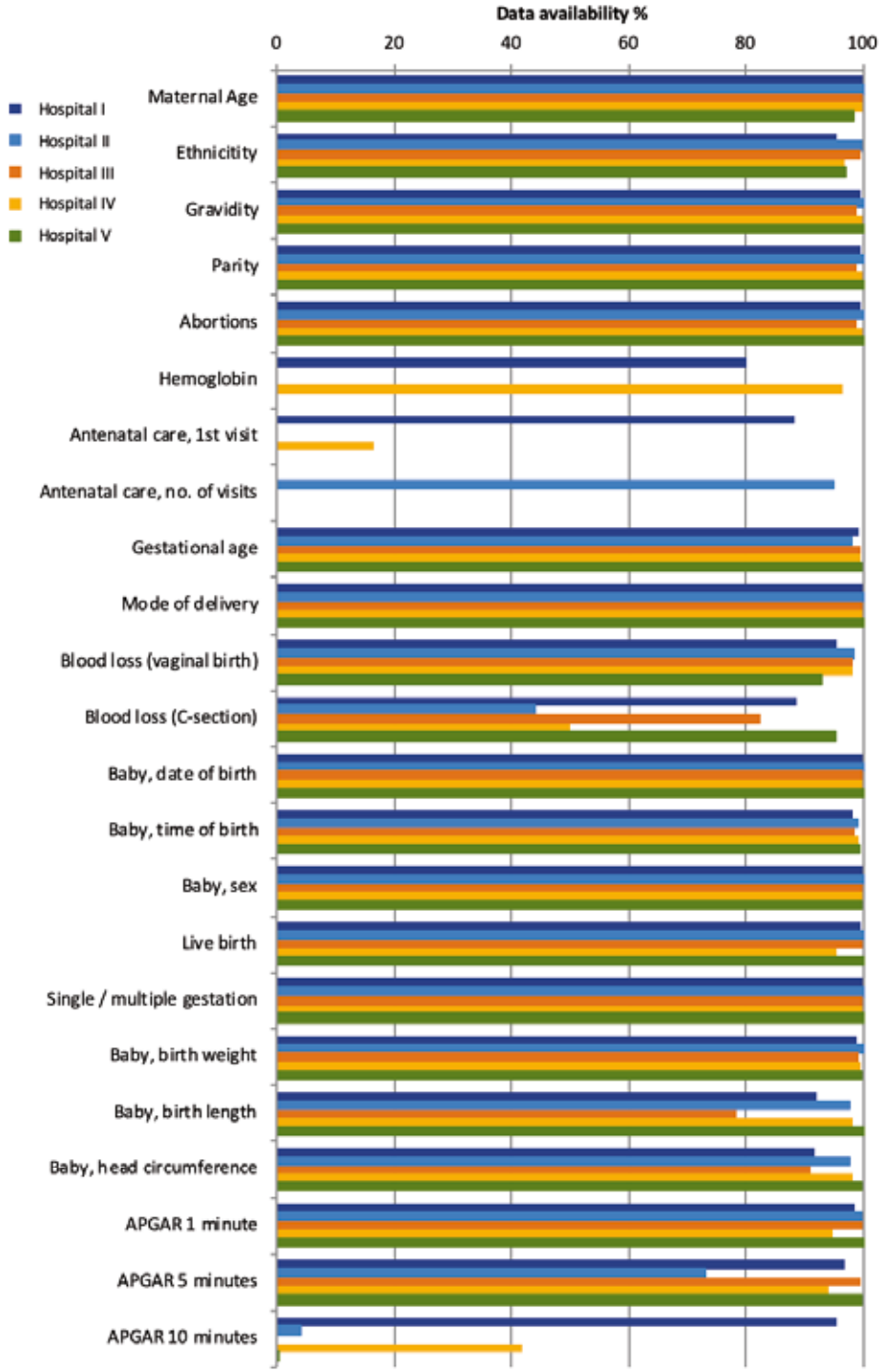
Supplementary file 1. Visual summary of data availability per hospital (I-V)



Supplementary file 2. Inter-hospital differences in characteristics and outcomes

	Hospital					p value
	I n = (%)	II n = (%)	III n = (%)	IV n = (%)	V n = (%)	
Deliveries	4380 (23.9)	5070 (27.7)	5089 (27.8)	3034 (16.6)	717 (3.9)	<0.05
2016	*2272 (24.7)*	*2418 (26.3)*	*2633 (28.6)*	*1531 (16.6)*	*348 (3.8)*	
2017	*2108 (23.2)*	*2652 (29.2)*	*2456 (27.0)*	*1503 (16.5)*	*369 (4.1)*	
Teenage pregnancy						
< 20 years	782 (17.9)	567 (11.2)	835 (16.4)	222 (7.3)	112 (15.9)	<0.05
20 – 35 years	3165 (72.6)	3762 (74.2)	3728 (73.3)	2446 (80.7)	545 (77.4)	
≥ 36 years	414 (9.5)	741 (14.6)	522 (10.3)	363 (12.0)	47 (6.7)	
Ethnicity						
Maroon	1758 (41.9)	1254 (24.8)	1746 (34.4)	189 (6.5)	3 (0.4)	< 0.05
Creole	1138 (27.1)	1342 (26.6)	1078 (21.2)	614 (20.9)	45 (6.5)	
Hindustani	700 (16.7)	940 (18.5)	808 (15.9)	554 (18.3)	393 (54.8)	
Mixed	168 (4.0)	654 (12.9)	735 (14.5)	579 (19.7)	117 (16.8)	
Javanese	251 (6.0)	605 (12.0)	422 (8.3)	594 (20.2)	76 (10.9)	
Inheems	166 (4.0)	170 (3.4)	247 (4.9)	54 (1.8)	45 (6.5)	
Chinees	14 (0.3)	62 (1.2)	29 (0.6)	260 (8.8)	16 (2.3)	
Other	1 (0.0)	25 (0.5)	14 (0.3)	96 (3.3)	1 (0.1)	
Parity						
0	1226 (28.1)	1942 (38.7)	1502 (29.5)	1295 (42.7)	278 (38.8)	<0.05
1 - 3	2333 (53.4)	2470 (49.2)	2770 (54.5)	1598 (52.7)	382 (53.4)	
≥ 4	810 (18.5)	609 (12.1)	815 (16.0)	138 (4.6)	56 (7.8)	
Mode of delivery						
Spontaneous	3595 (82.1)	3835 (75.6)	3733 (73.4)	1933 (63.7)	554 (77.3)	<0.05
Vacuum	12 (0.3)	135 (2.7)	44 (0.9)	2 (0.1)	38 (5.3)	
Caesarean	773 (17.6)	1100 (21.7)	1312 (25.8)	1099 (36.2)	125 (17.4)	
PPH						
500 - 999 mL	204 (4.9)	253 (5.3)	412 (9.6)	108 (4.4)	54 (8.1)	<0.05
≥ 1000 mL	59 (1.4)	67 (1.4)	90 (2.1)	24 (1.0)	16 (2.4)	
Gestational age						
< 28 weeks	113 (2.6)	44 (0.9)	39 (0.8)	15 (0.5)	6 (0.8)	<0.05
32 – 36 weeks	669 (15.4)	515 (10.2)	729 (14.6)	327 (10.8)	72 (10.1)	
≥ 37 weeks	3558 (82.0)	4484 (88.9)	4218 (84.6)	2673 (88.7)	636 (89.1)	
Total babies born	4444	5138	5147	3058	717	
Live Births	4281 (96.3)	5048 (98.2)	5052 (98.2)	3031 (99.1)	705 (98.3)	<0.05
Stillbirths ≥22 weeks or 1000 g	163 (3.7)	90 (1.8)	94 (1.8)	27 (0.9)	12 (1.7)	
Birth weight						
< 2500 grams	917 (20.8)	625 (12.3)	789 (15.3)	344 (11.3)	99 (13.8)	<0.05
2500 – 4000 grams	3373 (76.7)	4296 (84.3)	4234 (82.3)	2580 (84.7)	586 (82.0)	
≥ 4000 grams	109 (2.5)	176 (3.5)	120 (2.3)	123 (4.0)	30 (4.2)	
APGAR score 5 min						
Below 7	273 (6.3)	164 (3.2)	133 (3.5)	48 (1.7)	30 (4.2)	<0.05
Stillbirths ≥ 28 weeks						
n=	109	69	74	22	11	
SBR per 1000 births [1]	25.6	13.7	14.7	7.3	15.5	<0.05
Maternal deaths						
n=	8	3	4	5	-	
MMR per 100.000 live births [2,3]	186.9	59.4	79.1	165.0	-	<0.05

[1] SBR: stillbirth rate = per 1000 births ≥ 28 weeks or ≥ 1000 grams; [2] MMR: maternal mortality rate, maternal deaths per 100.000 live births (LB), hospital is location of death, n=5 occurred at home or in primary health care services; [3] Maternal deaths: one deaths in hospital I was a delivery from hospital II and one was a home delivery, one death in hospital II died during transport to the hospital, one death in hospital IV was a woman who gave childbirth in hospital I.

Part II

Global classification systems

Women are not dying because of disease we cannot treat; they are dying because societies have yet to make the decision that their lives are worth saving

~ Prof M Fathalla, Egypt

4

Classifying maternal deaths in Suriname using WHO ICD-MM; different interpretation by physicians, national and international maternal death review committees

Lachmi R. Kodan
Kim J. C. Verschueren
Affette M. McCaw-Binns
Ray Tjon Kon Fat
Joyce L. Browne
Marcus J. Rijken
Kitty W. M. Bloemenkamp

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Abstract

Background: Insight into the underlying causes of pregnancy-related deaths is essential to develop policies to avert preventable deaths. The WHO International Classification of Diseases-Maternal Mortality (ICD-MM) guidelines provide a framework to standardize maternal death classifications and enable comparison in and among countries over time. However, despite the implementation of these guidelines, differences in classification remain. We evaluated consensus on maternal death classification using the ICD-MM guidelines.

Methods: The classification of pregnancy-related deaths in Suriname during 2010-2014 was compared in the country (between the attending physician and the national maternal death review (MDR) committee), and among the MDR committees from Suriname, Jamaica and the Netherlands. All reviewers applied the ICD-MM guidelines. The inter-rater reliability (Fleiss kappa [κ]) was used to measure agreement.

Results: Out of the 89 cases certified by attending physicians, 47% (n=42) were classified differently by the Surinamese MDR committee. The three MDR committees agreed that 18% (n=16/89) of these cases were no maternal deaths, and, therefore, excluded from further analyses. However, opinions differed whether 15% (n=11) of the remaining 73 cases were maternal deaths. The MDR committees achieved moderate agreement classifying the deaths into type (direct, indirect and unspecified) (κ=0.53) and underlying cause group (κ=0.52). The Netherlands MDR committee classified more maternal deaths as unspecified (19%), than the Jamaican (7%) and Surinamese (4%) committees did. The mutual agreement between the Surinamese and Jamaican MDR committees (κ=0.69 vs κ=0.63) was better than between the Surinamese and the Netherlands MDR committees (κ=0.48 vs κ=0.49) for classification into type and underlying cause group, respectively. Agreement on the underlying cause category was excellent for abortive outcomes (κ=0.85) and obstetric haemorrhage (κ=0.74) and fair for unspecified (κ=0.29) and other direct causes (κ=0.32).

Conclusions: Maternal death classification differs in Suriname and among MDR committees from different countries, despite using the ICD-MM guidelines on similar cases. Specific challenges in applying these guidelines included attribution of underlying cause when comorbidities occurred, the inclusion of deaths from suicides, and maternal deaths that occurred outside the country of residence.

BACKGROUND

The maternal mortality ratio (MMR) is a robust indicator of health care quality, inequality and inequity in and among countries.[1] Most maternal deaths are preventable in low, middle and high resource settings, as was the case for 47% of maternal deaths in Suriname between 2010 and 2014.[2,3] To develop prevention strategies, accurate data on the number of maternal deaths and insight into underlying causes are essential.[2,4,5] However, the assignment of a reliable underlying cause of death and the subsequent classification can be a challenge.[6]

The World Health Organization (WHO) aimed to create uniform maternal death classification guidelines to enhance usability, improve comparability and decrease coding errors.[7-9] Therefore, the WHO launched the International Classification of Diseases-Maternal Mortality (ICD-MM) in 2012, an application of International Classification of Diseases-10th edition (ICD-10) to classify deaths during pregnancy, childbirth and the puerperium.[7]

Difficulties in attributing the underlying causes can result in inconsistencies in classification in and among countries, despite using the ICD-MM guidelines.[8,10] When a European expert panel reviewed pregnancy-related deaths across 13 European countries, they identified 14% more maternal deaths than what the national registries of the individual countries included.[11] Classification is especially complicated when comorbidities occur, and the start of the chain of events resulting in maternal death has to be determined.[10] Consequently, underlying cause attribution may vary, or the causes are unknown or unclear, resulting in underreporting. This is not only an issue in low- and middle-income countries but also in high-income countries and was reported by various Maternal Death Review

(MDR) committees, including those from Suriname, Jamaica and the Netherlands.[3,12,13]

Therefore, this study aimed to assess the applicability of the ICD-MM guidelines by investigating the classification of maternal deaths in one country and across three countries. First, the cause of death as determined by the attending physician was compared to the assessment of the Surinamese MDR committee. Second, cases were shared with the national MDR committees from Jamaica and the Netherlands, and their assessments were compared to the findings of the Surinamese MDR committee. Following these findings, the classification difficulties are discussed, and recommendations for improving the ICD-MM guidelines' applicability and international comparability of maternal mortality are provided.

METHODS

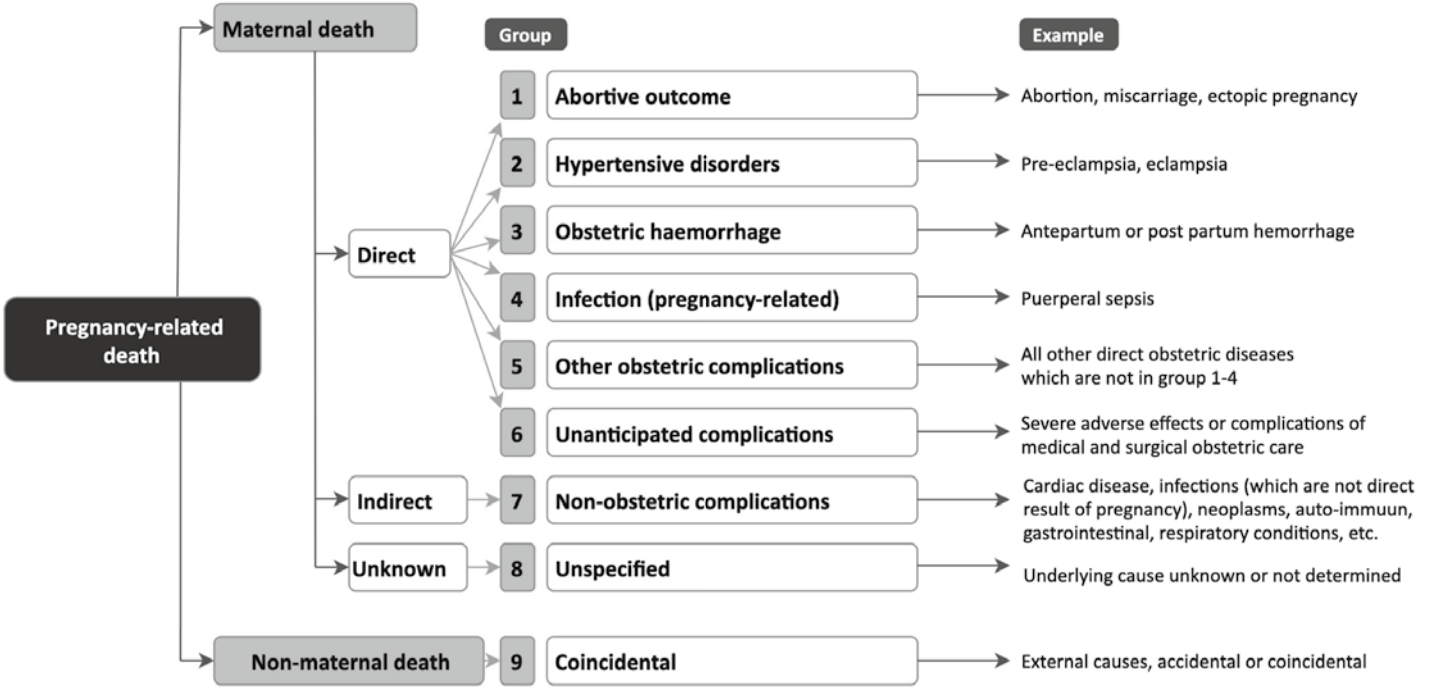
Study design: A population-based reproductive age mortality survey (RAMoS) was conducted in 2015 to identify pregnancy-related deaths in Suriname between 2010 and 2014.[3] A total of 89 possible maternal deaths were identified and reviewed by the national MDR committee of Suriname, Jamaica (both middle-income countries) and the Netherlands (high-income country).

Settings: Suriname is an upper middle-income South American country on the Caribbean coast with 570,496 inhabitants in 2017.[14,15] Out of the approximately 10,000 births annually, 86% occur in five hospitals, 6% in primary care centres and the remaining 8% deliver at home or is not registered.[16] When death occurs, the attending physician in Suriname has an obligation to complete a death certificate documenting the causes and circumstances of the death. The Bureau of Public Health codes the cause of death using ICD-10.[3,17] A national MDR committee was established to audit and classify the pregnancy-related cases. The committee consisted of specialists in obstetrics, internal medicine, midwifery and, on request, other specialists such as cardiologists, intensive care specialists and neurologists were invited. Classification was consensus-based, and according to the WHO ICD-MM guidelines.[3]

Jamaica, a Caribbean island nation with 2.9 million inhabitants, is an upper middle-income country.[18] Their MDR committee was established in 1998, and classified maternal deaths according to the ICD-MM.[12] Three members from this multidisciplinary committee (midwives, obstetricians, epidemiologists, public health practitioners, and pathologists), volunteered to review the Surinamese cases: a reproductive health epidemiologist and two obstetricians.
The Netherlands is a high-income country with 17.3 million inhabitants.[19] The MDR committee of the Dutch Society of Obstetricians and Gynaecology, was established in 1981 and currently uses the ICD-MM guidelines for maternal death classification.[13] Seven committee members classified the pregnancy-related deaths of this study independently. In case of uncertainty or unclarity, cases were discussed with other members to achieve consensus on the final classification.

Definitions: Pregnancy-related deaths occur during pregnancy, delivery and puerperium. Maternal deaths are defined as those occurring during pregnancy or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, where the cause of death is related to or aggravated by pregnancy or its management, not from coincidental or accidental causes.[7] Direct deaths are due to obstetric complications, while indirect deaths result from non-obstetric pre-existing diseases, or diseases developing during pregnancy, that is aggravated by the physiologic effects of pregnancy. If the underlying cause is unknown or undetermined, the death is classified as unspecified. Coincidental deaths are deaths that occur during pregnancy, childbirth and puerperium due to external causes that are not related to the pregnancy. Each pregnancy-related death can be assigned to one of nine groups: group 1-6 (direct deaths), group 7 (indirect deaths), group 8 (unspecified deaths), or group 9 (coincidental deaths) (figure 1).[7] The underlying cause of death is the disease or condition that initiated the chain of events leading to death.[6,7]

Figure 1. Groups of underlying causes of death during pregnancy, childbirth and the puerperium in mutually exclusive, totally inclusive groups[7]



Data collection and analysis: Pregnancy-related deaths (n=89) occurring in Suriname between 2010 and 2014 were identified by a Reproductive Age Mortality Survey (RAMoS).[3] Medical files were summarized, and the underlying causes of death, as attributed by the attending physicians, were extracted from the available death certificate. All possible pregnancy-related deaths were audited by the Surinamese MDR committee and classified according to the ICD-MM.[3] In Suriname, we compared the underlying cause attributed by the attending physicians (documented on the death certificate or in the medical record) to the findings of the national MDR committee.

The Jamaican and Dutch MDR committees reviewed and classified the same 89 pregnancy-related deaths into maternal death or not, type of maternal death and one of the nine ICD-MM groups. Cases classified as not maternal by all three review teams were excluded from further analysis. The classification in type of death (direct, indirect and unspecified) and the WHO group of underlying cause were compared, using correlation analysis to assess agreement among the three review teams (IBM SPSS version 24.0; Armonk, New York, USA). The inter-rater reliability (IRR) was calculated by Fleiss kappa (for three raters). The kappa (κ) value range from -1 to $+1$, where 0 represents no agreement and one perfect agreement. Negative values indicate that the observed agreement is less than that expected from chance alone.[20] A κ below 0.2 indicates poor agreement and above 0.8 very good agreement. The overall value of kappa is the weighted average of the individual kappa value per category. A p-value < 0.05 only indicates that agreement between raters is significantly better than expected by chance.[20,21] Discrepant cases were described to highlight sources of disagreement and facilitate further refinement of regional and global guidelines.

We performed two sensitivity analyses to evaluate the agreement across the MDR committees in type and underlying cause attribution. First, we excluded mortality cases that were not classified as maternal deaths by at least one MDR committee. Next, we assessed whether agreement on type and underlying cause attribution was better for maternal deaths with complete files.

Table 1. Pregnancy-related deaths lacking consensus among maternal death review (MDR) committees whether to classify as maternal deaths

Case	Gestation	Case description; cause of death	Classified as a maternal death by		
			Suriname	Jamaica	Netherlands
Doubt in classification of suicide in early pregnancy					
1	Unknown	Gramoxone[1] auto-intoxication	**No**	**Yes**	**No**
2	7 weeks	Gramoxone[1] auto-intoxication	**No**	**Yes**	**Yes**
3	9 weeks	Gramoxone[1] auto-intoxication	**No**	**Yes**	**Yes**
Doubt regarding evidence of pregnancy					
4	N/A	Following a curettage, chest pain and dyspnoea developed. Curettage pathology report showed no evidence of pregnancy.	**No**	**No**	**Yes**
5	N/A	Died at home from unknown cause. Verbal autopsy with family: early pregnancy. Examination: no fundal height palpable, but peripheral oedema of both feet.	**Yes**	**Yes**	**No**
6	N/A	Died in transit to hospital. Patient complained of abdominal pain, vaginal blood loss and chest pain. Verbal autopsy with family: could be pregnant.	**No**	**Yes**	**Yes**
Doubt whether the death was maternal or coincidental					
7	25 weeks	Severe burn wounds after explosion	**No**	**No**	**Yes**
8	29 weeks	Sepsis, meningoencephalitis/cerebral abscess	**Yes**	**Yes**	**No**
9	34 days postpartum	Sepsis with symptoms of high fever and diarrhoea	**Yes**	**No**	**Yes**
10	35 days postpartum	Normal delivery. Cause of death unknown.	**No**	**Yes**	**Yes**
Doubt in classification of maternal death of a local resident in another country					
11	29 weeks	Admitted in a Surinamese hospital with a severe sickle cell crisis. Ten days after discharge she died in neighboring French Guyana.	**No**	**Yes**	**No**

Legend: [1] Gramoxone is the tradename of paraquat, a contact herbicide, highly toxic to humans

RESULTS

Out of 89 pregnancy-related deaths, 53 (60%) medical files were complete, 14 (16%) were unavailable, and 22 were incomplete. The three MDR committees utilized all available information to analyse the 89 deaths.

Classification in Suriname: attending physicians vs national MDR committee

In 42 (47%) of 89 pregnancy-related deaths the cause attributed by the attending physician and the MDR committee differed; seventeen had no underlying cause attributed by the attending physician, and in 25 cases, different causes were concluded by the MDR committee. Differences were mostly due to the mode of death or symptoms having been recorded as the underlying cause. Two autopsies had been performed, one on a possible late maternal death and another on a woman who had developed a pulmonary embolism after a placental abruption.

Classification MDR committees Suriname, Jamaica and the Netherlands

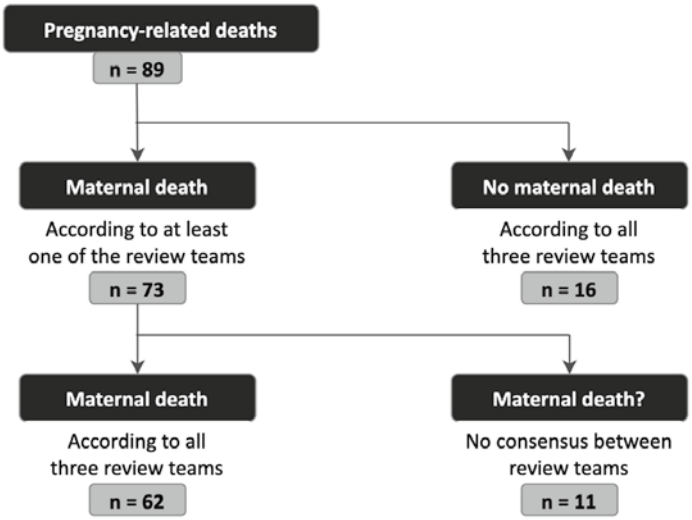
Maternal death classification

The Surinamese MDR committee classified 65 deaths as maternal, the Jamaican MDR committee 70 and the Netherlands MDR committee 69. Based on 50,051 live births in the audited period, this corresponded with an MMR of 130, 140 and 138 per 100.000 live births, respectively. The three MDR committees agreed unanimously that 18% (n=16/89) of the pregnancy-related deaths were not maternal deaths: 12 late maternal deaths, two coincidental deaths and two with negative pregnancy tests (supplementary file 1). Exclusion of these cases resulted in a total of 73 cases, used for further analyses (figure 2). However, opinions differed in 15% (n=11/73) of the cases (table 1).

Type of maternal deaths (direct, indirect and unspecified)

Of the 73 cases considered as maternal deaths by at least one MDR committee, classification into type of maternal death differed for 31 (42%) cases. The overall kappa was 0.53 (95% CI 0.44 - 0.62); $p < 0.001$ and was only fair for the unspecified category ($\kappa = 0.29$ (95% CI 0.16 – 0.43); $p < 0.001$) (table 2).

Figure 2. Flowchart of pregnancy-related deaths classified by MDR committees



The Netherlands committee (19%, n=14/73) classified more cases as unspecified compared to Surinamese (4%, n=3/73) and Jamaican committees (7%, n=5/73) (table 2 and supplementary file 2). Agreement between the MDR committees of Suriname and Jamaica (κ = 0.69 (95% CI 0.53 – 0.86); p < 0.001) was higher than between the committees of Suriname and the Netherlands (κ = 0.48 (95% CI 0.32 – 0.63); p < 0.001) (table 2). Out of 41 maternal deaths classified as direct by the Surinamese committee, the Jamaican committee classified five cases differently (four indirect, one unspecified), while the Dutch committee classified ten cases otherwise (three indirect, seven unspecified).

WHO ICD-MM groups of underlying causes

Table 3 compares the underlying causes of maternal deaths according to the nine ICD-MM groups as classified by the three MDR committees. Table 4 summarizes levels of agreement between the three MDR committees for each ICD-MM underlying cause group. The overall kappa was 0.52 (95% CI 0.47–0.58); p < 0.001, with the highest agreement for abortive outcomes (κ = 0.85) and obstetric haemorrhage (κ = 0.74) and the lowest for the unspecified (κ = 0.29) and other direct causes (κ = 0.32).

Table 2. Agreement among Maternal Death Review (MDR) committees in classification into the type of maternal death, n=73 (100%)

	MDR committees		
	Suriname	**Jamaica**	**The Netherlands**
	n (%)	n (%)	n (%)
Direct	41 (56)	41 (56)	36 (49)
Indirect	21 (29)	24 (33)	19 (26)
Unspecified	3 (4)	5 (7)	14 (19)
Not Maternal	8 (11)	3 (4)	4 (6)

Kappa = 0.53 (95% CI 0.44 - 0.62); p <0.001

Jamaican MDR committee		**Direct**	**Indirect**	**Un-specified**	**Not Maternal**	***Total Jamaica***
	Direct	36	1	0	4	***41***
	Indirect	4	19	0	1	***24***
	Unspecified	1	0	3	1	***5***
	Not Maternal	0	1	0	2	***3***
	Total Suriname	***41***	***21***	***3***	***8***	***73***

Kappa = 0.69 (95% CI 0.53 - 0.86); p<0.001

The Netherlands MDR committee		**Direct**	**Indirect**	**Un-specified**	**Not Maternal**	***Total Netherlands***
	Direct	31	3	0	2	***36***
	Indirect	3	14	0	2	***19***
	Unspecified	7	3	2	2	***14***
	Not Maternal	0	1	1	2	***4***
	Total Suriname	***41***	***21***	***3***	***8***	***73***

Kappa = 0.48 (98% CI 0.32 - 0.63); p<0.001

Agreement between the Surinamese and Jamaican MDR committees was higher (overall $\kappa = 0.63$; 95% CI: 0.53 – 0.73); $p < 0.001$ than between the Surinamese and Dutch committees (overall $\kappa = 0.49$; 95% CI: 0.39 – 0.59); $p < 0.001$. The lowest agreement between the Surinamese and the Jamaican MDR committees was for other direct obstetric causes ($\kappa = 0.36$) and highest for obstetric haemorrhage ($\kappa = 0.79$) and indirect deaths ($\kappa = 0.78$). Agreement was poor between the Surinamese and the Dutch MDR committee for unspecified ($\kappa = 0.14$) and other direct deaths ($\kappa = 0.25$).

The sensitivity analyses on the agreement between the MDR committees in type and underlying causes was performed on 62 cases (by excluding all mortality cases that were assessed as being not maternal). These showed slightly better overall agreement for classification in type of maternal death (κ = 0.61 vs 0.53) and underlying cause (κ = 0.58 vs 0.52) compared to the primary analysis (supplementary file 3). Fifty-three maternal death cases had complete files. Analysis of only the cases with complete files also showed better overall agreement for classification in type of maternal death (κ = 0.69 vs 0.53), and underlying cause (κ = 0.58 vs 0.52) than the primary analysis.

Evaluation of the level of agreement for the ICD-MM underlying cause among the MDR committees showed better agreement between Suriname and Jamaica (κ = 0.69 vs 0.66) than between Suriname and the Netherlands (κ = 0.54 vs 0.53) when applied to the 62 maternal deaths, as well as when applied to the 53 complete files respectively (supplementary file 3).

Table 3. Classification of maternal deaths underlying causes according to the ICD-MM by the three maternal death review (MDR) committees, n=73 (100%)

	Suriname n (%)	**Jamaica** n (%)	**The Netherlands** n (%)
Direct			
1. Abortive outcomes	2 (3)	3 (4)	2 (3)
2. Hypertensive disorders	7 (10)	11 (15)	6 (8)
3. Obstetric haemorrhage	13 (18)	16 (22)	14 (19)
4. Infection (pregnancy-related)	6 (8)	2 (3)	5 (7)
5. Other obstetric complications	13 (18)	9 (12)	9 (12)
6. Unanticipated complications	-	-	-
Indirect			
7. Non-obstetric complications	21 (29)	24 (33)	19 (26)
Unknown			
8. Unspecified	3 (4)	5 (7)	14 (19)
Not maternal			
9. Coincidental	8 (11)	3 (4)	4 (6)

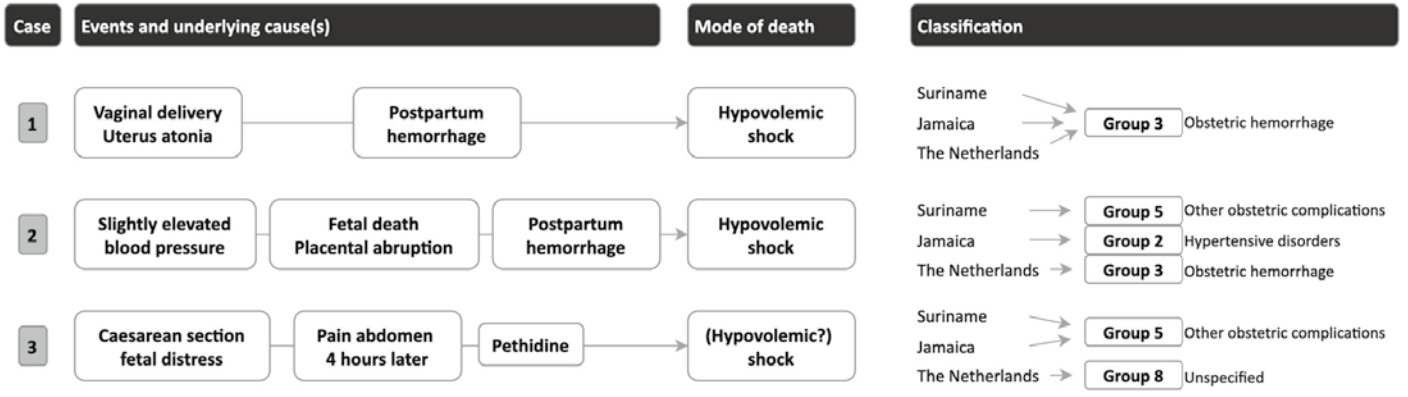
Table 4. Level of agreement of underlying causes according to WHO ICD-MM by MDR committees of Suriname, Jamaica and the Netherlands

Levels of Agreement	Suriname, Jamaica and Dutch MDR committee	Surinamese and Jamaican MDR committee	Surinamese and Dutch MDR committee
Almost perfect Kappa ≥ 0.81	Abortive outcomes	-	Abortive outcomes
Substantial Kappa 0.61 - 0.80	Obstetric haemorrhage Indirect	Abortive outcomes Hypertensive disorders Obstetric haemorrhage Indirect Unspecified	Obstetric haemorrhage
Moderate Kappa 0.41 - 0.60	Hypertensive disorders Obstetric infection	Obstetric infection	Hypertensive disorders Obstetric infection Indirect
Fair Kappa 0.21 - 0.40	Unspecified Other direct obstetric	Other direct obstetric	Other direct obstetric
Poor / Slight Kappa < 0.20	-	-	Unspecified

Morbid events leading to death

Consensus among the Surinamese, Jamaican and Dutch committees was fair for the other direct obstetric causes, with three cases identically classified (two presumed amniotic fluid embolisms, one suicide at 24 weeks) (table 4 and supplementary file 4). The cases with discrepancies in groups of underlying cause were characterized by either multiple comorbidities and longer chain of events or rapidly evolving death without opportunities for additional diagnostic evaluation (figure 3).

Figure 3. Maternal death classification difficulties in simple and complex chain of events



DISCUSSION

This study explored consistency in classifying pregnancy-related deaths in Suriname at two levels. First, underlying cause attribution by the attending physicians, and the Surinamese MDR committee was compared; conclusions differed in 47% of cases. Second, the classification of three national MDR committees of Suriname, Jamaica and the Netherlands were compared applying the WHO ICD-MM guidelines to the same cases. There was 15% disagreement among these committees on whether selected pregnancy-related deaths met the criteria to be defined as maternal deaths. They achieved moderate agreement (k = 0.53) on classifying cases as direct, indirect or unspecified, with greater consensus between the Surinamese and Jamaican MDR committees (k = 0.69) than the Surinamese and Netherlands MDR committees (k = 0.48). The MDR committee of the Netherlands, a high-income country, classified more deaths as unspecified than those from the middle-income countries of Suriname and Jamaica. There was higher concurrence among the three MDR committees in underlying cause attribution to abortive outcomes, obstetric haemorrhage and indirect maternal deaths, but only fair agreement on a mix of cases (other direct obstetric causes and unspecified).

The large difference (47%) in underlying cause attribution for maternal death between the attending physicians and the Surinamese MDR committee is not unusual. Similar differences were also seen in Malawi, where poor agreement between healthcare providers and the research team on maternal death classification was reported.[22] Another study found a 40% difference in underlying cause attribution in a multi-country survey that compared health provider findings with external reviewers among Low- and Middle-Income Countries (LMIC).[6] The abovementioned examples illustrate the importance of multidisciplinary case discussion and consensus-based underlying cause attribution.

Besides inconsistent underlying cause attribution, poor coding of pregnancy-related deaths, misidentification, or misclassification can result in inadequate certification and is associated with underreporting.[2,12,23] Due to underreporting, vital statistics could miss at least 50% of the maternal deaths.[24] Hence, since maternal death certificates are also completed by non-obstetricians (e.g. in the

rural interior or when indirect maternal deaths occurred), all clinicians would benefit from training to correctly complete death certificates.

The MDR committees in our study encountered specific challenges for which no clear guidance was available from the ICD-MM guidelines. These included (1) determining the fact of pregnancy with limited evidence; (2) inclusion of deaths from suicide, especially in early pregnancy and (3) whether and how to count maternal deaths outside the country of residence. It is unclear what the minimally acceptable evidence of pregnancy should be without medical confirmation and under which circumstances information from verbal autopsy alone could be used to confirm pregnancy. While the ICD-MM classifies suicide during pregnancy and puerperium as a direct maternal death, this is clearer for puerperal psychosis and postpartum depression than for events early in pregnancy.[7] The trigger for suicide may be social/circumstantial (partner rejection, domestic violence, unintended pregnancy), rather than clinical (pre-existing mental disorder or hormonal changes impacting mental health).[25,26] In addition, the ICD-MM guidelines do not elaborate on how to classify maternal deaths from suicide (direct vs indirect) when underlying mental disorders existed.[25] Finally, opinions differed in this study on the inclusion of a resident who had been under local care but died in another country. As no global guidance exists on whether to count such events in the country where the women dies or the country of residence, there is a chance that these cases are not reported at all (excluded in the country where she died and not reported in the country where she lived). Since all births are included in the national birth registry (denominator), we suggest including the mother also in the country where she died (numerator). Importantly, in these situations information is ideally exchanged between countries to facilitate local reporting and sharing of "lessons to be learned".

Consensus between the MDR committees of Suriname and Jamaica was higher than between those of Suriname and the Netherlands. The cases the Dutch committee considered unspecified but were assigned other diagnoses by the other committees had limited information on the disease course, and lacked confirmatory diagnostic tests such as laboratory results, ultrasounds, Computed Tomography (CT) or

Magnetic Resonance Imaging (MRI) scans compared to the cases with more agreement. Advanced diagnostics were often unavailable due to financial or logistic constraints, such as the minimal laboratory capacity in the rural interior areas. In these cases, the MDR committees in LIMCs must often rely on clinical judgement to make a diagnosis. Practicing medicine with greater uncertainty regarding diagnosis and treatment outcomes and fewer possibilities to provide evidence-based care is more commonplace in LMICs and possibly explains the more consistent results between the MDR committees of the two middle-income countries.

Classification into type of maternal death (direct, indirect and unspecified) differed in 42% of cases, only achieving moderate agreement among the three MDR committees. Dividing maternal deaths into direct and indirect conditions is pragmatic as preventive programs to avert direct deaths differ from indirect deaths.[27] However, this division has been questioned by the MDR committees in the United Kingdom (UK) and the Netherlands, especially for women with concurrent direct and indirect comorbidities.[28] In both middle and high-income countries, several pre-existing conditions such as obesity, diabetes mellitus, and hypertensive diseases are increasing and the risk of pregnant women to develop direct and indirect complications of pregnancy (e.g. postpartum haemorrhage, eclampsia, cardiovascular diseases).[28-30] This coexistence of multiple conditions in an individual is known as multimorbidity and is one of the challenges of modern medicine.[31,32] These conditions obfuscate the strict demarcation between direct and indirect deaths and reduce their relevance. Instead, adding multimorbidity categories, such as (non)communicable diseases and (pre-existing) mental disorders to the ICD-MM guidelines would be more pertinent.

We conducted a sensitivity analysis to explore whether consensus improved with the exclusion of (1) cases without consensus among the MDR committees in the classification as maternal deaths, and (2) cases with incomplete information. As expected, the exclusion of the cases with uncertainty improved the level of agreement. These exclusions strengthened the consensus that already existed between the Surinamese and Jamaican MDR committees. However, since

differences are small, these analyses suggest that, even with limited information, MDR committees can reach reliable conclusions on the probable types and underlying causes of maternal deaths.

Our data showed that when the cycle of events leading to death had fewer incidents (figure 3), underlying cause attribution was more straightforward (as with abortion-related and obstetric haemorrhage). Selecting the initiating event from a chain of multiple events is more difficult in complex cases, resulting in a discrepancy in underlying cause classification in our study. Two high-income countries, the United Kingdom (UK) and the Netherlands, also reported such differences in underlying cause attribution.[10] Their MDR committees discussed selected cases where disagreement was expected during a meeting attended by most members of both committees. While the Netherlands classified a death by the primary underlying pathology, the UK more pragmatically focused on the acute fatal complication.[10] They suggested that decision-making may be guided by what best informs local practice in the absence of global guidance. However, this approach could result in heterogeneity and complicates comparison among countries.

Reliable underlying cause attribution may be improved by combining clinical data with autopsy findings.[33,34] However, autopsy for maternal death is seldom performed in low resource countries such as Suriname, where only two cases were investigated.[3] It may be useful to revisit verbal autopsy techniques to improve collection and interpretation of information on signs, symptoms and risk factors.[35] Another possible option is the minimally invasive autopsy. This includes collection of blood, cerebrospinal fluid and tissue samples for histologic and microbiologic analysis.[36] This option could be explored to assist in identifying the underlying causes of maternal death.

Strengths and limitations: This study's strength is its unique comparison of the classification of the same cases by physicians and (inter)national MDR committees from three different settings applying the WHO ICD-MM guidelines. Limitations include difficulties in interpreting cases with limited information and, possibly, by

a high-income country being unfamiliar with the different contexts of LMIC. The inter-rater reliability should be carefully interpreted as the overall kappa may not be reliable for rare observations, such as group 1 (abortive outcomes) and group 4 (pregnancy-related infections).

CONCLUSION AND RECOMMENDATION

This is the first study comparing audit and ICD-MM classification of the same maternal deaths by MDR committees of different countries, revealing the difficulties and challenges. Accurately completing the death certificate, training in performing audits and applying the WHO ICD-MM guidelines to code and classify the death should be encouraged.[12,19] We suggest that the WHO guidelines should elaborate more on the following aspects:

1. Clearly define and describe how to classify suicide during (early) pregnancy or puerperium.
2. Provide guidance on the minimal acceptable evidence of early pregnancy in the absence of objective clinical evidence (e.g. a pregnancy test) and specify on the use of information obtained through verbal autopsy.
3. Specify where maternal deaths of citizens who die outside of their country of residence should be counted to ensure that all maternal deaths globally are counted.
4. Discuss the relevance of classification in direct or indirect causes and the addition of classification in multimorbidity categories.
5. Provide guidance on selecting the underlying causes when concurrent comorbid direct and indirect conditions exist, or multiple direct complications co-occur.

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Supplementary file 1. Case description pregnancy-related deaths classified as "no maternal death" by all three MDR committees

Case	Gestational age	Description
Pregnancy test negative		
1	Last menstruation 4 weeks ago	Pain in the belly, severe anaemia, pregnancy test negative
2	According to husband pregnant	Pain in the belly, pregnancy test negative, human chorionic gonadotrophins (HCG) < 1
Coincidental deaths		
3	24 weeks	Haemorrhagic shock following impact trauma
4	25 weeks	Trauma capitis and pneumo-sepsis
Late maternal deaths		
5	8 weeks postpartum	Tachypnoea, diarrhoea, vomiting
6	9 weeks after caesarean	Diarrhoea, fever, vomiting, acute respiratory distress
7	10 weeks postpartum	Pre-eclampsia. Developed meningitis/encephalitis
8	11 weeks postpartum	Breast cancer
9	11 weeks postpartum	Cervical cancer
10	12 weeks postpartum	Peripartum cardiomyopathy
11	16 weeks after early pregnancy	Probably early pregnancy (human chorionic gonadotrophins (HCG) 181), after 16 weeks pulmonary embolus, autopsy showed no pregnancy
12	16 weeks after caesarean	Pregnancy complicated by pre-eclampsia. Died at home suddenly
13	19 weeks postpartum	Oesophageal cancer
14	24 weeks postpartum	Delivered premature (at 35 weeks), lupus erythematosus and sickle cell anaemia.
15	24 weeks postpartum	Peripartum cardiomyopathy
16	41 weeks post caesarean	Laparotomy due to ileus, many adhesions

Supplementary file 2. Case description of the 2010-2014 maternal deaths of Suriname classified as "unspecified"

	Gestation	Case description	Classification by MDR Committees		
			Suriname	Jamaica	Netherlands
1	9 months pregnant	Came from the interior, died in the car and was immediately transferred to the mortuary.	Unspecified	Unspecified	Unspecified
2	23 weeks according to family	Died at home in the interior. Complained of headache and dizziness 3 months before.	Unspecified	Unspecified	Unspecified
3	Verbal autopsy: early pregnancy	Died at home from unknown cause. Verbal autopsy with family: early pregnancy. Examination: no fundal height palpable, but peripheral oedema of both feet.	Unspecified	Unspecified	No Maternal death
4	35 days postpartum	Uncomplicated childbirth. Died at home 35 days later. No further information available.	No Maternal death	Unspecified	Unspecified
5	3 days postpartum	Uncomplicated childbirth. Died 3 days later with pain in legs and belly. No further information available.	Other Direct causes	Unspecified	Other Direct causes
6	Early pregnancy	Died before reaching hospital. Had abdominal pain, vaginal blood loss and chest pain. Verbal autopsy with family: could be pregnant	No Maternal death	Direct	Unspecified
7	25 weeks	Severe hypertension and severe dyspnoea followed by respiratory arrest	Direct	Direct	Unspecified
8	35 weeks	Grande multiparous, breech delivery in interior, retained placenta, died during transport to city. Blood loss not recorded.	Direct	Direct	Unspecified

Supplementary file 2. Continued

	Gestation	Case description	Classification by MDR Committees		
			Suriname	**Jamaica**	**Netherlands**
9	37 weeks	Obstructed labour, died in interior 3 hours after full dilation and ruptured membranes.	Direct	Direct	Unspecified
10	1 week postpartum	Two previous caesareans. Delivery of dead child at 27 weeks, curettage postpartum. One week later died at ER with normal vitals, normal laboratory results.	Direct	Direct	Unspecified
11	5 hours after caesarean	Caesarean for foetal distress at 41 weeks, stillbirth born. Post-caesarean hypotensive and found dead an hour later.	Direct	Direct	Unspecified
12	40 weeks	Died suddenly during delivery after rupture of membranes.	Direct	Direct	Unspecified
13	+/- 27 weeks	Found in vomit, unconscious with fever and high pulse and died. Abnormal kidney and liver enzymes.	Direct	Indirect	Unspecified
14	35 weeks	Atypical pneumonia, respiratory insufficiency and died after one week.	Indirect	Indirect	Unspecified
15	2 weeks postpartum	AIDS with heart failure and sepsis. No medical file available.	Indirect	Indirect	Unspecified
16	+/- 30 weeks	Known with an unknown illness before pregnancy. Vomits and probably had an exacerbation of disease. Did not seek medical help and died in interior.	Indirect	Indirect	Unspecified

Supplementary file 3. Sensitivity analysis for agreement among MDR committees in type of maternal death and ICD-MM underlying causes, expressed in Kappa (95% CI)

Type of maternal death			
	Overall	**Suriname - Jamaica**	**Suriname - the Netherlands**
All files (n=73)	0.53 (0.44-0.62)	0.69 (0.53-0.86)	0.48 (0.32-0.63)
Only cases with consensus on classification as maternal death (n= 62)	0.61 (0.49-0.72)	0.80 (0.58-1.0)	0.52 (0.33-0.72)
Complete files only (n=53)	0.69 (0.58-0.79)	0.80 (0.60-0.99)	0.64 (0.46-0.82)
WHO ICD-MM group of underlying causes			
	Overall	**Suriname - Jamaica**	**Suriname - the Netherlands**
All files (n=73)	0.52 (0.47–0.58)	0.63 (0.53–0.73)	0.49 (0.39–0.59)
Only cases with consensus on classification as maternal death (n= 62)	0.58 (0.52–0.65)	0.69 (0.57–0.81)	0.54 (0.43–0.66)
Complete files only (n=53)	0.58 (0.51-0.65)	0.66 (0.54-0.78)	0.53 (0.42-0.64)

Supplementary file 4. Case description of the 2010-2014 maternal deaths of Suriname classified as "other direct obstetric causes"

Case	Gestation	Case description	Classification by MDR Committees		
			Suriname	Jamaica	Netherlands
1	39 weeks	Collapsed during delivery, amniotic fluid embolism	Other Direct Causes	Other Direct Causes	Other Direct Causes
2	41weeks	Collapsed during delivery, amniotic fluid embolism	Other Direct Causes	Other Direct Causes	Other Direct Causes
3	24 weeks	Suicide by autointoxication	Other Direct Causes	Other Direct Causes	Other Direct Causes
4	0 days postpartum	Hypertension, abruption complicated by massive blood loss after childbirth.	Other Direct Causes	Hypertensive	Haemorrhage
5	30 days postpartum	Pre-eclampsia complicated by intra-cranial cerebral bleeding postpartum.	Other Direct Causes	Hypertensive	Other Direct Causes
6	27 weeks	Home delivery stillbirth. Normotensive with headache and vomiting. Died one week later.	Other Direct Causes	Hypertensive	Unspecified
7	3 days postpartum	Lupus and hypertension with thrombocytopenia complicated by massive blood loss.	Other Direct Causes	Haemorrhage	Haemorrhage
8	0 days postpartum	Hypertension and abruption placentae. Uterine torsion, hysterec-tomy and massive bleeding.	Other Direct Causes	Haemorrhage	Hypertensive
9	37 weeks	Obstructed labour, died in interior 3 hours after full dilation and ruptured membranes.	Other Direct Causes	Haemorrhage	Unspecified
10	11 days postpartum	Severe pre-eclampsia, stillbirth of one of twins, caesarean section, followed by severe hematemesis, coagulation disorder and respiratory insufficiency.	Other Direct Causes	Indirect	Indirect

Supplementary file 4. Continued

Case	Gestation	Case description	Classification by MDR Committees		
			Suriname	Jamaica	Netherlands
11	41 days postpartum	Pulmonary hypertension with respiratory insufficiency six weeks after childbirth. No pulmonary embolism.	Other Direct Causes	Indirect	Indirect
12	40 weeks	Died instantly during labour when the membranes ruptured	Other Direct Causes	Other Direct Causes	Unspecified
13	0 days postpartum	Found dead in her bed five hours after caesarean section	Other Direct Causes	Other Direct Causes	Unspecified
14	34 weeks	Immune thrombocytopenic purpura. Pulmonary bleeding and respiratory insufficiency.	Indirect	Other Direct Causes	Indirect
15	Early pregnancy	Suicide by autointoxication	No maternal death	Other Direct Causes	Other Direct Causes
16	Early pregnancy	Suicide by autointoxication	No maternal death	Other Direct Causes	No maternal
17	10 weeks	Suicide by autointoxication	No maternal death	Other Direct Causes	Indirect
18	1 day postpartum	Caesarean section complicated by respiratory insufficiency, history of severe mitral valve stenosis	Indirect	Indirect	Other Direct Causes
19	0 days postpartum	Severe pre-eclampsia, pulmonary oedema, eclampsia, cardiac arrest	Hypertensive	Hypertensive	Other Direct Causes
20	0 days postpartum	Hypovolemic shock due to uterus rupture	Haemorrhage	Haemorrhage	Other Direct Causes
21	Early pregnancy	Died before hospital admission. Abortion, chest pain and dyspnoea. Curettage pathology: no evidence of pregnancy.	No maternal death	No maternal death	Other Direct Causes

Applicability of the WHO maternal near-miss tool: a nationwide surveillance study in Suriname

5

Kim J. C. Verschueren
Lachmi R. Kodan
Raëz R. Paidin
Sarah M. Samijadi
Rubinah R. Paidin
Marcus J. Rijken
Joyce L. Browne
Kitty W. M. Bloemenkamp

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ABSTRACT

Background: Maternal near-miss (MNM) is an important maternal health quality-of-care indicator. To facilitate comparison between countries, the World Health Organization (WHO) developed the 'MNM-tool'. However, several low- and middle-income countries have proposed adaptations to prevent underreporting, i.e. Namibian and Sub-Sahara African (SSA)-criteria. This study aims to assess MNM and associated factors in middle-income country Suriname by applying the three different MNM tools.

Methods: A nationwide prospective population-based cohort study was conducted, using the Suriname Obstetric Surveillance System (SurOSS). We included women with MNM-criteria defined by WHO-, Namibian- and SSA-tools during one year (March 2017-February 2018) and used hospital births (86% of total) as a reference group.

Results: There were 9114 hospital live births in Suriname in the one-year study period. SurOSS identified 71 women with WHO-MNM (8/1000 live births, mortality-index 12%), 118 with Namibian-MNM (13/1000 live births, mortality-index 8%), and 242 with SSA-MNM (27/1000 live births, mortality-index 4%). Namibian- and SSA-tools identified all women with WHO-criteria. Blood transfusion thresholds and eclampsia explained the majority of differences in MNM prevalence. Eclampsia was not considered a WHO-MNM in 80% (n=35/44) of cases. Nevertheless, mortality-index for MNM with hypertensive disorders was 17% and the most frequent underlying cause of maternal deaths (n=4/10, 40%) and MNM (=24/71, 34%). Women of advanced age and maroon ethnicity had twice the odds of WHO-MNM (respectively aOR 2.6, 95%CI 1.4-4.8 and aOR 2.0, 95%CI 1.2-3.6). The stillbirths rate among women with WHO-MNM was 193/1000births, with six times higher odds than women without MNM (aOR 6.8, 95%CI 3.0-15.8). While the prevalence and mortality-index differ between the three MNM tools, the underlying causes of and factors associated with MNM were comparable.

Conclusions: The MNM ratio in Suriname is comparable to other countries in the region. The WHO-tool underestimates the prevalence of MNM (high mortality-index), while the adapted tools may overestimate MNM and compromise global comparability. Contextualised MNM-criteria per obstetric transition stage may improve comparability and reduce underreporting. While MNM studies facilitate international comparison, audit will remain necessary to identify shortfalls in quality-of-care and improve maternal outcomes.

BACKGROUND

Sustainable Development Goal target 3.1 aims to eliminate preventable maternal deaths and reduce the global maternal mortality ratio (MMR) to less than 70 per 100.000 live births (LB) by 2030.[1] Women who die represent just the tip of the iceberg: for each woman who dies, at least ten suffer from severe maternal complications and narrowly escape death by chance or because of the care they receive: a maternal near-miss (MNM).[2] With the decline of maternal deaths, MNM is used as a proxy to measure the quality of obstetric care.[2,3] MNM has the advantage that it occurs more frequently and that the survival of the woman makes it less threatening to report by health care providers.[2-4] In Suriname, a middle-income country in South America, the MMR is 130 per 100.000 LB, one of the highest in the Caribbean & America's, but the absolute number of deaths is "only" ten to fifteen per year.[5] This makes MNM studies crucial to develop justified recommendations and finally reduce maternal mortality.[2-4]

To standardise the MNM definition and facilitate comparison between different countries, the World Health Organization (WHO) developed the "Maternal near-miss approach" in 2011.[2] The classification includes three types of criteria: disease-, intervention,- and organ dysfunction-based. If any organ dysfunction criteria are met, the MNM approach defines the case as 'life-threatening' and therefore, MNM. The choice for organ-dysfunction criteria follows the concept that the following sequence of events leads from good health to death: clinical disease, systemic inflammatory response syndrome, organ dysfunction, organ failure and finally death.[6,7] Following this concept, organ dysfunction markers (25 criteria) define

MNM.[2] However, several studies in different settings demonstrated that the organ-dysfunction criteria may not be suitable and proposed adapted criteria to prevent underreporting of life-threatening disorders.[8-12] In 2017, a Delphi study suggested adaptations to the WHO-criteria for low-resource settings in Sub-Sahara Africa (SSA).[10] The adapted MNM tool included several clinical conditions, such as eclampsia, sepsis and uterine ruptured and a lower threshold for blood transfusion, and performed well in Ethiopia.[11] A recent study in Namibia suggested that both tools were not suitable for middle-income countries and proposed criteria 'in-between' WHO-MNM and SSA-MNM.[12] However, the resulting heterogeneity of these adapted MNM criteria compromises comparability[3], which the WHO approach specifically intended to avoid.

The goal of studying maternal near-miss in Suriname would be to (1) find a reason for the relatively high maternal mortality, and stillbirth rate in the country[5,13,14], (2) compare findings to other countries and (3) improve the quality of care. Due to the variety of (adapted) MNM-criteria, it is unclear which criteria are most applicable to achieve the abovementioned aims.

Therefore, this nationwide study in Suriname first aims to apply the WHO-MNM tool and adapted Namibian and SSA-tools to evaluate differences in prevalence, mortality-index, underlying causes, and factors associated with maternal near-miss. The comparison of MNM in a clinical setting may facilitate possible amendments of the global WHO near-miss criteria to assure uniformity and applicability.

METHODS

Study design and setting: A prospective nationwide population-basd cohort study, using the Suriname Obstetric Surveillance System (SurOSS), was performed during one year (March 2017 to February 2018). Suriname is situated on the Northern coast of South-America, with a population of approximately 560.000 and 10.000 live births a year.[15] The five hospitals conduct approximately 86% of all births, 4% women deliver at home, 6% of women deliver at the primary health care services and in 4% the place of birth is unknown.[15] In general, all women with (severe)

morbidity are referred to a hospital. Maternal deaths (in facilities and the community) are reported to the Surinamese Maternal Mortality Committee. For a detailed description of the health care system, see our previous publications on maternal mortality and childbirth outcomes.[5,13-16]

Maternal near-miss case definition: Within SurOSS we identified all women with potentially-life threatening complications (PLTC, i.e. disease- and intervention-criteria) and life-treatening complications (LTC, i.e. MNM, organ dysfunction criteria) according to the WHO near-miss approach.[2] Per Surinamese Maternal Mortality Committee consensus directions, the criteria were minorly, contexually adaptated to clarify definitions and prevent inclusion of women without PLTC (table 1), as follows:

1. Transfusion of one blood product was increased to ≥ three blood products and women were excluded who were transfused for only anaemia without any other complications;
2. Laparotomy for ectopic pregnancy was only included if blood loss was ≥1000 mL, blood was transfused or if patient was hemodynamically unstable[12];
3. Definition of maternal sepsis and eclampsia were harmonised with the United Kingdom (UKOSS) and International Network of Obstetric Surveillance System (INOSS).[17,18]

Data collection: Eligible women were identified by the research coordinator (doctor) of each hospital during daily rounds. The authors weekly screened the medical files of all discharged women on the gynaecology and obstetric wards, in the intensive care of all hospitals. Additionally, the hospital registries reported whether patients on non-obstetric departments were consulted by a gynaecologist or obstetrician or had a ICD-code related to pregnancy. The research coordinator of the primary health care centres were contacted every quartile and reported women who were not transferred to a hospital. Medical files were retrieved of all discharged women with PLTC and digitalised using an anonymous 188-item digital case report form on a password-secured Kobotoolbox.

Table 1. Definition of potentially life-threatening and life-threatening complications in pregnancy defined by WHO and minor adaptations within the Suriname Obstetric Surveillance System (SurOSS).

Potentially life-threatening complications (PLTC) Disease-based criteria		
	WHO	**SurOSS**
Severe post-partum haemorrhage	Genital bleeding after delivery, with at least one of the following: perceived abnormal bleeding (1000 ml or more) or any bleeding with hypotension or blood transfusion.	• 1000 mL blood loss and/or; • Any bleeding (antepartum, intrapartum or postpartum) with hypotension or transfusion of at least 3 products
Severe pre-eclampsia	Persistent systolic blood pressure of 160 mmHg or more or a diastolic blood pressure of 110 mmHg; proteinuria of 5 g or more in 24 hours; oliguria of <400 ml in 24 hours; and HELLP syndrome or pulmonary oedema. Excludes eclampsia.	• Systolic blood pressure of 160 mm Hg or more, or diastolic 110 mm Hg or more twice at least 4 hours apart and/or; • Thrombocytopenia (platelet count of <100x9 10^9/l) • Raised plasma ALT or AST (twice the upper limit of normal) • Renal insufficiency (twice the normal serum creatinine) • Pulmonary oedema • Pre-eclampsia complaints, not attributed to other causes
Eclampsia	Generalised fits in a patient without previous history of epilepsy. Includes coma in pre-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 or ≥90 mmHg diastolic) • Proteinuria [at least 1 g/l [‘2 +’] on dipstick testing] • Thrombocytopenia (platelet count of <100x9 10^9/l) • Raised plasma ALT or AST (twice the upper limit of normal)

Table 1. Continued

Potentially life-threatening complications (PLTC) **Disease-based criteria**		
	WHO	**SurOSS**
Severe sepsis	Presence of fever (body temperature >38°C), a confirmed or suspected infection (e.g. chorioamnionitis, septic abortion, endometritis, pneumonia), and at least one of the following: heart rate >90, respiratory rate >20, leukopenia (white blood cells <4000), leucocytosis (white blood cells >12 000).	Any pregnant or recently pregnant woman (up to 6 weeks postpartum) diagnosed with severe sepsis (irrespective of the source of infection). Clinical diagnosis of severe sepsis, associated with two or more of the following: • Temperature >38C or <36C measured on two occasions at least 4 hours apart • Heart rate >100 beats/minute measured on two occasions at least 4 hours apart • Respiratory rate >20/minute measured on two occasions at least 4 hours apart • White cell count >17x10^9/L or <4x10^9/L or with >10% immature band forms, measured on 2 occasions
Ruptured uterus	Rupture of uterus during labour confirmed by laparotomy.	A visually confirmed, complete rupture of the myometrium and serosa
Severe complications of abortion	Not further defined	Severe haemorrhage (≥1000mL, hypotension, blood transfusion of at least 3 products), severe sepsis or complications due lesion of intestines or other organs or complications related to anaesthesia
Intervention-criteria		
Intensive care unit admission	Not further defined	Admission to a ward where mechanical ventilation and administration of continous vasoactive drugs are possible
Intervention radiology	Not further defined	Not available in Suriname

Table 1. Continued

Intervention-criteria		
	WHO	**SurOSS**
Laparotomy excluding caesarean section	Not further defined	Excluding uncomplicated laparotomy for ectopic pregnancy when patient remains hemodynamically stable and blood loss is less than 1000 mL and less than three blood products
Use of blood products	Not further defined	Use of at least 3 blood products Excluding blood transfusion for anaemia without any other complications
Life-threatening Organ-dysfunction criteria		
Cardiovascular	Shock, cardiac arrest (absence of pulse/ heart beat and loss of consciousness), use of continuous vasoactive drugs, cardiopulmonary resuscitation, severe hypoperfusion (lactate >5 mmol/l or >45 mg/dl), severe acidosis (pH <7.1)	
Respiratory	Acute cyanosis, gasping, severe tachypnoea (respiratory rate >40 breaths per minute), severe bradypnea (respiratory rate <6 breaths per minute), intubation and ventilation not related to anaesthesia, severe hypoxemia (O2 saturation <90% for ≥60 minutes or PAO2/FiO2 <200)	
Renal	Oliguria non-responsive to fluids or diuretics, dialysis for acute renal failure, severe acute azotaemia (creatinine ≥300 µmol/ml or ≥3.5 mg/dl)	
Coagulation / haematology	Failure to form clots, massive transfusion of blood or red cells (≥5 units), severe acute thrombocytopenia (<50 000 platelets/ml)	
Hepatic	Jaundice in the presence of pre-eclampsia, severe acute hyperbilirubinemia (bilirubin >100 µmol/l or >6.0 mg/dl)	
Neurologic	Prolonged unconsciousness (lasting ≥12 hours)/coma (including metabolic coma), stroke, uncontrollable fits/status epilepticus, total paralysis	
Uterine dysfunction	Uterine haemorrhage or infection leading to hysterectomy	

Data on demographics, general and obstetric history, occurrence of maternal and perinatal adverse outcomes were retrieved. The Surinamese Maternal Mortality Committee conducted verbal autopsy and audits of all maternal deaths and shared the elaborate case summaries. For the purpose of this study, all maternal deaths in the study period and women with any WHO-MNM, Namibian-MNM or SSA-MNM were extracted for analysis (table 2). The SSA-MNM criteria were developed after our study commenced.[10] This resulted in women who received two units of red blood cells without any other MNM-criteria not being included. We used hospital births (86% of total births in Suriname) as a reference group. Data were collected through the childbirth books of all hospitals of babies with birth weight of at least 500 grams.

Outcome measures: The prevalence was calculated per 1000 live births and mortality-index was calculated by dividing maternal deaths (MD) with (MD+MNM). Causes were classified according to the International Classification of Diseases Maternal Mortality (ICD-MM).[19] The underlying cause of maternal deaths and MNM diagnosis was the primary event in the chain-of-events.[19,20] Risk indicators were analyzed by comparing women who gave birth with MNM (numerator) to those who gave birth without MNM (denominator). No sample size calculation was performed due to the descriptive character of this study.

Statistical analysis: SPSS version 25 (IBM, Armonk, NY, USA) was used and simple descriptive statistics were performed (frequencies, proportions, bar charts and pie charts). No data imputation was conducted as missing data was <5% and completely at random. Univariate binary logistic regression was performed to assess factors associated with MNM, reported in crude odds ratio (OR) with 95% confidence intervals (95% CI). Multivariate logistic regression included variables with $p<0.1$ in the univariate analysis and the hypothesis-driven variables age, parity and ethnicity, and was reported in adjusted OR (aOR, 95% CI). Maternal near-miss was the dependent variable for the association with maternal characteristics. Each adverse perinatal outcome (preterm birth, low birth weight, low Apgar score

and stillbirth) was the dependent variable for the associon with maternal-near miss. Possible explanatory factors such as BMI, socio-economic status and medical history could not be included due to the lack of this data in the reference group. The risk of MNM related to caesarean section (CS) could not be studied, due to bias by indication (CS could be both the cause and result of MNM).

Ethical considerations: This research was approved by the ethical review board of the Surinamese Committee on Research Involving Human Subjects (#VG21-16) on October 4th, 2016. Informed consent was not deemed necessary as data were obtained from medical records without identification of the woman.

Figure 1. Number of women in the spectrum to life-threatening conditions

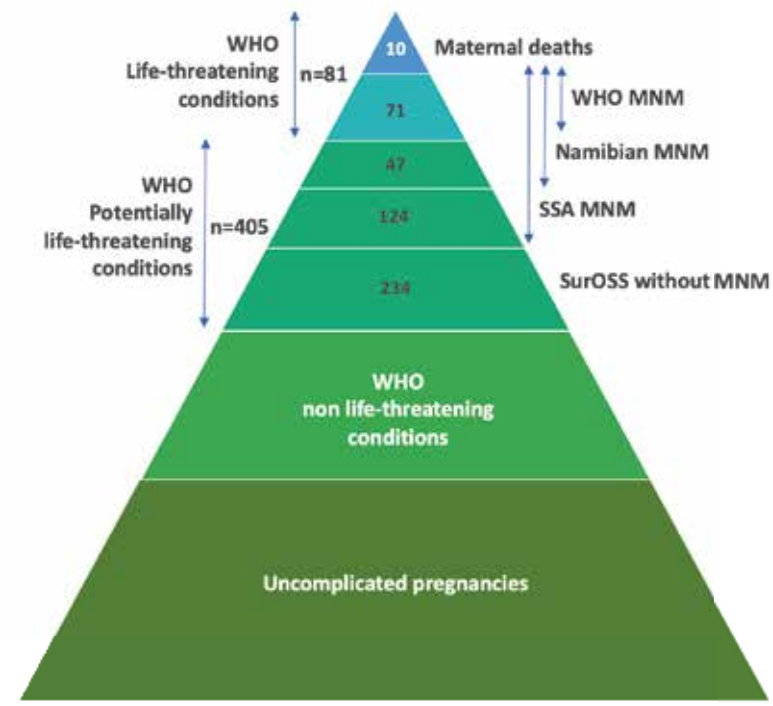


Table 2. MNM criteria according to WHO, Namibian and Sub-Sahara Africa tools

	WHO	Nam	SSA
Clinical criteria			
Acute cyanosis	✓	✓	✓
Gasping	✓	✓	✓
Respiratory rate >40 or <6/min	✓	✓	✓
Shock	✓	✓	✓
Oliguria non responsive to fluids or diuretics	✓	✓	✓
Failure to form clots	✓	✓	✓
Loss of consciousness lasting more than 12 h	✓	✓	✓
Cardiac Arrest	✓	✓	✓
Stroke	✓	✓	✓
Uncontrollable fits / total paralysis	✓	✓	✓
Jaundice in the presence of pre-eclampsia	✓	✓	✓
Eclampsia	✗	✓	✓
Ruptured uterus	✗	✓	✓
Sepsis or severe systemic infection	✗	✗	✓
Pulmonary oedema	✗	✗	✓
Severe complications of abortion	✗	✗	✓
Severe malaria	✗	✗	✓
Severe pre-eclampsia with ICU admission	✗	✗	✓
Laboratory criteria			
Oxygen saturation <90% for >60 minutes	✓	✓	✓
PaO2/FiO2 <200 mmHg	✓	✓	✗
Creatinine ≥300µmol/l or ≥3.5 mg/dl	✓	✓	✓
Bilirubin >100 µmol/l or > 6.0 mg/dl	✓	✓	✗
pH <7.1	✓	✓	✗
Lactate >5 mEq/mL	✓	✓	✗
Acute thrombocytopenia (<50 platelets/ml)	✓	✓	✓
Loss of consciousness, gluc/keto in urine	✓	✓	✓
Management-based criteria			
Use of continuous vasoactive drugs	✓	✓	✗
Hysterectomy due to infection / haemorrhage	✓	✓	✓
Transfusion of … units of blood or red cells	5	4	2
Intubation/ventilation unrelated to anaesthesia	✓	✓	✓
Dialysis for acute renal failure	✓	✓	✗
Cardiopulmonary resuscitation	✓	✓	✓
Laparotomy other than CS	✗	✗	✓
Laparotomy other than CS/ectopic pregnancy	✗	✓	✗

	WHO	Nam	SSA
Cardiovascular dysfunction			
Shock	✓	✓	✓
Cardiac Arrest	✓	✓	✓
Use of continuous vasoactive drugs	✓	✓	✗
Cardiopulmonary resuscitation	✓	✓	✓
Lactate >5mml/l	✓	✓	✗
pH <7.1	✓	✓	✗
Respiratory dysfunction			
Acute cyanosis	✓	✓	✓
Gasping	✓	✓	✓
Respiratory rate >40 or <6/min	✓	✓	✓
Intubation/ventilation unrelated to anaesthesia	✓	✓	✓
Oxygen saturation <90% for >60 minutes	✓	✓	✓
PaO2/FiO2 <200 mmHg	✓	✓	✗
Renal dysfunction			
Oliguria non responsive to fluids or diuretics	✓	✓	✓
Dialysis for acute renal failure	✓	✓	✗
Creatinine ≥300µmol/l or ≥3.5 mg/dl	✓	✓	✓
Coagulation/haematological dysfunction			
Failure to form clots	✓	✓	✓
Transfusion of .. units of blood or red cells	5	4	2
Acute thrombocytopenia (<50.000/ml)	✓	✓	✓
Hepatic dysfunction			
Jaundice in the presence of pre-eclampsia	✓	✓	✓
Bilirubin >100 µmol/l or > 6.0 mg/dl	✓	✓	✗
Neurological dysfunction			
Loss of consciousness lasting more than 12 h	✓	✓	✓
Loss of consciousness, gluc/keto in urine	✓	✓	✓
Stroke	✓	✓	✓
Uncontrollable fits / total paralysis	✓	✓	✓
Uterine dysfunction			
Hysterectomy due to infection/ haemorrhage	✓	✓	✓
Additional parameters			
Eclampsia	✗	✓	✓
Ruptured uterus	✗	✓	✓
Sepsis or severe systemic infection	✗	✗	✓
Pulmonary oedema	✗	✗	✓
Severe complications of abortion	✗	✗	✓
Severe malaria	✗	✗	✓
Severe pre-eclampsia with ICU admission	✗	✗	✓
Laparotomy other than CS	✗	✗	✓
Laparotomy other than CS/ectopic pregnancy	✗	✓	✗

Legend ✓ Criterion according to the specified tool; ✗ Not a criterion according to the specified tool

RESULTS

During the one-year study period, there were 9114 live births and ten maternal deaths, which results in an MMR 110 per 100.000 live births. SurOSS identified 486 women with PLTC, of whom 234 had no MNM criteria (figure 1). The primary health care centres reported ten women with PLTC who were not referred to a hospital, and none had MNM criteria. The WHO-tool identified 71 MNM (ratio 7.8 per 1000 LB, mortality-index 12% (n=10/81)), the Namibian-tool identified 118 MNM (ratio 12.9 per 1000 LB, mortality-index 8% (n=10/128)) and the SSA-tool 242 MNM (ratio 26.5 per 1000 LB, mortality-index 4% (n=10/252)) (Table 3). Namibian and SSA-MNM identified all women with WHO-MNM.

Table 3. Demographics and maternal health indicators in Suriname

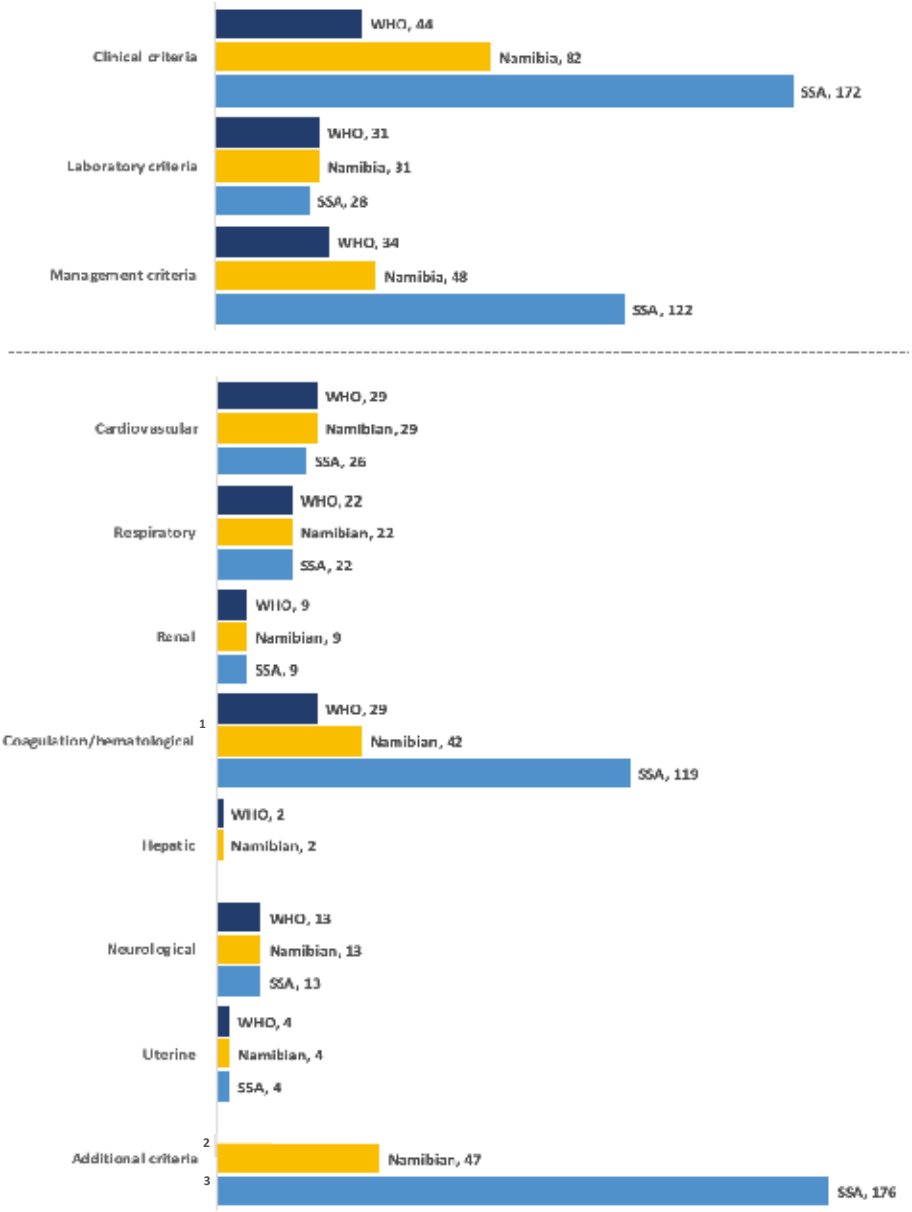
	n=		
Deliveries	9190		
Total babies born	9313		
Live births	9114		
Maternal deaths	10		
Maternal mortality ratio[1]	110		
Near miss tools	**WHO**	**Namibian**	**SSA**
Maternal near miss, n=	71	118	242
MNM ratio[2]	7.8	12.9	26.5
One MNM-criterion, n= (%)	*40 (56%)*	*79 (67%)*	*135 (56%)*
Two or three MNM-criteria, n= (%)	*20 (28%)*	*26 (22%)*	*83 (34%)*
Four or more MNM-criteria, n= (%)	*11 (16%)*	*13 (11%)*	*24 (10%)*
Total amount of MNM-criteria	*146*	*218*	*458*
Severe maternal outcomes, n=	81	128	252
SMO ratio[3]	8.8	14.0	27.6
Maternal near miss : mortality ratio	7 : 1	12 : 1	24 : 1
Mortality index[4]	12.3 %	7.8 %	4.0 %
Severity score, mean (SD)[5]	2.5 (2.2)	2.1 (2.0)	2.1 (1.8)

Legend [1] Maternal mortality ratio: maternal deaths per 100.000 live births; [2] Maternal near miss ratio: near miss cases per 1000 live births; [3] Severe maternal outcome ratio: near miss cases and maternal deaths per 1000 live births; [4] Mortality index: number of maternal deaths divided by number of women with severe maternal outcomes (near miss and maternal deaths), expressed in percentages; [5] Average no of severity markers (near-miss criteria) in all SMO cases

Table 4. Patient characteristics of women with MNM (not mutually exclusive) and all hospital births in the study period

	WHO		Namibian		SSA		Hospital births	
	n=71	%	n=118	%	n=242	%	n=9190	%
Hospital								
I	24	33.8	47	39.8	81	33.5	2189	23.8
II	24	33.8	31	26.3	62	25.6	2647	28.8
III	15	21.1	24	20.3	58	24.0	2496	27.2
IV	7	9.9	12	10.2	29	12.0	1481	16.1
V	1	1.4	4	3.4	12	5.0	377	4.1
Age								
< 20 years	8	11.3	16	13.6	31	12.8	1214	13.2
20 - 35	43	60.6	79	66.9	163	67.4	6807	74.1
> 35 years	20	28.2	23	19.5	48	19.8	995	10.8
Parity								
Nullipara	22	31.0	46	39.0	83	34.3	3151	34.3
1-3	34	47.9	50	42.4	110	45.5	4785	52.1
≥ 4	15	21.1	22	18.6	49	20.2	1221	13.3
Ethnicity							*Missing n=43*	
Maroon	32	45.1	48	40.7	89	36.8	2639	28.9
Creole	14	19.7	27	22.9	56	23.1	1993	21.8
Hindustani	9	21.7	17	14.4	31	12.8	1737	19.0
Javanese	6	8.5	8	6.8	18	7.4	943	10.3
Mixed	7	9.9	10	8.5	27	11.2	1135	12.4
Indigenous	2	2.8	5	4.2	12	5.0	348	3.8
Other	1	1.4	3	2.5	9	3.7	352	3.8
Residency	*Missing n=3*		*Missing n=7*		*Missing n=17*			
Urban	57	83.8	96	86.5	194	86.2	-	-
Coastal	7	10.3	8	7.2	18	8.0	-	-
Rural	4	5.6	7	6.3	13	5.8	-	-
Insurance	*Missing n=1*		*Missing n=3*		*Missing n=5*			
State	49	70.0	79	68.7	167	70.5	-	-
Private	14	20.0	25	21.7	52	21.9	-	-
None	7	10.0	11	9.6	18	7.6	-	-
Gestational age								
< 22 weeks	9	12.7	13	11.0	25	10.2	-	-
22 – 28 weeks	3	4.2	5	4.2	16	6.6	160	1.7
28 – 36 weeks	30	42.3	52	44.1	89	36.8	1143	12.4
≥ 37 weeks	29	40.8	48	40.7	112	46.3	7887	85.8
Pregnancy outcome								
Miscarriage	7	9.9	10	8.5	20	8.3	-	-
Ectopic	2	2.8	3	2.5	5	2.1	-	-
Vaginal delivery	34	47.9	53	44.9	119	49.2	6904	75.1
Vacuum or forceps	1	1.4	2	1.7	2	0.8	123	1.3
Caesarean section	27	38.0	50	42.4	96	39.7	2163	23.5

Figure 2. No. of women per MNM category and tool, reported in events



Legend

[1] Coagulation dysfunction high due to transfusion of two units (SSA-MNM, n=112) and four units (Namibian-MNM, n=31) vs WHO-MNM five units (n=15); [2] Additional criteria for [3] Namibia-MNM included eclampsia (n=44), uterine rupture (n=1) and laparotomy other than for CS or ectopic pregnancy (n=2); and for [3]SSA-MNM: eclampsia (n=44), uterine rupture (n=1), severe sepsis (n=40), pulmonary oedema (n=13), severe complications of abortion (n=21), severe pre-eclampsia with ICU-admission (n=103) and laparotomy other than CS (n=6).

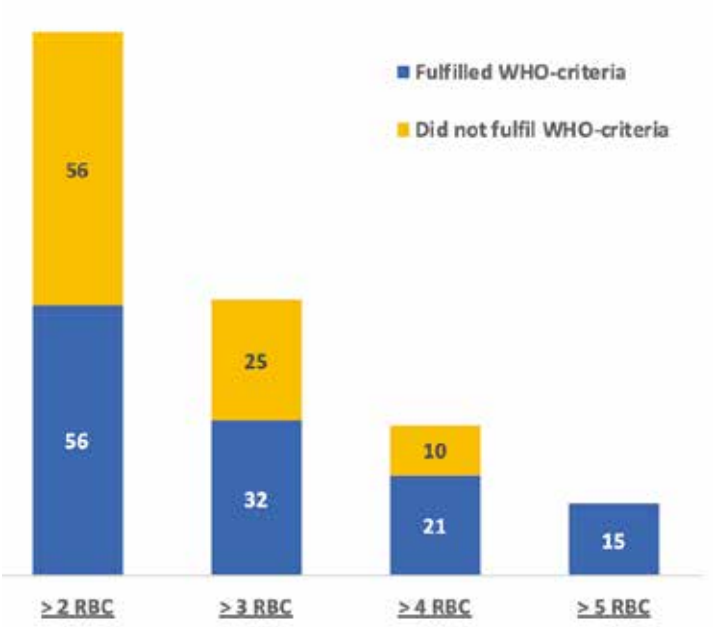
The three MNM-tools identified all maternal deaths. Patient characteristics are reported in Table 4. The proportion of women with MNM is highest in hospital I (34-40% compared to 24% of total births), which is the only referral hospital. Women of Maroon-descent represent majority of MNM (37-45%), while they account for 29% of total births.

Differences between MNM criteria

Figure 2 (and supplementary file 1 and 2) presents the distribution of MNM events. Laboratory MNM-events played a small role in the SSA-tool (9%, n=28/322) compared to WHO-tool (28%, n=31/109). The most important criteria were organ-dysfunction cardiovascular (27%), coagulation (27%) and respiratory (20%) for WHO-MNM, additional criteria (28%), coagulation (25%) and cardiovascular dysfunction (17%) for Namibian and additional criteria (48%) and coagulation dysfunction (32%) for the SSA tool. Transfusion of >4 red blood cell (RBC) products (Namibian-criteria), instead of the WHO threshold >5, led to an additional 10 cases of women without any WHO-MNM, while transfusion of >2 RBC (SSA-criteria) led to an additional 91 women without any WHO-MNM being included (figure 3). The transfusion of blood products was responsible for 21% (n=15/71) of WHO-MNM, 26% (n=31/118) of Namibian-MNM, and 46% (n=112/242) of SSA-MNM. Eclampsia was not considered a WHO-MNM in 80% (n=35/44) of cases as these women had no organ-dysfunction. Women with pre-eclampsia admitted to the ICU (n=64) had no WHO-MNM criteria in 62% (n=64/103).

Text box 1 illustrates disputable case examples of (1) women who were included in SurOSS but did not meet any MNM-criteria; (2) women included by Namibian- or SSA-MNM (not included by WHO-tool); (3) women included solely by SSA-MNM (not included by WHO or Namibian-tool); and (4) women with MNM in whom the severity of their disease is debatable.

Figure 3. Number of women who received red blood cell (RBC) products and fulfilled WHO MNM-criteria



Underlying causes

Hypertensive disorders of pregnancy (HDP) was the most frequent primary diagnosis in women with MNM (34% WHO-MNM, 52% Namibian-MNM) (figure 4). The case fatality-rate for HDP was 17% (n=4/24, WHO-MNM), 7% (n=4/61, Namibian-MNM), and 4% (n=4/97, SSA-MNM). Women had multiple diagnosis in 8-14%, for example: severe pre-eclampsia and thrombocytopenia followed by massive haemorrhage. The primary diagnosis of this case would be HDP (figure 4). In supplementary file 3 and 4 all diagnoses are reported (in number of events) and its underlying causes. The low number of maternal deaths (n=10) limited analysis of case fatality rates for the other diseases. However, 'other obstetric complications' and 'indirect, non-obstetric complications' are responsible for 60% (n=6/10) of maternal deaths, while they represent only 12-17% of underlying causes of MNM (12% Namibian- and SSA-MNM and 17% WHO-MNM).

Text box 1. Case examples of cases included with certain criteria

Severe morbidity according to SurOSS without any MNM criteria

1. Woman admitted with HELLP syndrome at 30 weeks of gestation, delivered a girl of 950 grams by CS who died two days later.
2. Woman had a severe post-partum psychosis post-partum, walked away and was never seen again.
3. ICU admission for severe hypokalaemia (1.8 mEq/L) and rhabdomyolysis (CK 10.000) due to pemba (clay) consumption.
4. Woman developed peri-partum cardiomyopathy three months post-partum and was admitted to ICU with moderate heart failure

Namibian- and SSA-MNM, not included by the WHO-criteria

1. A woman had three fits at home, was admitted with pre-eclampsia, stabilized and a caesarean section was performed. She had two fits post-partum.
2. A uterine rupture was discovered per-operatively in a woman with two previous CS. The woman received three packed cells and three fresh frozen plasma and was admitted to the ICU for severe haemorrhage (1500 mL). Her baby was in good condition.
3. Severe haemorrhage due to miscarriage at 19 weeks of gestation with haemoglobin level of 2.4 g/dL, for which patient was transfused 4 units RBC.
4. Laparotomy performed with suspicion for ectopic pregnancy, yet showed no ectopic mass. Post-operatively she developed a sepsis. Re-laparotomy showed an appendicitis and perforation of her intestines. An appendectomy and intestine repair were performed. Her pregnancy ended in a miscarriage.

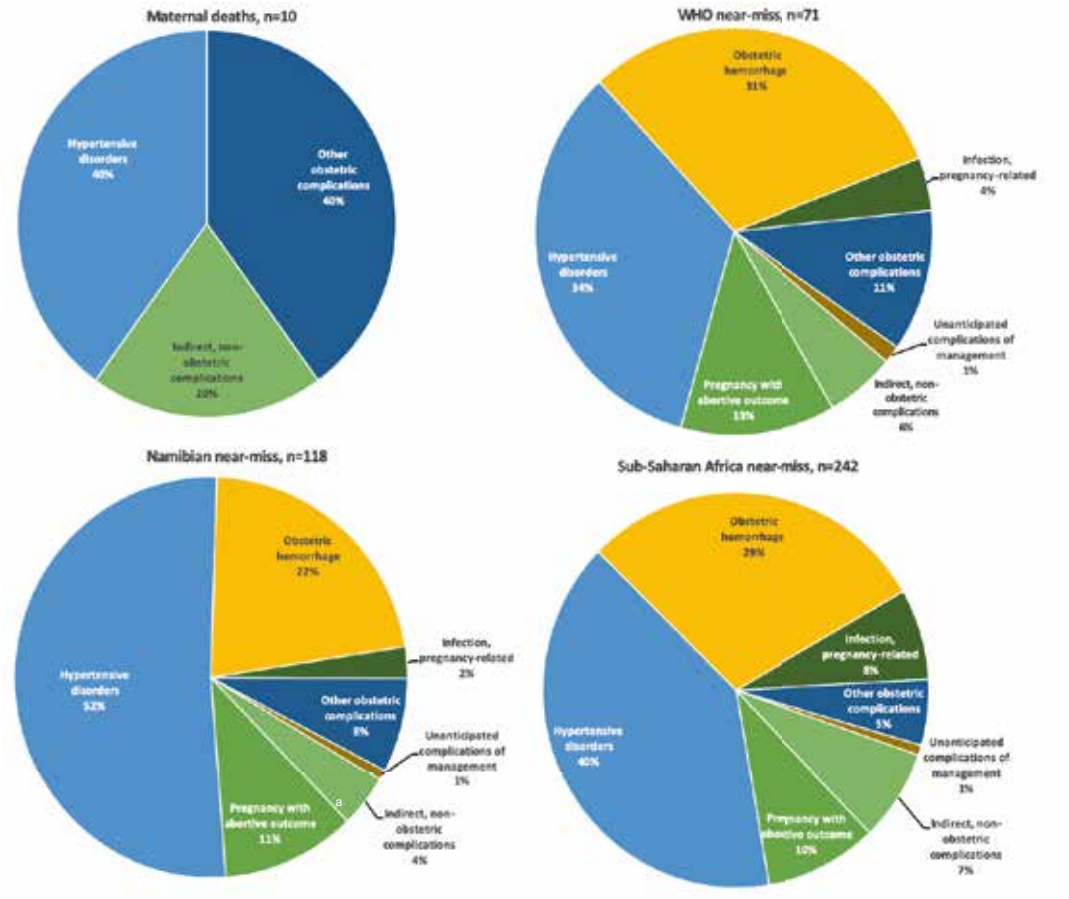
Additional SSA-MNM, not included by the WHO- or Namibian-criteria

1. Ruptured ectopic pregnancy, operated and complicated by a sepsis due to bilateral pneumonia for which she received intravenous antibiotics.
2. Severe pre-eclampsia, CS performed at 33 weeks. ICU admission for pulmonary oedema (received 4-litre fluids in first 24 hour).
3. A woman from the interior with a septic and haemorrhagic miscarriage referred from interior clinic to hospital and arrived 12 hours later. She was admitted to the ICU, treated with intravenous antibiotics and was transfused 3 units of RBC.
4. Severe antepartum haemorrhage due to placental abruption at 36 weeks of gestation with vaginal birth of stillbirth baby. She was diagnosed with HELLP syndrome and transfused three units of RBC, six units of fresh frozen plasma and two platelet suspensions.

MNM and debatable severity

1. Mild pre-eclampsia, uncomplicated term delivery with post-partum thrombocytopenia of 48,000 (platelets/mL) which resolved spontaneously. *(included by all MNM-tools)*
2. Transfusion of two units of RBC for post-partum haemorrhage of 700 mL and pre-delivery haemoglobin level of 9.4 g/dL. *(included by SSA MNM-tool)*
3. Post-partum pre-eclampsia ICU-admission for monitoring of blood pressure and magnesium sulfate therapy. No complications. *(included by SSA MNM-tool)*
4. In labour with fever, tachycardia with suspected chorioamnionitis for which antibiotics and CS. She recovered well. *(included by SSA MNM-tool)*

Figure 4. Primary underlying causes of maternal deaths and underlying diseases causing MNM according to the different tools



Legend: In the case of more than one near-miss event, the primary underlying cause was reported according to the ICD-MM guideline. Maternal death "other obstetric complications" was caused by amniotic fluid embolism (n=1), pulmonary embolism (n=4) and peri-partum cardiomyopathy (n=1).

Table 5. Association between WHO MNM and perinatal outcomes (MNM n=57, no MNM n=9123)

Maternal characteristics										
	MNM[1]	**No MNM**	**cOR**	**95% CI**		**p-value**	**aOR**	**95% CI**		**p-value**
Teen pregnancy	6 / 56 (10.7%)	1208 / 8950 (13.5%)	0.76	0.33	1.78	0.529	-			
Advanced mat age	15 / 56 (26.8%)	978 / 8950 (10.9%)	3.12	1.79	5.44	**<0.001**	**2.59**	**1.37**	**4.88**	**0.003**
Maroon ethnicity	27 / 56 (48.2%)	2608 / 9082 (28.7%)	2.31	1.37	3.91	**0.002**	**2.04**	**1.15**	**3.61**	**0.015**
Nullipara	17 / 57 (29.8%)	3132 / 9091 (34.5%)	0.81	0.46	1.43	0.464	-			
Grande multipara	16 / 57 (28.1%)	1203 / 9091 (13.2%)	2.56	1.43	4.57	**0.002**	1.63	0.83	3.21	0.158
Multiple pregnancy	1 / 57 (1.8%)	120 / 9123 (1.3%)	1.34	0.18	9.76	0.773	-			
Perinatal outcomes										
	MNM[2]	**No MNM**	**cOR**	**95% CI**		**p-value**	**aOR**	**95% CI**		**p-value**
Low birth weight	27 / 55 (49.1%)	1299 / 9076 (14.3%)	5.77	3.39	9.83	**<0.001**	1.02[3]	0.41	2.57	0.960
Preterm birth	31 / 57 (54.4%)	1270 / 9123 (13.9%)	7.37	4.36	12.46	**<0.001**	2.65[4]	0.97	7.23	0.058
Low Apgar 5 min	6 / 43 (14.0%)	227 / 8850 (2.6%)	6.16	2.57	14.74	**<0.001**	2.45[5]	0.84	7.13	0.100
Late stillbirth	11 / 57 (19.3%)	111 / 9123 (1.2%)	19.42	9.80	38.47	**<0.001**	**6.83[5]**	**2.96**	**15.76**	**<0.001**

Legend: GA: gestational age; [1] MNM is the dependent variable; [2] MNM is the independent variable; Adjusted for [3] age, parity ethnicity, gestational age, Apgar score and stillbirth; [4] age, parity ethnicity, birth weight, Apgar score and stillbirth; [5] age, parity, ethnicity, gestational age and birth weight

Factors associated with MNM

For the WHO-criteria advanced maternal age and maroon ethnicity were associated with MNM, with respectively aOR 2.59 (95%CI 1.37-4.88) and aOR 2.04 (95%CI 1.15-3.61) after adjustment for age, parity, and ethnicity (table 5). For the Namibian-criteria only maroon ethnicity was associated with MNM, aOR 1.93 (95%CI 1.25-2.99) after adjustment for age and parity (supplementary file 5). For the SSA-criteria, next to advanced maternal age and maroon ethnicity, multiple pregnancy was significantly associated with MNM (aOR 3.38, 95%CI 1.68-6.81) (supplementary file 6).

The stillbirth rate among women with WHO-MNM is 193/1000 births (n=11/57), and 153/1000 births (n=15/98) and 110/1000 births (n=23/209) for respectively Namibian-and SSA-MNM. Women without MNM had a stillbirth rate of 12/1000 births (n=111/9123). Univariate analysis showed highly significant association between MNM and adverse perinatal outcomes (low birth weight, preterm birth, low Apgar score, and stillbirths) for the three MNM-criteria (table 5, supplementary files 5 and 6). In multivariate analysis only stillbirths remained significantly associated with MNM (WHO MNM: aOR 6.83, 95%CI 2.96-15.76, Namibian-MNM: aOR 4.75, 95%CI 2.34-9.62 and SSA-MNM: aOR 3.98, 95%CI 2.24-7.06) after adjustment for age, parity, ethnicity, gestational age and birth weight.

DISCUSSION

This nationwide population-based study in Suriname demonstrated that for every woman who died, between seven and twenty-four women experienced MNM, depending on the type of MNM criteria used. The WHO-MNM criteria detected all maternal deaths and resulted in a mortality-index of 12% (n=10/71), which justified the WHO terminology life-threatening. However, WHO-criteria underestimate the prevalence of severe complications as certain disease-based complications such as eclampsia with a high case fatality rate are not included. Namibian-MNM (which included disease- and intervention) criteria led to more cases and a lower mortality-index (8%, n=10/118). Application of the SSA-MNM (excluded the majority of laboratory-criteria and added several disease-based criteria) resulted

in more cases and a lower mortality-index (4%, n=10/242). SSA-MNM may have overestimated the prevalence of MNM since not all complications directly threatened the woman's life. For all three MNM tools, hypertensive disorders of pregnancy contributed most frequently to MNM. Advanced maternal age and maroon ethnicity were associated with MNM and women with MNM had six times the odds of a stillbirth. The absence of applicable and globally comparable MNM-criteria prevents countries such as Suriname from the sustainable implementation of MNM-registration.

Maternal near-miss criteria and obstetric transition stages

The fundamental aim of studying MNM is twofold: 1) to have globally comparable data on MNM and 2) to capture MNM cases and determine causes of MNM, which ultimately improve maternal health care and reduces maternal mortality.[2] The global universal WHO-MNM tool best achieves the first aim. Because MNM criteria are not as clear cut as other maternal health indicators (e.g., MMR, stillbirth rate), underreporting is inevitable and will occur in all settings, most substantially in low-income settings.[9-12,21,22] If the purpose is to find solutions for the most critical problems associated with severe maternal outcomes (the second fundamental aim), local adaptations are unavoidable, though this subverts the first aim of globally comparable data.

Contextually-tailored MNM criteria may be the answer to achieve both fundamental aims of uniformity and applicability of MNM criteria. One contextual approach could be to incorporate the 'obstetric transition framework', which assimilates context-specific analysis and recommendations to improve the quality of care.[23] The framework, developed by Souza et al. (2014), describes the transition from higher MMR/fertility to low MMR/fertility within and between countries.[23] The problems and solutions for countries in obstetric transition stage I and II are incomparable to countries in stage III and IV. For example, in the first two stages, many maternal deaths occur and access to care and the availability of educated staff and resources play the most crucial role in reducing maternal mortality in these stages. Studying maternal mortality is of primary importance, and MNM studies

play a limited role. However, if MNM studies are to be performed in these stages (e.g., in rural settings with a low number of deaths), criteria should focus on 'direct' causes of maternal mortality (e.g., severe haemorrhage and eclampsia). Stage III is known as a complicated stage as access to care is improved, and quality of care becomes a significant determinant of health outcomes. As maternal mortality decreases, MNM studies play an increasingly important role. The threshold of specific criteria (e.g., blood transfusion) is higher than in stage I-II, and more focus is needed on 'indirect' causes. In stage IV, maternal mortality rates are low and severe outcomes are often the result of 'overmedicalization' and more high-risk pregnancies (high maternal age, non-communicable diseases, and pregnancies in women with severe comorbidities).[23] MNM criteria in these stages need to focus on rare diseases with high case fatality rates (e.g., abnormally invasive placentation, amniotic fluid embolism as proposed by the INOSS[18]), to reduce maternal mortality and reach the mostly aspirational stage V.

Organ-based versus disease-based criteria

Case identification is more feasible when using disease-based criteria, than organ-dysfunction criteria (25-item list with many cut-off values).[2,17,24-26] For example, clinicians easily identify a woman with eclampsia, while women with transient tachypnoea or thrombocytopenia are more difficult to identify. Another advantage of disease-based criteria is that the underlying problem is better understood and risk factors and case-fatality rates are easier to interpret. This makes it easier to identify gaps in the quality of care and find potential solutions to these problems. An illustrative example is the impact of disease-based criteria comparison between the Netherlands and the United Kingdom.[24] The observation that the Netherlands had a five-fold incidence of eclampsia, stemming from differences in clinical management, prompted rapid eclampsia incidence reductions through the implementation of different management protocols.[25]

The WHO working group on Maternal Mortality and Morbidity Classification stated that organ dysfunction captures the severest diseases, and that disease-based criteria often have too low threshold to be considered ‘severe’ morbidity, and risk

variation in definition and identification [6,7]. While organ-dysfunction are in the sequence of events leading from good health to death, it is not always measurable. An example is that only a small percentage of women with eclampsia in Suriname had measurable organ-dysfunction criteria, despite being very ill and nearly dead.[26] Although the inclusion threshold for near-miss is lower with most WHO disease-based criteria (e.g. severe post-partum haemorrhage, sepsis and pre-eclampsia), it does not outweigh the benefits of clinical relevance and more feasible case identification. This would justify the initiation of a global consensus process for (higher threshold) definitions of severe morbidity and near-miss, as done by INOSS and the Core Outcomes in Women' and Newborn (CROWN) Health initiative.[18,27]

Comparing prevalence and case-fatality rates

When comparing the prevalence of WHO-MNM to the region, Suriname has a similar prevalence to Brazilian referral hospitals (9.4 per 1000 live births).[28] No comparison with other Latin America/Caribbean countries is possible, as the studies are conducted in single sites, have limited case numbers, and have modified the criteria.[3,9,29] The lack of comparison possibilities emphasises how crucial it is to apply uniform MNM criteria (as proposed by the WHO-tool) to report the prevalence of MNM in countries reliably. The proportion of maternal deaths and WHO-MNM due to hypertensive disorders of pregnancy in Suriname was high, 40%, and 34%, respectively. HDP are known to contribute significantly to maternal deaths in Latin America (22%), and for unclear reasons as the coverage of medication such as magnesium sulfate is adequate.[4] Currently, women with eclampsia are not included in MNM-criteria, while this disease is on the severest side of the spectrum of HDP. Only 80% of women with eclampsia in Suriname had WHO-MNM criteria, similar to previous studies.[11,12] Excluding eclampsia from MNM limits analysis of the factors contributing to the high burden of HDP. We are more likely to eliminate preventable maternal deaths if MNM studies were to include disease-based criteria with high case-fatality rates (such as eclampsia). While MNM studies serve to monitor the quality of care by reporting numbers and trends, they barely facilitate the development of quality improvement strategies.[3,8-

[12] Near-miss audits are necessary to identify the lessons learned and to develop justified recommendations. The action and response to these findings and recommendations will finally reduce severe maternal (and perinatal) outcomes.[25]

Risk factors and adverse outcomes

Identifying risk factors is vital to guide interventions to reduce severe maternal and perinatal outcomes. However, as maternal near-miss consists of different diseases in different proportions, risk factors can be challenging to interpret. For example, while post-partum haemorrhage is associated with grand multiparity, eclampsia is prevalent among younger nulliparous women.[29-31] If the proportion is similar, the net result might be no association between parity and maternal near-miss (including both post-partum haemorrhage and eclampsia), as seen in our study. Similarly, old maternal age is a well-known risk factor for a broad spectrum of obstetric complications[31] and is strongly correlated with MNM in our study, as well as in a large multi-country study.[32] However, if the proportion of eclampsia-related MNM increases (in Namibian-MNM), the association between maternal age and MNM disappears. Equivalent to previous studies in Suriname, women of Maroon descent are at increased risk of adverse pregnancy outcomes as they have twice the odds of MNM compared to women of other ethnicities (for all three tools).[13,14] These ethnic disparities may reflect socioeconomic inequalities and inequity within the healthcare system and need more attention. Ethnic disparities in severe maternal outcomes have also been reported in Brazil and high-income countries (e.g., the United States, the Netherlands, and Germany).[33-36]

Although it is clear that complications leading to MNM also contribute to adverse perinatal outcomes, the magnitude and causes of perinatal deaths among women with MNM are mainly unknown in low- and middle-income countries. The stillbirth rate among women with WHO-MNM in Suriname (193/1000 births) is higher than reported in Brazil (140/1000 births)[37] or other Latin American countries (128/1000 births)[30], and lower than in low-resource settings (e.g., Ethiopia 284/1000 births)[38]. The higher stillbirth rate among women with WHO-criteria (than Namibian- or SSA-criteria) further confirms that the WHO-tool

comprises of the most clinically severe criteria. Improving national data collection of childbirth outcomes, disaggregated for maternal conditions, is necessary to improve identification and quantify factors that contribute to maternal complications and adverse perinatal outcomes.

Finally, compared to solely MNM registration, an audit of maternal near-miss is more likely to identify shortfalls in clinical practice and lead to improvements in both maternal and perinatal outcomes. While MNM-tools register the number of severe maternal outcomes, an audit is necessary to reveal the actual 'lessons to be learned'.[39] Recommendations can be formed through these 'lessons learned', which encourage targeted action and response (e.g. guideline updates, enabling policies and legislation, conduct research to fulfil knowledge gaps). This cycle of continuous evaluation, 'maternal death and near-miss surveillance and response', is essential in the elimination of preventable severe maternal outcomes and deserves a more prominent place in MNM studies.[39-41]

Strengths and limitations

Our study's strengths are the nationwide setting, prospective identification and robust data collection over a long period, and availability of background data on all deliveries. Several limitations need to be considered. First, we extracted data from patient records after discharge, and specific parameters (socioeconomic status, BMI) were unavailable. Second, reference data was limited to simple characteristics as no perinatal registry is yet in place and included no primary care and home births. Finally, we were not able to apply all SSA-criteria (e.g., transfusion >2 RBC products) as SSA-criteria were published after the initiation of our study. The SSA-MNM prevalence is, therefore, higher than reported in our study.

CONCLUSION

The MNM-ratio in middle-income country Suriname is 8 per 1000 live births according to the WHO-MNM tool. The Namibian- and SSA-MNM ratios are 13 and 27 per 1000 live birth. MNM may be underreported by the WHO (mortality-index 12%) and overreported by Namibian- and SSA-MNM (mortality-index 8% and 4%). Solutions to prevent under- and overreporting without compromising comparability can be to (1) create context-specific MNM-criteria per obstetric transition stage and; (2) use disease-based criteria. Advanced maternal age and maroon ethnicity were associated with MNM and women with MNM had six times the odds of a stillbirth. While MNM allows identification of women with severe outcomes, an audit is necessary to identify shortfalls in clinical practice and reduce severe maternal and perinatal outcomes.

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Supplementary file 1. MNM events by WHO, Namibian and SSA clinical, laboratory and management criteria

	WHO n=71	Namibian n=118	SSA n=242
Clinical criteria	**44**	**82**	**174**
Acute cyanosis	0	0	0
Gasping	2	2	2
Respiratory rate >40 or <6/min	11	11	11
Shock	24	24	24
Oliguria non responsive to fluids or diuretics	6	6	6
Failure to form clots	4	4	4
Loss of consciousness lasting more than 12 h	10	10	10
Cardiac Arrest	2	2	2
Stroke	2	2	2
Uncontrollable fits / total paralysis	6	6	6
Jaundice in the presence of pre-eclampsia	0	0	0
Eclampsia[1]	✘	44	44
Ruptured uterus[1]	✘	1	1
Sepsis or severe systemic infection[2]	✘	✘	40
Pulmonary oedema[2]	✘	✘	13
Severe complications of abortion[2]	✘	✘	21
Severe malaria[2]	✘	✘	0
Severe pre-eclampsia with ICU admission[2]	✘	✘	103
Laboratory criteria	**31**	**31**	**28**
Oxygen saturation <90% for >60 minutes	8	8	8
PaO2/FiO2 <200 mmHg[3]	0	0	✘
Creatinine ≥300µmol/l or ≥3.5 mg/dl	4	4	4
Bilirubin >100 µmol/l or > 6.0 mg/dl[3]	2	2	✘
pH <7.1[3]	2	2	✘
Lactate >5 mEq/mL[3]	1	1	✘
Acute thrombocytopenia (<50.000 platelets/ml)	17	17	17
Loss of consciousness and glucose/ketoacids in urine	1	1	1
Management-based criteria	**34**	**48**	**122**
Use of continuous vasoactive drugs[3]	7	7	✘
Hysterectomy following infection or haemorrhage	4	4	4
Transfusion of .. units of blood or red cells	15[4]	31[5]	112[6]
Intubation and ventilation not related to anaesthesia	15	15	15
Dialysis for acute renal failure	1	1	✘
Cardiopulmonary resuscitation	2	2	2
Laparotomy other than for caesarean section[2]	✘	✘	6
Laparotomy other than for caesarean or ectopic pregnancy[7]	✘	2	✘

Legend: [1]Criterion added by Namibian and SSA-tools; [2]Criterion added by SSA-tool; [3]Criterion excluded by SSA-tool; [4]Five blood products; [5]Four blood products; [6]Two blood products; [7]Criterion added by Namibian-tool;

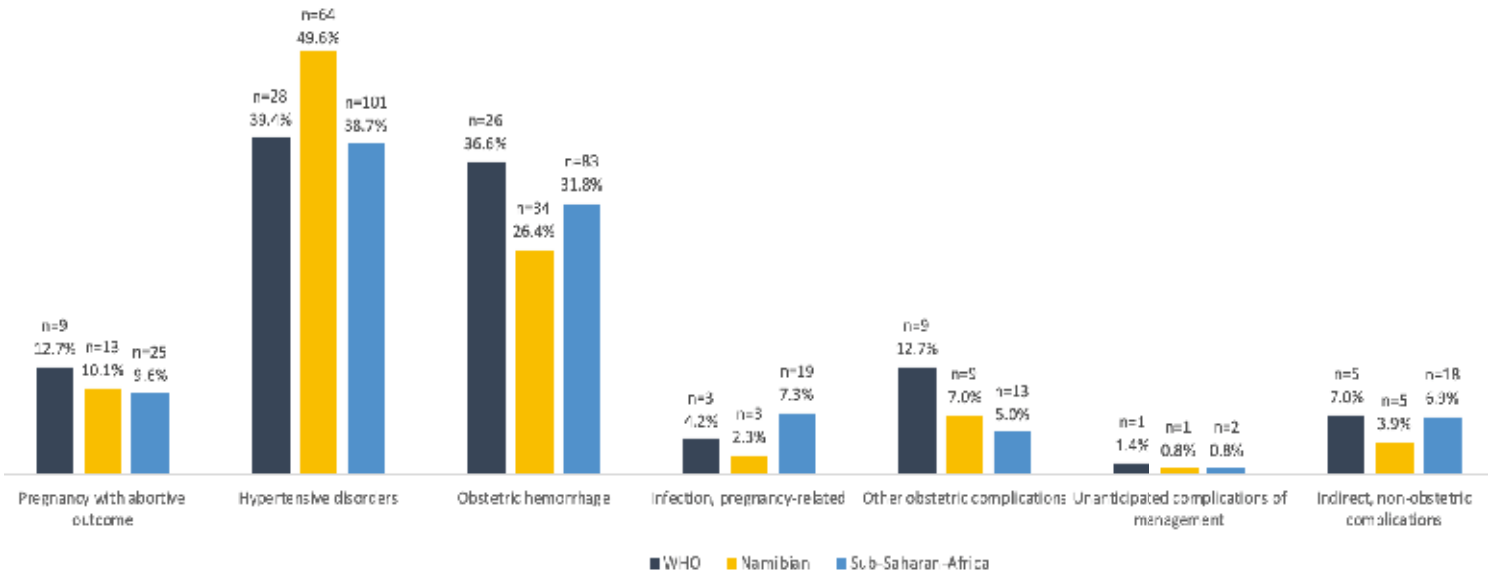
✘ Not a criterion according to the specified tool

Supplementary file 2. MNM events by WHO, Namibian and SSA organ-dysfunction

	WHO n=71	Namibian n=118	SSA n=242
Cardiovascular dysfunction	**29**	**29**	**26**
Shock	24	24	24
Cardiac Arrest	2	2	2
Use of continuous vasoactive drugs[1]	7	7	✘
Cardiopulmonary resuscitation	2	2	2
Lactate >5mml/l[1]	1	1	✘
pH <7.1[1]	2	2	✘
Respiratory dysfunction	**22**	**22**	**22**
Acute cyanosis	0	0	0
Gasping	2	2	2
Respiratory rate >40 or <6/min	11	11	11
Intubation/ventilation not related to anaesthesia	15	15	15
Oxygen saturation <90% for >60 minutes	8	8	8
PaO2/FiO2 <200 mmHg[1]	0	0	✘
Renal dysfunction	**9**	**9**	**9**
Oliguria non responsive to fluids or diuretics	6	6	6
Dialysis for acute renal failure[1]	1	1	✘
Creatinine ≥300µmol/l or ≥3.5 mg/dl	4	4	4
Coagulation/haematological dysfunction	**29**	**42**	**119**
Failure to form clots	4	4	4
Transfusion of .. units of blood or red cells	15[5]	31[6]	112[7]
Severe acute thrombocytopenia (<50.000/ml)	17	17	17
Hepatic dysfunction	**2**	**2**	**0**
Jaundice in the presence of pre-eclampsia	0	0	0
Bilirubin >100 µmol/l or > 6.0 mg/dl[3]	2	2	✘
Neurological dysfunction	**13**	**13**	**13**
Loss of consciousness lasting more than 12 h	10	10	10
Loss of consciousness, glucose/ketoacids in urine	1	1	1
Stroke	2	2	2
Uncontrollable fits / total paralysis	6	6	6
Uterine dysfunction	**4**	**4**	**4**
Hysterectomy following infection or haemorrhage	4	4	4
Additional parameters	✘	**47**	**176**
Eclampsia[2]	✘	44	44
Ruptured uterus[2]	✘	1	1
Sepsis or severe systemic infection[3]	✘	✘	40
Pulmonary oedema[3]	✘	✘	13
Severe complications of abortion[3]	✘	✘	21
Severe malaria[3]	✘	✘	0
Severe pre-eclampsia with ICU admission[3]	✘	✘	103
Laparotomy other than for CS[3]	✘	✘	6
Laparotomy other than for CS or ectopic pregnancy[4]	✘	2	✘

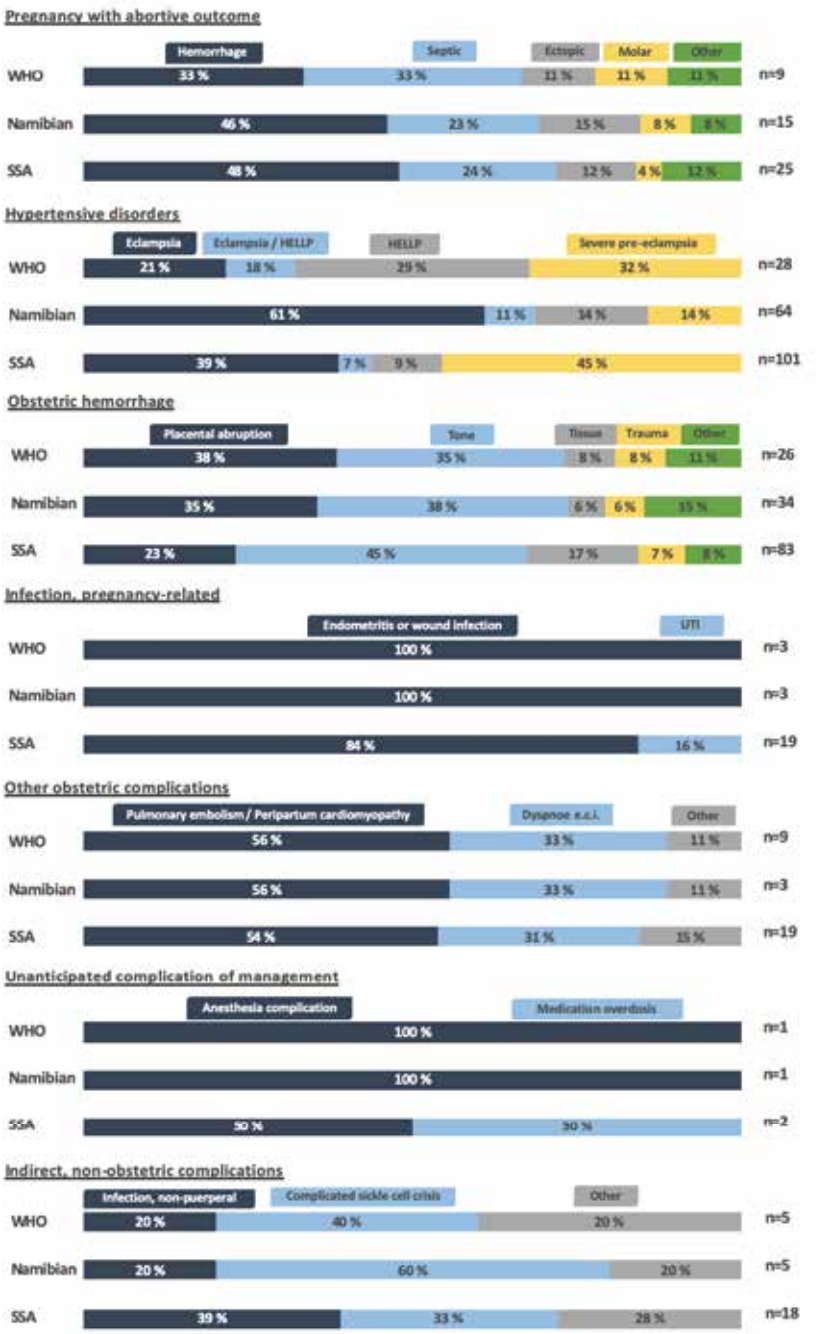
Legend: [1]Criterion excluded by SSA-tool; [2] Criterion added by Namibian and SSA-tools; [3]Criterion added by SSA-tool;[4]Criterion added by Namibian-tool; [5]Five blood products; [6]Four blood products; [7]Two blood products;
✘ Not a criterion according to the specified tool

Supplementary file 3. Underlying causes of MNM for the different tools, number of events



Legend: Number of events reported, therefore not mutually exclusive. [1] WHO-MNM: one underlying cause (n=61) and two underlying causes (n=10); [2] Namibian-MNM: one underlying cause (n=107) and two underlying causes (n=11); [3] SSA-MNM: one underlying cause (n=223) and two underlying causes (n=19).

Supplementary file 4. Distribution of the underlying causes and differences between the MNM criteria, number of events



Supplementary file 5. Association between Namibian MNM and perinatal outcomes (MNM n=98, no MNM n=9082)

Maternal characteristics										
	MNM[1]	**No MNM**	**cOR**	**95% CI**		**p-value**	**aOR**	**95% CI**		**p-value**
Teen pregnancy	13 / 98 (13.3%)	1201 / 8989 (13.4%)	0.99	0.55	1.78	0.978				
Advanced mat age	20 / 97 (20.6%)	1275 / 8980 (14.2%)	1.57	0.96	2.58	0.075				
Maroon ethnicity	43 / 97 (44.3%)	2592 / 9041 (28.7%)	1.98	1.32	2.97	**0.001**	1.93	1.25	2.99	**0.003**
Nullipara	39 / 98 (39.8%)	3110 / 9050 (34.4%)	1.26	0.84	1.90	0.261				
Grande multipara	22 / 98 (22.4%)	1197 / 9050 (13.2%)	1.90	1.18	3.06	**0.009**	1.47	0.86	2.53	0.162
Multiple pregnancy	1 / 98 (1.0%)	120 / 9082 (1.3%)	0.77	0.11	5.57	0.796				
Perinatal outcomes										
	MNM[2]	**No MNM**	**cOR**	**95% CI**		**p-value**	**aOR**	**95% CI**		**p-value**
Low birth weight	48 / 94 (51.1%)	1278 / 9037 (14.1%)	6.34	4.21	9.53	**<0.001**	1.34[3]	0.67	2.67	0.41
Preterm birth	53 / 98 (54.1%)	1248 / 9082 (13.7%)	7.39	4.95	11.05	**<0.001**	**2.25[4]**	**1.11**	**4.56**	**0.025**
Low Apgar 5 min	9 / 78 (11.5%)	224 / 8815 (2.5%)	5.00	2.47	10.15	**<0.001**	1.91[5]	0.83	4.39	0.128
Late stillbirth	15 / 98 (15.3%)	107 / 9082 (1.2%)	15.2	8.5	27.1	**<0.001**	**4.74[5]**	**2.34**	**9.62**	**<0.001**

Legend: GA: gestational age; [1] MNM is the dependent variable; [2] MNM is the independent variable; Adjusted for [3] age, parity ethnicity, gestational age, Apgar score and stillbirth; [4] age, parity ethnicity, birth weight, Apgar score and stillbirth; [5] age, parity, ethnicity, gestational age and birth weight

Supplementary file 6. Association between SSA-MNM and perinatal outcomes (MNM n=209, no MNM n=8971)

Maternal characteristics										
	MNM[1]	**No MNM**	**cOR**	**95% CI**		**p-value**	**aOR**	**95% CI**		**p-value**
Teen pregnancy	23 / 208 (11.1%)	1191 / 8879 (13.4%)	0.80	0.52	1.24	0.324				
Advanced mat age	45 / 207 (21.7%)	1250 / 8870 (14.1%)	**1.69**	**1.21**	**2.37**	**0.002**	**1.50**	**1.03**	**2.20**	**0.036**
Maroon ethnicity	76 / 208 (36.5%)	2559 / 8930 (28.7%)	**1.43**	**1.08**	**1.91**	**0.014**	**1.42**	**1.04**	**1.94**	**0.027**
Nullipara	74 / 208 (35.6%)	2075 / 8940 (34.4%)	1.05	0.79	1.40	0.723				
Grande multipara	43 / 208 (20.7%)	1176 / 8940 (13.2%)	**1.72**	**1.22**	**2.42**	**0.002**	1.36	0.93	1.99	0.113
Multiple pregnancy	9 / 209 (4.3%)	112 / 8971 (1.2%)	**3.56**	**1.78**	**7.12**	**<0.001**	**3.38**	**1.68**	**6.81**	**0.001**
Perinatal outcomes										
	MNM[2]	**No MNM**	**cOR**	**95% CI**		**p-value**	**aOR**	**95% CI**		**p-value**
Low birth weight	92 / 202 (45.5%)	1234 / 8929 (13.8%)	**5.22**	**3.93**	**6.92**	**<0.001**	1.45[3]	0.92	2.92	0.114
Preterm birth	101 / 209 (48.3%)	1200 / 8971 (13.4%)	**6.06**	**4.59**	**8.00**	**<0.001**	**2.57[4]**	**1.62**	**4.11**	**<0.001**
Low Apgar 5 min	20 / 172 (11.6%)	213 / 8721 (2.4%)	**5.26**	**3.23**	**8.54**	**<0.001**	**2.41[5]**	**1.36**	**4.30**	**0.003**
Late stillbirth	23 / 209 (11.0%)	99 / 8971 (1.1%)	**11.08**	**6.88**	**17.84**	**<0.001**	**3.98[5]**	**2.24**	**7.06**	**<0.001**

Legend: GA: gestational age; [1] MNM is the dependent variable; [2] MNM is the independent variable; Adjusted for [3] age, parity ethnicity, gestational age, Apgar score and stillbirth; [4] age, parity ethnicity, birth weight, Apgar score and stillbirth; [5] age, parity, ethnicity, gestational age and birth weight

Investigation of stillbirth causes in Suriname: application of the WHO ICD-PM tool to national-level hospital data

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Zita D. Prust*
Kim J. C. Verschueren*
Gieta A.A. Bhikha-kori
Lachmi R. Kodan
Kitty W. M. Bloemenkamp
Joyce L. Browne
Marcus J. Rijken
**Contributed equally*

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ABSTRACT

Background: Suriname has one of the highest stillbirth rates in Latin America and the Caribbean. To facilitate data comparison of perinatal deaths, the World Health Organization developed the International Classification of Diseases-10 Perinatal Mortality (ICD-PM).

Objective: We aimed to (1) assess characteristics and risk indicators of women with a stillbirth, (2) determine the timing and causes of stillbirths according to the ICD-PM with critical evaluation of its application, and (3) propose recommendations for the reduction of stillbirths in Suriname.

Methods: A hospital-based, nation-wide, cross-sectional study was conducted in all hospitals within Suriname during one-year (2017). The medical files of stillbirths (gestation ≥28 weeks/birth weight ≥1000 grams) were reviewed and classified using ICD-PM. We used descriptive statistics and multiple logistic regression analyses to identify risk indicators.

Results: The stillbirth rate in Suriname was 14.4/1000 births (n=131 stillbirths, n=9089 total births). Medical files were available for 86% (n=113/131) of stillbirths. Women of African descent had the highest stillbirth rate and two times the odds of stillbirth (OR 2.1, 95%CI 1.4-3.1) compared to women of other ethnicities. One third (33%, n=37/113) of stillbirths occurred after hospital admission. The timing of the stillbirth was antepartum in 85% (n=96/113), intrapartum in 11% (n=12/113) and unknown in 4% (n=5/113) of cases. Antepartum stillbirths were caused by *hypoxia* in 46% (n=44/96). In 41% (n=39/96) the cause was unspecified. *Maternal medical and surgical conditions* were present in 50% (n=57/113), mostly hypertensive disorders.

Conclusion: Stillbirth reduction strategies in Suriname call for targeting ethnic disparities, improving antenatal services, implementing perinatal death audits, and post-mortem investigations. ICD-PM limited the formulation of recommendations

due to many stillbirths of 'unspecified' causes. The diagnostic work-up of stillbirths needs to be improved to increase knowledge of stillbirth causes. Based on our study findings, we also recommend addressing some challenges with applying the ICD-PM.

BACKGROUND

Stillbirth is one of the most common adverse pregnancy outcomes. It is often related to severe maternal morbidity and associated with long-lasting psychosocial distress for mothers and their families. However, stillbirths often remain hidden from society.[1] The estimated worldwide stillbirth rate (SBR) is 18.4 per 1000 births, yet the numbers vary substantially per country (1.3 to 43.1 per 1000 total births).[2] Most stillbirths (98%) occur in low- and middle-income countries (LMIC), affecting the most marginalised communities. Therefore, this also makes it an equality and equity issue.[1,2] Although the Sustainable Development Goals do not explicitly state a stillbirth reduction target, it is an essential indicator for the quality of care in pregnancy and childbirth and a sensitive marker of a healthcare system's strength.[3,4] The World Health Organization's (WHO) *Every Newborn Action Plan (ENAP)* aims to reduce stillbirths globally, with the target of no more than 12 stillbirths per 1000 total births in every country by 2030.[1] Despite the endorsement of the ENAP and an increase in the number of studies on stillbirths, most countries have not yet defined a stillbirth reduction target in their national health plans.[4,5]

Stillbirths should be systematically assessed to identify risk factors and causes and provide strategies for reducing the SBR.[6] Obtaining reliable statistics is challenging since stillbirths are often poorly documented by the vital registry.[4-7] A literature review[8] revealed that, between 2009 and 2014, more than 81 systems were in place to classify causes of perinatal deaths, complicating cross-country comparison.[8] In response, the WHO developed a universal classification system, the International Classification of Disease 10 Perinatal-Mortality (ICD-PM) to harmonise classifications and facilitate global data comparison on causes of perinatal deaths.[9] A pilot study in South-Africa and the United Kingdom validated the ICD-PM as the

global standard for perinatal death classification.[10] Thus far, no countries in Latin America or the Caribbean have applied the ICD-PM to stillbirths.

A previous nationwide study on perinatal outcomes in Suriname, South America, in 2016 and 2017 reported an SBR of 14.8 per 1000. This ranked Suriname with the second-highest SBR of Latin America and the Caribbean.[11,12] The reason for Suriname's high stillbirth rate is unknown. Similar to many other LMIC, no stillbirth registry or classification system is in place, and no perinatal death audits are performed.[4,5,11] To develop an adequate stillbirth reduction strategy, in-depth investigation into stillbirths is necessary to identify risk factors, causes, and contributing factors. Therefore, we introduced the WHO ICD-PM tool and applied this to national-level hospital data. This study aimed to (1) assess pregnancy characteristics and risk indicators of women with stillbirths in Suriname, (2) determine the timing and causes of stillbirths according to the ICD-PM and evaluate the applicability of the tool and (3) propose recommendations for the reduction of stillbirths in Suriname.

METHODS

Study design: A nationwide, hospital-based, cross-sectional study was conducted in all five hospitals in Suriname over 1 year, from 1 January to 31December, 2017.

Study Setting: Suriname is a multi-ethnic, upper-middle-income country on the northeast coast of South America.[13] In 2018, the population counted 575,991 people, of which approximately 90% live in Paramaribo or along the coastline.[14,15] Of the five hospitals in the country, four are located in the capital Paramaribo (including one tertiary hospital), and one in Nickerie, a town on the northwest coast. About 86% of all deliveries in Suriname occur in these five hospitals (one public tertiary facility and four public secondary facilities). The public primary healthcare centres perform 6% of births, mostly in the interior and rural coastal areas. Of the remaining 8%, half are home births and half unknown.[15] Suriname has one of the most ethnically diverse populations globally, with each group preserving

its own culture.[15] The ethnic distribution in Suriname is Hindustani (27%), Maroon (22%), Creole (16%), Javanese (14%), Mixed (13%), Indigenous (4%), Chinese (1%) and Other (3%) in 2018.[12,14,15] Suriname's ethnic diversity reflects its history. Indigenous people, also known as Amerindians, are the original inhabitants of the country. Maroons and Creoles are of (West-) African descent, as they were enslaved and brought to Suriname in the seventeenth and eighteenth centuries. In contrast to Creoles, Maroon people escaped from slavery and fled into Suriname's interior where they lived separately from the rest of the population for decades. Following the abolition of slavery in 1863, Creoles gained their freedom. They sometimes have mixed African-European (Dutch and British) ancestry. People of Asian descent, Hindustani (from East-India), Javanese (from Indonesia, then a Dutch-ruled colony) and Chinese people, came to Suriname in the late nineteenth century as contract workers. Mixed ethnicities are the result of interchanging identities between almost all ethnicities. Other ethnicities include Brazilians, Caucasians (descendants of Dutch colonists) and a few Lebanese.[12,15] Maroon and Indigenous women belong to the poorest quartile of Suriname.[15] We classified ethnicities with the necessary ethical considerations: the principles of autonomy were embraced (by self-reporting of ethnicity by patients), there were no interventions (observational study), and reporting of disparities aimed to reduce inequity at the beneficence of women with poorer outcomes.

Eligibility Criteria: We included all live births and stillbirths of babies at or beyond 28 weeks of gestation or with a birth weight of $\geq$ 1000 grams (WHO definition) in Suriname's hospitals.[9,16] The SBR was defined as the number of late stillbirths per 1000 total births.[9] Gestational age was determined using early ultrasound examination, as this is a standard procedure during antenatal care visits. If no early ultrasound examination had been performed, later ultrasound examinations or the estimated last menstruation were used to estimate gestational age. Live births during the study period were used as the reference group to analyse risk indicators.

Variables: Age categories were based on definitions used in previous studies of teenage pregnancies (<20 years) and pregnancies at advanced maternal age (≥35 years).[17,18] Grand multiparity was defined as four or more previous births beyond 22 weeks of gestation.[19] Ethnicity was self-reported, similar to the national Multiple Indicator Cluster Survey.[15] Moderate anaemia was defined as a haemoglobin level below 100 g/L (6.2 mmol/L) and severe anaemia as a haemoglobin level below 70 g/L (4.3 mmol/L), according to the WHO definition.[20] Preterm birth was defined as a delivery before 37 weeks of gestation.[19,21] Categories of preterm deliveries were set according to the WHO definition: late preterm (32 to 37 weeks) and extremely preterm (below 32 weeks).[21] A birth weight lower than 2500 grams was considered a low birth weight (LBW).[19] Small for gestational age was defined as weight under the 10th percentile according to INTERGROWTH 21st charts.[21] A macerated foetus was defined as a stillbirth with skin and soft tissue changes such as redness, peeling and skin discolouration.[9,11] Congenital malformations were determined by reported macroscopic abnormalities.

Data collection: In Suriname, midwives and doctors are responsible for the registration of each birth, which is done manually in childbirth books in maternity wards. Each hospital digitalised the childbirth book of 2017 with the assistance of one of the authors (ZP). The availability of variables was described elsewhere.[12] In brief, basic childbirth data (e.g. maternal age and parity) were available, while information on socio-economic status, BMI, medical history and current pregnancy was unavailable.[12] The medical files were located and examined in detail when it was unclear whether the foetus was born dead or alive. Death certificates were not used for identification of stillbirths, as they are often not completed until several weeks after the birth of a stillborn baby. The medical files of all stillbirths were reviewed and summarised. Maternal and neonatal characteristics and clinical information were entered into Microsoft Office Excel. Early neonatal deaths were not included because the childbirth books did not provide information on neonatal deaths after transfer or discharge of the baby. Two independent clinicians (ZP, GB) classified the stillbirths according to the ICD-PM. If no consensus was achieved, the

advice was obtained from an external expert (MR). Autopsy or placental histopathological examinations were not performed for stillbirths, as this is not a standard post-mortem investigation in Suriname.

Application of the ICD-PM: The ICD-PM classifies perinatal deaths according to a three-step process[9]: (1) identify the timing of death, which can be either antepartum or intrapartum. Neonatal deaths were not assessed in this study, (2) assign the causes, with six options (A1-A6) in the antepartum group and seven options (I1-I7) in the intrapartum groups. These ICD-PM groups represent the main causes of foetal deaths and are linked to ICD-10 codes, (3) identify the main maternal condition affecting the foetus, consisting of five main groups (M1-M5).
Antepartum or intrapartum deaths were distinguished by foetal heart rate (FHR) on admission, cardiotocography (CTG) on the maternity ward, information on cervical dilation and presence of painful uterine contractions. If no information on FHR or stage of labour was available, the timing of death was classified as *'unable to classify timing'*. If the cause of the stillbirth could not be determined, it was classified as '*unspecified cause'*. Placental abruption was classified as antepartum hypoxia, similar to previous studies.[9,10]
Maternal condition *M1 'Complications of placenta and membranes'* included placenta praevia, placental abruption and prolapsed cord. The *M4 'Maternal medical and surgical conditions'* included maternal conditions such as hypertensive disorders, gestational diabetes and sickle cell disease. When more than one assignable cause was identified (for example a woman with severe pre-eclampsia, foetal growth restriction and placental abruption), the causes were classified by the first event in the chain: the underlying problem (in this example severe pre-eclampsia).[23] If there were several, independent maternal factors, the factor contributing most significantly was used for classification.

Data analysis: Descriptive data analysis consisted of frequency (percentages), mean (standard deviation) and median (interquartile range (IQR)) if variables were not normally distributed. Categorical variables were analysed using cross-tabulations

and chi-square test for significance ($p<0.05$). Denominator data for assessment of associated risk indicator consisted of all hospital deliveries of live births. We performed no data imputation, as missing data were <5% and assumed missed at random. Univariate binary logistic regression was performed to assess factors associated with stillbirths, reported in odds ratios (OR) with 95% confidence intervals (95% CI). Multiple logistic regression was performed for variables with $p<0.1$ in the univariate analysis. We also included variables that were risk indicators reported in previous studies (age, parity and ethnicity[7,12,17,18]). The results of the multiple logistic regression were reported as adjusted odds ratio (aOR). Several possible explanatory variables could not be included in our regression analysis as these variables were not available for the reference population (socio-economic status, residency, BMI, or pre-existing maternal conditions and information on current pregnancy). IBM-SPSS version 25 was used for data analysis.

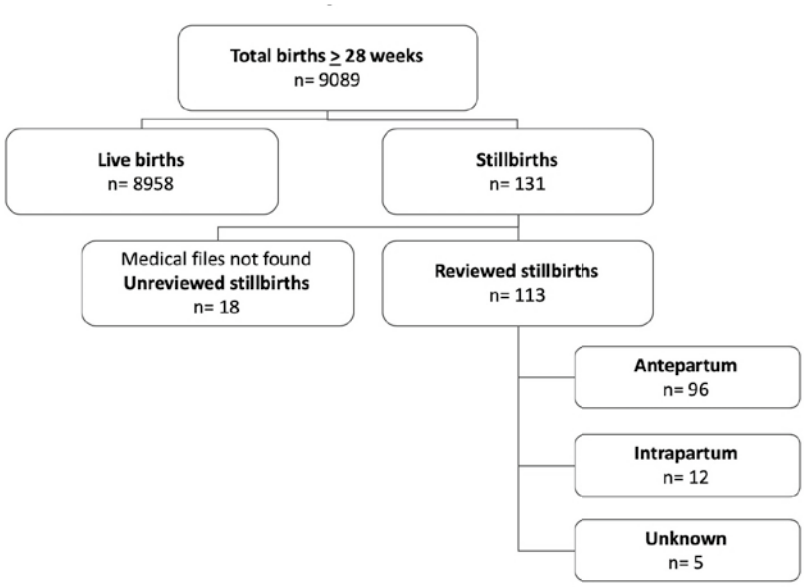
RESULTS

In 2017, a total of 9089 babies were born to 8985 women in hospitals in Suriname (figure 1). There were 131 stillbirths, resulting in an SBR of 14.4 per 1000 births. One woman with a twin pregnancy delivered two stillborn babies. The total number of deliveries of live births was 8855.

Characteristics and risk indicators of women with stillbirths: Table 1 displays maternal and foetal characteristics of stillbirths compared to live births. Hospital I, the only referral hospital, had the highest SBR of 26.3 per 1000 births and hospital IV had the lowest SBR of 8.6 per 1000 live births. Maternal age (mean 28.4, SD 6.6 years) did not differ between women who experienced a stillbirth and those who did not. The highest SBR was among women of African descent (Maroons and Creole), with 20.2 stillbirths per 1000 total births. Women of Asian descent (Hindustani, Javanese, Chinese) had the lowest SBR with 8.3 stillbirths per 1000 total births. Table 2 presents the multivariable analysis and the factors associated with stillbirth. There was no association between maternal age and stillbirth after

adjusting for confounders. Women of African descent had two times the odds of stillbirth compared to women of other ethnicities (aOR 2.1; 95%CI 1.4-3.1), after adjustment for confounders maternal age and parity.

Figure 1. Flowchart of the total births and stillbirths in Suriname in 2017



Medical files were available in 86.3% of stillbirths (n=113/131) (figure 1). The timing and causes of death of the remaining 18 stillbirths could not be determined. Stillbirths were small for gestational age (SGA) in 26.5% (n=30/113) of cases. However, foetal death could not be determined in 34.5% (n=39) of cases due to unreliable pregnancy dating or timing of death. Maceration was described in 48.7% (n=55) of stillbirths and congenital abnormalities in 8.0% (n=9) of stillbirths (table 1). The stillbirth occurred at home or during transportation to the hospital in 67.3% (n=76/113) of cases and after hospital admission in 32.7% (n=37/113) of cases. In total, there were seven women with a stillbirth delivered by caesarean section. In two cases the stillbirth was not yet diagnosed. In five cases the foetal death was known, and caesarean section was performed on a maternal indication, of which there was one perimortem caesarean section for a woman who died due to a cardiac arrest.

Table 1. Characteristics of stillbirths compared to live deliveries in 2017

	Stillbirths n= 131 (%)	**Deliveries of live births** n= 8855 (%)	**p-value**
Hospitals			
I	54 (41.2)	1998 (22.6)	
II	29 (22.1)	2599 (29.4)	**p < 0.001**
III	29 (22.1)	2409 (27.2)	
IV	13 (9.9)	1488 (16.8)	
V	6 (4.6)	361 (4.1)	
Age (years)			
12 – 19	15 (11.5)	1254 (14.2)	
20 - 34	93 (71.0)	6264 (70.9)	p = 0.532
≥ 35	23 (17.6)	1323 (15.0)	
Ethnicity			
African-descendants	91 (69.5)	4410 (50.7)	
Hindustani	16 (12.3)	1625 (18.7)	
Mixed	13 (10.0)	1153 (13.3)	**p 0.003**
Javanese	6 (4.5)	946 (10.9)	
Indigenous	4 (3.1)	334 (3.8)	
Chinese	1 (0.8)	173 (2.0)	
Other[1]	0 (0.0)	60 (0.7)	
Parity			
0	30 (22.9)	3047 (34.5)	
1 – 3	69 (52.7)	4625 (52.4)	**p < 0.001**
≥ 4	32 (24.4)	1155 (13.1)	
Antenatal care (missing n=10)			
No	18 (14.9)	*N/A*	
At least one visit	103 (85.1)		-
Insurance (missing n=23)			
Yes	89 (82.4)	*N/A*	-
No	19 (17.6)		
Anaemia			
Severe (Hb <4.3)	6 (6.3)	56 (2.0)	
Moderate (Hb 4.3 -6.1)	35 (36.5)	986 (35.1)	**p = 0.015**
None (Hb ≥ 6.2)	55 (57.3)	1768 (62.9)	
Missing	*35*	*6045*	
HIV (missing n=10)			
Positive	9 (7.4)	*N/A*	
Negative	112 (92.6)		
Gestational age (missing n=6)			
28 - 32 weeks	46 (36.8)	151 (1.7)	
32 - 36 weeks	52 (41.6)	925 (10.5)	**p < 0.001**
≥ 37 weeks	27 (21.6)	7758 (87.8)	

Table 1. continued

	Stillbirths n= 131 (%)	**Deliveries of live births** n= 8855 (%)	**p-value**
Mode of delivery			
Spontaneous delivery	123 (93.9)	6577 (74.3)	
Instrumental delivery	1 (0.8)	144 (1.6)	**p < 0.001**
Caesarean section	7 (5.3)	2134 (24.1)	
Sex (missing n=1)			
Female	71 (54.6)	4339 (49.0)	
Male	59 (45.4)	4511 (51.0)	p = 0.206
Birth weight (missing n=1)			
< 1500 gr	52 (40.0)	132 (1.5)	
1500 – 2500 gr	49 (37.7)	1002 (11.4)	**p < 0.001**
≥ 2500 gr	29 (22.3)	7687 (87.1)	

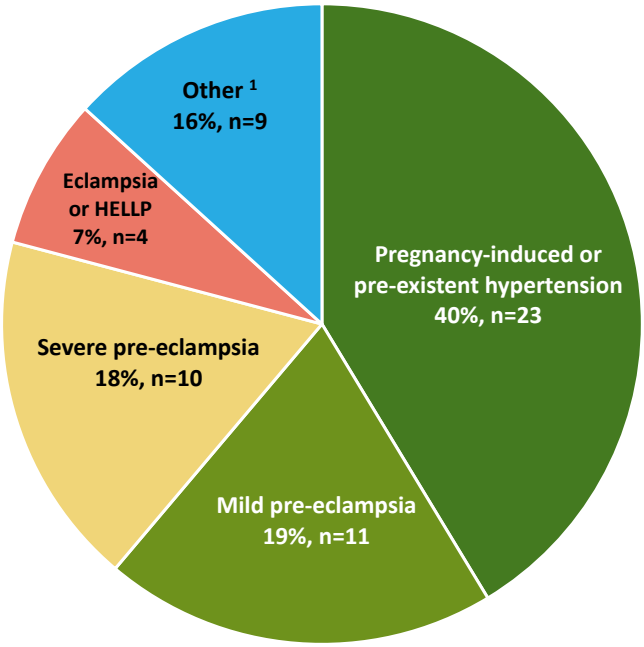
Legend [1] Brazilian (n=44), Caucasian (n=12), Guyanese (n=3), Caribbean (n=1). N/A: not available

Table 2. Multivariate regression analysis for factors associated with stillbirths in Suriname (n=130)

	Odds ratio (95% CI)	**Adjusted Odds ratio**
Age (vs. 20-34 years)		*Adjusted for parity and ethnicity*
< 20 years	0.81 (0.47 – 1.40)	0.88 (0.50 – 1.55)
≥ 35 years	1.17 (0.74 – 1.86)	0.89 (0.54 – 1.48)
Parity (vs. para 1-3)		*Adjusted for age and ethnicity*
Primiparous	0.66 (0.43 – 1.01)	0.69 (0.43 – 1.09)
Para ≥ 4	**1.86 (1.22 – 2.84)**	1.48 (0.92 – 2.37)
Ethnicity (vs. all other ethnicities)		*Adjusted for age and parity*
African descendants	**2.29 (1.58 – 3.33)**	**2.11 (1.43 – 3.11)**
Hindustani	**0.62 (0.37 – 1.05)**	0.70 (0.41 – 1.20)
Javanese	**0.40 (0.18 – 0.91)**	0.44 (0.19 – 1.00)
Anaemia		*Adjusted for age, parity and ethnicity*
Yes (vs. no anaemia)	1.27 (0.84 – 1.91)	0.92 (0.60 – 1.42)

Classification of stillbirths: Of the 113 stillbirths that were classified, 85.0% (n=96) occurred antepartum and 10.6% (n=12) intrapartum. In 4.4% (n=5) of cases, the timing of death could not be determined despite the availability of the medical file (figure 1). The classification of stillbirths, according to the ICD-PM, is reported in table 3. In 34.5% (n=39/113) of all classified stillbirths, the cause remained unknown. Women had hypertensive disorders of pregnancy in 42.5% (n=48) of cases (figure 2) and 23.0% (n=26) of stillbirths were due to a placental abruption.

Figure 2. Women with stillbirths classified as M4; Maternal medical and surgical conditions (n=57, includes four women with unknown timing of death)



Legend: Includes antepartum and intrapartum stillbirths, as well as stillbirths with an unknown timing of death (n=4/5 unknown timing with M4). [1] Other consists of women with (gestational) diabetes (n=3), sickle cell disease (n=3), HIV (n=1), Zika virus (n=1), car-accident (n=1)

Antepartum (n=96): The leading cause of antepartum stillbirths was 'Antepartum hypoxia (A3)' (45.8%, n=44), which was most frequently associated with 'Maternal medical and surgical conditions (M4)' (70.5%, n=31) and 'Complications of placenta, cord and membranes (M1)' (25.0%, n=11). The second main group consisted of stillbirths of 'Unspecified cause (A6)' (40.6% of all antepartum stillbirths, n=39/96), mostly to women without a medical condition (64.1%, n=25/39) (table 3).

Intrapartum (n=12): The majority of deaths during the intrapartum period were caused by an 'Acute intrapartum event (I3)' (91.7%, n=11) (table 3). In four cases, there was a placental abruption during labour and in three cases, obstructed labour, e.g. complicated breech delivery.

Table 3. Classification of stillbirths in Suriname, according to the ICD-PM

	Maternal medical condition					
	M1 Complications of placenta, cord and membranes	**M2** Maternal complications of pregnancy	**M3** Other complications of labour and delivery	**M4** Maternal medical and surgical conditions	**M5** No maternal condition	**Causes** Total (%)
Causes of antepartum deaths						
A 1: Congenital malformations and chromosomal abnormalities	1				1	**2 (2.1)**
A 2: Infection				1		**1 (1.0)**
A 3: Antepartum hypoxia	11	1	1	31		**44 (45.8)**
A 4: Other specified disorder		1		1		**2 (2.1)**
A 5: Related to foetal growth	1			2	5	**8 (8.3)**
A 6: Unspecified cause		1		13	25	**39 (40.6)**
Causes of intrapartum deaths						
I 1: Congenital malformations and chromosomal abnormalities				1		**1 (8.3)**
I 2: Birth trauma						**-**
I 3: Acute intrapartum event	2	1	3	4	1	**11 (91.7)**
I 4: Infection						**-**
I 5: Other specified disorder						**-**
I 6: Related to foetal growth						**-**
I 7: Unspecified cause						**-**
Unknown timing of death						
Total				**4**	**1**	
Maternal condition total (%)	**15 (13.3)**	**4 (3.5)**	**4 (3.5)**	**57 (50.4)**	**33 (29.2)**	**113 (100)**

Maternal condition (n=80): The majority of stillbirths (70.8%, n=80) were classified with at least one maternal condition. The most frequently determined maternal conditions were 'Maternal medical and surgical conditions (M4)' (71%, n=57/80)

Classification difficulties: Figure 3 illustrates the challenges encountered in this study during ICD-PM classification. The most critical difficulties were as follows: (1) the fact that one attributable cause of death had to be assigned, while there were often competing conditions within the chain-of-events (e.g. hypertensive disorders, growth restriction and placental abruption); (2) the large proportion of antenatal deaths of unknown cause; (3) the difficulty of determining foetal growth (when gestational age or timing of death was unknown); (4) the inability to reliably determine the timing of death (antepartum or intrapartum); (5) the inability to assign a cause of death to stillbirths of unknown timing and (6) discussion of whether certain conditions should be classified as a maternal condition when they are a foetal condition (umbilical cord prolapse).

DISCUSSION

This study is the first to apply the WHO ICD-PM tool on stillbirths in the Americas. Stillbirths have not previously been studied in Suriname, and the SBR of 14.4 per 1000 births found in this study is higher than in most other LMIC in Latin America and the Caribbean.[11] Women of African descent were at higher risk of a stillbirth compared to women of other ethnicities. Stillbirths occurred predominantly during the antepartum period (85%) and before arrival at the hospital (67%). When a stillbirth cause was determined, the death was mostly attributable to hypertensive disorders. However, a major group of antepartum stillbirths remained of unknown cause (39%), often due to a lack of information and poor diagnostic evaluation.

The SBR among women of African descent in our study is two and a half times higher than among women of Asian descent. Previous studies in Suriname have also reported substantial ethnic disparities in maternal deaths and stillbirths, with similar increased odds of adverse outcomes among women of African descent.[12]

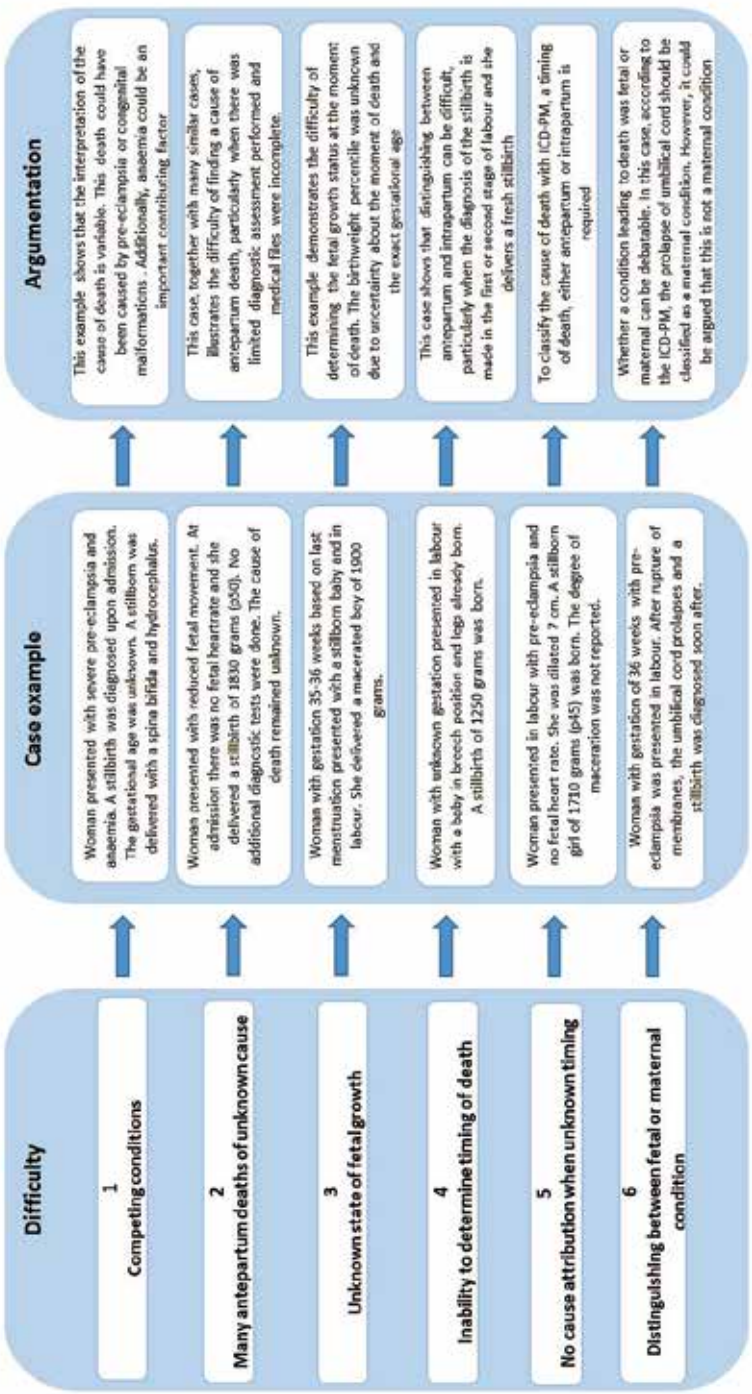


Figure 3. Difficulties encountered in the application of the ICD-PM in Suriname

These differences may reflect inequity within the healthcare system and need further investigation.[12,24] Body Mass Index (BMI) and socio-economic circumstances could have also contributed to the ethnic disparity seen in the SBR. Adjustment for these variables (BMI, level of income, education, place of residence) was not possible as they were not available from routinely collected data. Well-designed prospective studies are urgently needed to identify high-risk women and develop effective stillbirth prevention strategies.

A gradually shifting pattern is seen globally, from high SBRs with mostly intrapartum deaths in low-income countries to low SBRs with mostly antepartum deaths in high-income countries (see supplementary file 1).[10,25-29] The SBR and timing of stillbirth can be incorporated into the 'obstetric transition' framework, which describes five stages in which countries shift from high maternal mortality and fertility and many communicable diseases (stage I-II) to low maternal mortality and fertility and more non-communicable diseases.[30] These stages help to understand the context and provide justification for appropriate interventions for reducing maternal (and perinatal) mortality.[30] In various low-resource settings, half of stillbirths (51%) occurred in the intrapartum period. In addition to ensuring access to care, these findings emphasise the need to improve the quality of intrapartum care (e.g. foetal monitoring) to reduce perinatal mortality.[25-27]
In middle-income countries, the proportion of antepartum (80%) and intrapartum (20%) stillbirths suggests that intrapartum quality of care is gradually improving and antenatal quality of care improvement is essential for further reduction of perinatal mortality.[10,28,29] Suriname follows these trends with 85% of stillbirths in the antepartum period and serves as an example of a country, which has largely overcome barriers for women to access care. However, a high maternal and perinatal mortality remains due to suboptimal quality of care.[15,24] In the United Kingdom, a high-income country, the SBR is low, and the majority of stillbirths occur in the antepartum period (91%).[10] Advanced maternal age, rare (pre-existent) and non-communicable maternal diseases and congenital malformations are the main contributors to stillbirths in this high-income setting.

Previous studies have reported a wide variation in the distribution of causes, even between countries with similar settings and economies.[10,25-29] While we classified placental abruption as antepartum hypoxia, similar to the ICD-PM pilot study in the United Kingdom and South Africa (2016)[10], a later study in South Africa (2018) classified placental abruption as *'Other specified antepartum disorders (A4)'*.[28] Consequently, this led to *'Antepartum hypoxia (A3)'* being classified as the stillbirth cause in South Africa in 53% in the first study (2016) compared to 0% in the second study (2018).[10,28] Variations in cause identification and diverse interpretations of the ICD-PM classification make stillbirth study comparisons within and between settings difficult.

A large proportion of stillbirths in Suriname (39%) remained unknown due to an unknown cause or unknown timing after application of the ICD-PM tool, despite the availability of medical files and adequate documentation of the chain of events once admitted to the hospital. Previous studies on applications of the ICD-PM have reported similar figures with *unknown causes* representing between 89% of antepartum stillbirths in low-income settings[26] and 38% in high-income settings[10] (see supplemental file 1). A large amount of *unknown causes* hinders healthcare providers, researchers and policymakers, in establishing interventions to reduce the number of stillbirths. Explanations for the high proportion of *unknown causes* in Suriname were (1) the lack of diagnostic assessment tools (no autopsy, no histological examination of the placenta, no swabs or cultures, and minimal maternal blood tests) used in stillbirths, and (2) the lack of stillbirth audits. Determination of causes remains challenging due to the pathophysiological interaction between mother, foetus and placenta and multiple co-existing conditions that can contribute.[31,32] Previous studies have shown that diagnostic assessments, such as post-mortem autopsy or minimal invasive perinatal autopsy, reduced the percentage of unexplained deaths.[32-35] Global consensus on standardisation of necessary diagnostic assessments in stillbirths would not only improve classifications globally but also motivate healthcare providers, researchers and policymakers to reduce preventable stillbirths. It is vital to consider, not only

the direct cause leading to death but the chain of events as well. This includes preliminary medical conditions and contributing substandard care factors. The ICD-PM needs to be extended with the addition of perinatal audit to develop country-specific strategies and recommendations for stillbirth reduction.

Maternal conditions occurred in 71% of stillbirths in Suriname, in 59% of stillbirth in South Africa and in 76% of stillbirths in low-resource settings.[26,28] A systematic review[36] on global causes and contributing factors of stillbirths in 2018 reported that maternal conditions contribute to only 37% of global stillbirths, which is much lower than in the studies applying the ICD-PM classification.[25-29,36] Mirroring a recently published commentary by Lavin et al.[31], these different numbers in the attribution of maternal conditions reflect the variance between classification systems on what conditions are classified as a 'maternal condition'. For example, the ICD-PM maternal condition group *M1 Complications of placenta, cord and membranes* includes cases of 'cord around neck' and 'prolapsed cord'. However, arguably this is not a maternal condition. It is crucial to enable accurate reporting of maternal complications in stillbirths to target and invest in the right actions.[31]

Challenges using ICD-PM

Based on our study findings, we make the following recommendations to address the current challenges with applying the ICD-PM (Figure 3):

1. To make recommendations on wherein the chain of events the cause of stillbirth classification should be set, especially when there are multiple contributing factors.[36]
2. To add a checklist of the minimal data (events and outcomes (not mutually exclusive)) that are required to use the ICD-PM classification.
3. To elaborate on the definition of antepartum versus intrapartum stillbirth and make recommendations on the classification of causes when the timing of death is unclear.
4. To gain a global consensus on which conditions/events should be included as a maternal complication.

Addressing these issues will ensure better quality and more consistent reporting, necessary to significantly impact the current global priority of reducing preventable perinatal deaths.

Strengths and limitations

This study's main limitation was that underreporting might have occurred. This study collected data from all national hospitals, that cover 86% of all deliveries in the country. Therefore, results could be an under- or overestimation of the stillbirth rate in Suriname (depending on the stillbirth rate in primary health care facilities and at home). The documentation in the childbirth books was generally complete; however, stillbirths could have been missed (e.g. an infant could have been recorded as a neonatal death in case a 1-minute APGAR score of 1 was reported while the baby was stillborn).

Additionally, this study did not include early neonatal deaths, although these are generally closely related to pregnancy and delivery and should be investigated to assess the whole burden of perinatal mortality. Furthermore, only basic information was available from the reference group of live births. Since no perinatal registry is yet in place, no information was available on demographics, general or obstetric history, or current pregnancy. This lack of data hindered analysis of risk factors for stillbirths. It is crucial to establish a high-quality national data registry, which includes the abovementioned variables for future studies on risk factors of severe maternal and perinatal outcomes. We believe that our study can serve as an example for other LMIC.

We emphasise the importance of (1) establishing a perinatal data registry with a list of essential variables, and (2) discussing and addressing stillbirth classification challenges in order to obtain reliable and valuable statistics for the reduction of perinatal mortality. Even though this study provided classification and indications regarding causes of death, our experience with ICD-PM was that it was insufficient for generating the evidence needed to inform researchers, health care providers and policymakers as to why these stillbirths occurred and how the burden of

stillbirths can be reduced in Suriname. To develop more country-specific strategies for the reduction of stillbirths, more insight into the causes of stillbirth is necessary. Recommendations include:

1. accurate, prospective monitoring of stillbirths;
2. installation of a perinatal audit committee and;
3. development of national guidelines for diagnostic assessment of stillbirth, including routine blood tests, cultures, radiology and minimally invasive autopsy.

CONCLUSION

Suriname has a high stillbirth rate of 14.4 per 1000 births and requires a stillbirth reduction action plan. Women of African descent are at the highest risk of stillbirth, and further studies need to assess socio-economic background and health services related factors contributing to the high SBR and ethnic disparities. The majority of stillbirths occurred before hospital admission, and hypertensive disorders formed the primary cause of stillbirths, emphasising the importance of improving the quality of antenatal care services. A significant proportion of stillbirths were classified as 'unspecified', limiting further development of recommendations for the reduction of stillbirths in Suriname. Perinatal death audits, post-mortem investigations and guidelines for the diagnostic assessment are necessary to improve the knowledge about the causes and development of recommendations. Addressing the challenges described in this study may improve ICD-PM feasibility and applicability in Suriname and other LMIC settings.

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Supplementary file 1. Literature overview of all studies conducted on perinatal mortality using the ICD-PM

		High-income	Middle-income				Low-income		
		United Kingdom (2016)	South-Africa (2016)	South Africa (2018)	Sri-Lanka (2017)	Suriname (2020)	Multi-country[2] (2019)	Zambia (2019)	Tanzania (2020)
Total perinatal deaths, n=		9067	689	26810	291	N/A	N/A	75	661
Total stillbirths, n=		4834	418	19344	205	131	1267	32	413
Total neonatal deaths, n=		4233	271	7466	86	N/A	N/A	43	248
Perinatal death rate per 1000 births		N/A	N/A	N/A	N/A	N/A	N/A	N/A	71
Stillbirth rate per 1000 births		N/A	N/A	N/A	N/A	14	Malawi: 20.3 Zimbabwe 34.7 Kenya 38.8	N/A	44
Timing	**Antepartum**	91%	82%	81%	97%	85%	42%	9%	31%
	Intrapartum	8%	18%	19%	3%	11%	51%	33%	31%
	Unknown	0%	0%	0%	-	4%	7.3%	57%	38%
Main causes Antepartum deaths	**A1**	22%	?	3%	14%	2%	2%	14%	3%
	A2	?	?	3%	4%	1%	9%	0%	1%
	A3	?	53%	0%	42%	46%	0%	14%	46%
	A4	?	?	19%	18%	2%	0%	0%	0%
	A5	15%	?	8%	5%	8%	0%	0%	0%
	A6	38%	42%	68%	17%	39%	89%	71%	50%
Main causes Intrapartum deaths	**I1**	?	?	5%	72%	8%	4%	16%	2%
	I2	?	?	0%	0%	0%	0%	0%	0%
	I3	65%	93%	69%	14%	92%	31%	84%	67%
	I4	?	?	1%	0%	0%	4%	0%	0%
	I5	?	?	13%	0%	0%	0%	0%	0%
	I6	?	?	2%	14%	0%	0%	0%	1%
	I7	?	?	10%	0%		61%	0%	30%
Main Maternal condition	**M1**	21%	?	18%	?	13%	27%	1%	12%
	M2	11%	?	5%	?	4%	10%	9%	6%
	M3	?	18%	21%	?	4%	26%	54%	9%
	M4	?	26%	33%	35%	47%	14%	4%	18%
	M5	50%	36%	31%	?	28%	24%	35%	34%

Legend

[1] Twenty-nine countries, HIC and LMIC [2] Kenya, Malawi, Sierra Leone and Zimbabwe

Abbreviations: A1= Congenital malformations, deformations and chromosomal abnormalities, A2= infection, A3= Antepartum hypoxia, A4= Other specified antepartum disorder, A5= Disorders related to fetal growth, A6= unspecified cause. I1= Congenital malformations, deformations and chromosomal abnormalities, I2 = birth trauma I3= Acute intrapartum event, I4= Infection, I5= Other specified intrapartum disorders, I6= Disorders related to fetal growth, I7= Unspecified cause. M1= Complications of placenta, cord and membranes, M2= Maternal complications of pregnancy, M3=Other complications of labor and delivery, M4= Maternal medical and surgical conditions, M5= No maternal condition identified

Part III

Beyond the numbers

Not everything that can be counted counts, and not everything that counts can be counted

~ Albert Einstein

Why magnesium sulfate 'coverage' only is not enough to reduce eclampsia: lessons learned in a middle-income country

7

Kim J.C. Verschueren
Rubinah R. Paidin
Annabel Broekhuis
Olivier S.S. Ramkhelawan
Lachmi R. Kodan
Humphrey H.H. Kanhai
Joyce L. Browne
Kitty W. M. Bloemenkamp
Marcus J. Rijken

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ABSTRACT

Objectives: Determine the eclampsia prevalence and factors associated with eclampsia and recurrent seizures in Suriname and evaluate quality-of-care indicator 'magnesium sulfate ($MgSO_4$) coverage'.

Study design: A two-year prospective nationwide cohort study was conducted in Suriname and included women with eclampsia at home or in a healthcare facility.

Main outcome measures: We calculated the prevalence by the number of live births obtained from vital registration. Risk factor denominator data concerned hospital births. Descriptive statistics and multivariate regression analysis were performed.

Results: Seventy-two women with eclampsia (37/10.000 live births) were identified, including two maternal deaths (case-fatality 2.8%). Nulliparity, African-descent and adolescence were associated with eclampsia. Adolescents with eclampsia had significantly lower BPs (150/100mmHg) than adult women (168/105mmHg). The first seizure occurred antepartum in 54% (n=39/72), intrapartum in 19% (n=14/72) and postpartum in 26% (n=19/72). Recurrent seizures were observed in 60% (n=43/72). $MgSO_4$ was administered to 99% (n=69/70) of women; however 26% received no loading dosage and, in 22% of cases $MgSO_4$ duration was <24 hours, i.e. guideline adherence existed in only 43%. $MgSO_4$ was ceased during CS in all women (n=40). Stable BP was achieved before CS in 46%. The median seizure-to-delivery interval was 27 hours, and ranged from four to 36 hours.

Conclusion: Solely '$MgSO_4$ coverage' is not a reliable quality-of-care indicator, as it conceals inadequate $MgSO_4$ dosage and timing, discontinuation during CS, stabilization before delivery, and seizure-to-delivery interval. These other quality-of-care indicators need attention from the international community in order to reduce the prevalence of eclampsia.

BACKGROUND

Hypertensive disorders of pregnancy (HDP) are responsible for 14% of maternal deaths globally.[1] In Latin America and the Caribbean, HDPs are the most common causes of maternal deaths (22%).[1] Middle-income country Suriname is known to have a high maternal mortality ratio (MMR) (130/100,000 live births)[2] and a high rate of stillbirths (14/ 1,000 births)[3,4], both caused or aggravated by HDP in 30-40% of cases. Eclampsia, seizures related to HDPs, is a severe and life-threatening complication leading to significant mortality and morbidity.[5,6] The prevalence of eclampsia varies globally from 1 to 400 per 10,000 live births, with a case fatality rate of up to 10% in low-income countries.[7] The Eclampsia-trial (1995) established the efficacy of magnesium sulfate ($MgSO_4$) in preventing recurrent seizures following eclampsia.[8] Subsequently, the Magpie-trial (1998-2001), in which 85% of recruited women were in low- and middle-income countries (LMIC), established that administration of $MgSO_4$ reduces the risk of death due to eclampsia by more than 50%.[9] Following these findings, the increasingly used $MgSO_4$ in high-income countries went hand in hand with a steady decrease in maternal mortality and prevalence of eclampsia.[10-12]

To monitor effective interventions to reduce maternal mortality, the World Health Organization (WHO) developed the process indicator 'proportion of women with eclampsia who received $MgSO_4$' and defined inadequate 'coverage' as below 95%.[13] However, in a study among twenty-nine LMICs (2010-2011), mortality due to eclampsia was not reduced, despite high $MgSO_4$ 'coverage'.[14] Therefore, using $MgSO_4$ alone may not achieve the intended effect. In all likelihood, additional, more difficult to measure dimensions of quality-of-care such as prevention strategies, pre-delivery stabilization, including hypertension management and timing of childbirth, are also important.[10,15,16] These dimensions of quality-of-care need more research attention.

Suriname, a middle-income country with a small population (roughly half a million) in South America, has a well-structured health care system with the majority of deliveries by qualified birth attendants and adequate availability of essential medication.[17-19] Since 2016, the Surinamese Maternal Mortality

committee consistently reviews maternal deaths[2], conducts studies on maternal near-miss[18] and stillbirths[3,4], and implemented national guidelines on HDP.[17]
These activities provide the necessary infrastructure for high-quality audits of eclampsia quality-of-care. The aims of this nationwide study in Suriname were to (1) determine the nationwide prevalence of eclampsia, (2) assess factors associated with eclampsia, and (3) audit the different dimensions of quality-of-care, with particular attention to the timing and dosage of $MgSO_4$.

METHODS

Study Design and Setting: A two-year, nationwide, prospective cohort study was conducted in Suriname between March 2017 and February 2019.[18] Suriname is situated on the Northern coast of South-America, with a population of approximately 560,000 and 10,000 live births a year.19 Approximately 86% of all births occur in the country's five hospitals, while 4% of women deliver at home, 6% of women deliver at the two primary health care services, and in 4%, the place of birth is unknown.[19] In general, all women with severe morbidity are referred to a hospital.[18] Maternal deaths (both those that take place in facilities and also in the community) are reported to the Surinamese Maternal Mortality Committee.

Data sources: Our previous publication elaborately described details of the data collection process.[18] Suriname Obstetric Surveillance Study (SurOSS), a study on severe maternal morbidity, prospectively identified all women with eclampsia by weekly screening of all discharged patients' files. The authors retrieved the data from their medical records: demographics, general and obstetric history, complications and laboratory values and management ($MgSO_4$ dosage, duration, and continuation during delivery, fluid charts, blood pressures (BP) at different time points, anti-hypertensive medications, time intervals between events). Additionally, an elaborate case summary was made of all cases of eclampsia (supplementary file 1). The Surinamese Maternal Mortality Committee conducted verbal autopsies and maternal death reviews of each maternal death.

The number of live births were obtained from vital registration to assess eclampsia prevalence. We used hospital deliveries (babies with a birth weight of >500 grams) without eclampsia during one year (2017-03 to 2018-02) as a reference group to assess risk indicators.

Definitions, variables, and quality-of-care indicators: We defined eclampsia using the Delphi-validated International Network of Obstetric Surveillance System (INOSS)[6], as seizure(s) in a woman during pregnancy or up to 14 days postpartum, without any other attributable cause, and with at least one of the following conditions:

- Hypertension (≥140 mmHg systolic or ≥90 mmHg diastolic)
- Proteinuria (at least 1 g/l ['2 +'] on dipstick testing)
- Thrombocytopenia (platelet count of <100 x 109/L)
- Raised plasma ALT or AST (twice the upper limit of normal).[6]

The characteristics and clinical outcomes examined for women with eclampsia included adolescent pregnancy (childbirth below the age of 20 years[20]), ethnicity (self-reported[19]), preterm delivery (before 37 weeks[21]), low birth weight (below 2500 grams[21]), low Apgar score (below seven at five minutes[21]), obstetric haemorrhage (at least 500mL blood loss during birth and in the first 24 hours following birth[22]), pre-existing hypertension (BP>140/90 mmHg, before the 20th week of pregnancy[17,23,24]) and severe hypertension (BP>160/110 mmHg[17,23,24]) as measured by manual or automatic manometers. Eclampsia during the third stage of labour was considered 'postpartum'. A maternal near-miss, a woman who survived a life-threatening complication, had organ-dysfunction according to WHO criteria.[13] We assessed quality-of-care by using previously conducted criteria-based audits[25-27] and the Surinamese HDP guideline[17], which is based on international recommendations[23,24]:

- Aspirin prevention < 20 weeks of gestation in women with HDP during a previous pregnancy;
- Anti-hypertensive medication by oral administration in cases of BP 150/100–159/109mmHg and intravenous administration where BP >160/110mmHg;

- $MgSO_4$ regimen loading dosage 4-6 grams in 5-30 minutes, followed by a maintenance dosage of 1 gram/hour during at least 24 hours;
- $MgSO_4$ bolus of 2 grams in 5 minutes in recurrent seizure(s) under $MgSO_4$.
- Stabilization was defined as adequate $MgSO_4$ therapy and BP<160/110mmHg before initiation of the caesarean section.

The national HDP guideline was developed in Suriname in November 2017.[17] The guideline development process was initiated by committee Maternal Mortality Suriname (MaMS) in close collaboration with local health care providers and international experts. They compared the five hospitals' local protocols or standards of care, international indicators and recommendations and distributed the drafted guideline. During a national conference for all maternal health care professionals and policymakers, the guideline indicators and recommendations were discussed and finalized.[17] The guideline was first distributed in February 2018 and renewed in May 2019, following the second national maternal care guideline conference organised by committee MaMS.

Statistical analysis: SPSS (IBM version 25) was used for statistical analyses. The prevalence of eclampsia was calculated per 10,000 live births using the number of national live births during the study period, obtained from the Surinamese Central Bureau of Statistics. We calculated the 95% confidence interval for the prevalence and case fatality rate manually. The Mann–Whitney U test tested differences between continuous data. Univariate and multivariate logistic regression was performed to assess factors associated with eclampsia, reported in (adjusted) odds ratios (OR) with 95% confidence intervals (95% CI). Multivariate analysis included the variables with p-value ≤0.05 in the univariate analysis. Eclampsia was the dependent variable for maternal characteristics (explanatory variables). Eclampsia was the independent variable for each adverse perinatal outcome measure (e.g., stillbirths, low Apgar score), with maternal characteristics (p-value >0.05 in univariate analysis) were the other possible explanatory variables. Missing data were <5% and presumed to miss at random. The significance level was set at a p-value <0.05.

Ethical approval: The ethical review board of the Surinamese Committee on Research Involving Human Subjects (#VG21-16) approved this research on October 4, 2016. The review board required no additional approval for the analysis of anonymous medical record data.

RESULTS

During the nationwide two-year prospective study period, Suriname registered 19,652 live births. Of these live births, seizures were reported in 74 women (0.38%). Two women were excluded because seizures were attributed to other causes (epilepsy and hypoglycaemia). The resulting prevalence was 37 per 10,000 live births since 72 women fulfilled the eclampsia definition (95% CI 32-41 per 10,000 live births). Supplementary file 1 depicts all women with eclampsia in Suriname. There were two maternal deaths related to eclampsia, resulting in a case fatality rate of 2.8% (95% CI 0.8-4.7%). One of these women died during a caesarean section (CS), and the second woman, who did not receive prenatal care despite a history of eclampsia, died at home due to eclampsia.

The prevalence of eclampsia varied between the hospitals, with referral hospital I reporting the most cases, 58 per 10,000 live births, and hospital IV reporting the least number of cases, 13 per 10,000 live births. Characteristics of women with and without eclampsia are shown in table 1, and risk indicators are demonstrated in table 2. Nulliparity, adolescent pregnancy, and women African-descent were significantly associated with eclampsia and had two to three times the odds of eclampsia. Adverse perinatal outcomes were more likely in women with eclampsia than in women without, with aORs between 5.2-15.5 (95% CI between 2.5-36.9 after adjustment for maternal factors) (table 2).

The clinical condition of women with eclampsia is depicted in Table 3. In women with eclampsia in Suriname, the first seizure occurred antepartum in 54% (n=39), intrapartum in 19% (n=14), and postpartum in 26% (n=19). In 35% (n=25/72) women had their first seizure at home, and in 65% (n=47/72), they had their first seizure at the hospital. In 58% of cases (n=42/72) HDP was diagnosed before eclampsia.

Table 1. Perinatal characteristics of women with and without eclampsia

	Eclampsia n=72 (%)	**No eclampsia**[a] n=9148 (%)	**p-value**
Age			
Median, IQR	23, 19-28	27, 22-32	**0.002**
< 20 years	22 (31)	1237 (13)	
20 – 34 years	44 (61)	6549 (72)	**<0.001**
> 35 years	6 (8)	1346 (15)	
Missings	-	227	
Parity			
Median, IQR	0, 0-1	1, 0-2	**<0.001**
Nullipara	46 (64)	3124 (34)	
1-3	23 (32)	4772 (52)	**<0.001**
≥ 4	3 (4)	1220 (13)	
Missings	-	32	
Ethnicity			
Hindustani	9 (12)	1733 (19)	
African-descent	51 (71)	4606 (51)	
Javanese	2 (3)	941 (10)	**0.010**
Mixed / other	7 (10)	1482 (16)	
Indigenous	3 (4)	347 (4)	
Missings	-	39	
Residency			
Urban	62 (88)	N/A	
Coastal	4 (6)	N/A	
Rural	4 (6)	N/A	
Missings n=	2		
Insurance			
None	6 (8)	N/A	
Private	20 (28)	N/A	
State	46 (64)	N/A	
Antenatal care			
Yes	59 (89)	N/A	
No	7 (11)	N/A	
Missings	6		
Multiple pregnancy			
Singleton	71 (99)	9028 (99)	0.954
Twins	1 (1)	120 (1)	
Chronic hypertension	7/71 (10)	N/A	
HDP in prior pregnancy	13/26 (50)	N/A	
Caesarean section scar	7/26 (27)	N/A	

Table 1. continued

	Eclampsia n=72 (%)	No eclampsia[1] n=9148 (%)	p-value
Gestational age at delivery			
Median, IQR	36, 33-38	39, 38-40	**0.002**
< 34^0 weeks	19 (26)	452 (5)	
34^0 - 36^6 weeks	20 (28)	819 (9)	
≥ 37^0 weeks	33 (46)	7846 (86)	**<0.001**
Missings	1	31	
Mode of delivery			
Vaginal delivery	26 (37)	7003 (77)	**<0.001**
Caesarean section	45 (63)	2142 (23)	
Missings	1	3	
Blood loss			
Median, IQR	200, 150-400	150, 100-250	**0.001**
< 500 mL	54 (78)	8051 (91)	
500 - 999 mL	9 (13)	631 (7)	**<0.001**
1000 - 1999 mL	6 (9)	164 (2)	
Missings	3	302	
Birth weight			**<0.001**
Median, IQR	2380, 1600-2975	3070, 2735-3390	
< 1500 grams	15 (22)	279 (3)	
1500 - 2499 grams	22 (32)	1026 (11)	**<0.001**
≥ 2500 grams	32 (46)	7795 (86)	
Missings	*3*	48	
NICU admission			
Yes	17 (27)	N/A	
No	46 (73)	N/A	
APGAR 5 minutes			
7 or higher	52 (84)	8742 (98)	**<0.001**
< 7	10 (16)	159 (2)	
Missings	10	247	
Stillbirth			
Yes	9 (13)	175 (2)	**<0.001**
< 28^0 weeks	2		
≥ 28^0 weeks	7		
Neonatal death			
Early (0 – 7 days)	1 (16)	N/A	
Late (8 - 28 days)	1 (16)	N/A	

Legend

[1] Hospital deliveries during one year, represent approximately 86% of live births in the country. Vital statistics could not be used due to lack of national disaggregated perinatal data for all (live) births.

Table 2. Association between maternal characteristics and eclampsia and perinatal outcomes, odds ratio's with 95%CI

	Eclampsia n=72 (100%)	No eclampsia n=9148 (100%)	p-value	cOR [95% CI]	p-value	aOR [95% CI]
Characteristics[1]						
Nulliparous	46/72 (64%)	3124/9116 (34%)	**<0.01**	**3.4 [2.1-5.5]**	**<0.01**	**3.0 [1.7-5.1]**
African-descent	51/72 (71%)	4604/9109 (51%)	**<0.01**	**2.4 [1.4-4.0]**	**<0.01**	**2.9 [1.7-4.9]**
Adolescent	22/72 (31%)	1237/9132 (13%)	**<0.01**	**2.8 [1.7-4.7]**	**0.01**	**2.2 [1.3-4.0]**
Cesarean section	45/71 (63%)	2142/9145 (23%)	**<0.01**	**5.3 [3.3-8.6]**	**<0.01**	**6.0 [3.6-10.1]**
Obstetric hemorrhage	15/69 (22%)	795/8846 (9%)	**<0.01**	**2.8 [1.6-5.0]**	0.07	1.8 [1.0-3.2]
Perinatal outcomes[2]						
Preterm	39/71 (55%)	1271/9117 (14%)	**<0.01**	**7.5 [4.7-12.1]**	**<0.01**	**6.8 [4.2-11.2]**
Low birth weight	37/69 (54%)	1305/9100 (14%)	**<0.01**	**6.9 [4.3-11.1]**	**<0.01**	**5.8 [3.6-9.5]**
Low Apgar score	10/62 (16%)	234/8901 (3%)	**<0.01**	**7.1 [3.6-14.2]**	**<0.01**	**5.2 [2.5-11.0]**
Stillbirth	9/72 (13%)	175/9148 (2%)	**<0.01**	**7.3 [3.6-15.0]**	**<0.01**	**15.5 [6.5-36.9]**

Legend

[1] Eclampsia is the dependent variable; [2] Eclampsia is the independent variable, adjusted for maternal characteristics with p<0.05 in univariate analysis

Hypertension was present in 93% (n=65/69, missing n=3) of women with eclampsia, and severe hypertension was present in 72% (n=50/69). Sixty percent (n=43/72) of women with eclampsia had more than one seizure. Recurrent seizures during hospitalization were reported in 46% of women (n=33/71, n=1 woman died at home). Women with eclampsia met WHO near-miss criteria (i.e. organ-dysfunction) in 31% of cases (n=22/72).

Of the Surinamese adolescents with eclampsia (n=22), 50% (n=11) had severe hypertension, 32% (n=7) had mild hypertension, and 18% (n=4) were normotensive. In general, adolescents had a significantly lower BP before or during the seizure than adults. Adolescents' median systolic BP was 150 (IQR 140-170) mmHg compared to 168 (IQR 160-180) mmHg in adults (p=0.041). Their diastolic BP was 100 (IQR 90-100) mmHg compared to 105 (IQR 100-112) mmHg in adults(p=0.004). The median time between a woman's first seizure and her hospital admission was two (IQR 01:21 – 03:00) hours. Women who experienced a seizure at home (n=18) arrived at the hospital within one hour in 17% of cases (n=3), within two hours in 50% (n=9) of cases, and in more than two hours in 33% (n=6).

Table 4 describes the audit of eclampsia quality-of-care. None of the thirteen women with HDP in their obstetric history received prophylactic aspirin before the 20th week of gestation. Women with a first seizure in the hospital received prophylactic $MgSO_4$ in 17% (n=8/47). Further, all but one women with eclampsia received therapeutic MgSO4 therapy during hospital admission (99%, n=69/70, one maternal death at home, and one missing file). However, the loading dosage was inadequate in 26% of these women (n=17/65, n=7 missing), and the duration was shorter than 24 hours in 22% of the cases (n=15/69, n=3 missing). Women with recurrent seizures during $MgSO_4$ therapy received a bolus in 25% of cases (n=4/16). Women received $MgSO_4$ before CS in 97% of cases (n=39/40). However, in 21% of these cases (n=8/39), no loading dosage was administered. Intra-operative seizures occurred in 25% (n=10/40) of women with (pre-)eclampsia who received a CS. $MgSO_4$ was ceased during the CS in all women. Fifteen minutes prior to the CS, 53% (n=20/37, missing n=3) of women had a BP>160/110mmHg. The median interval between first antepartum seizure and delivery was 27 hours; this ranged from four

(> 37 weeks) to 36 hours (gestation <34 weeks) (table 4). Figure 1 summarizes the problems identified during the case studies and recommendations based on the quality-of-care audits.

DISCUSSION

In this nationwide prospective surveillance study in Suriname, eclampsia prevalence was 37 per 10,000 live births (1 in 270 live births), with 60% of women experiencing recurrent seizures. Eclampsia was associated with adolescence, nulliparity, and African-descent. Adolescents with eclampsia had lower median blood pressures than adults, leading to diagnostic delay or failure of pre-eclampsia and the possible sequelae of eclampsia. Practically all women with eclampsia received $MgSO_4$ (99%). Beyond the associations indicated above, factors that may have contributed to the high prevalence of eclampsia and recurrent seizures included suboptimal dosing, short duration of $MgSO_4$, and cessation of $MgSO_4$ during CS. Other factors included unstable BP during CS and a long seizure-to-delivery interval. Reporting the prevalence of eclampsia and '$MgSO_4$ coverage' alone is not a reliable to assess quality-of-care indicator and additional indicators are necessary to develop justified recommendations for the reduction of eclampsia-related maternal and perinatal mortality. A study in fourteen tertiary hospitals in six Latin American countries (2012) reported a prevalence of eclampsia of 17 per 10,000 live births[28], much lower than in Suriname. Brazilian researchers (2009-2010) reported a prevalence of 22 out of 10,000 live births in the Southeast region (a higher-income locality), while they found 83 out of 10,000 live births in the North (a lower-income region) of the country.[29]

The contrast in prevalence emphasizes the persisting global inequity in access and quality-of-care for women living in different geographical environments.[30] Ethnic disparities, with African-descendants at highest risk, are seen within and between countries and are most likely a consequence of socioeconomic inequality and healthcare inequity.[3,30]

Table 3. Clinical condition of women with eclampsia

	Eclampsia n=72 (100%)
Time of first fit	
Antepartum	39 (54)
Intrapartum	14 (19)
Postpartum	19 (26)
Within first hour (n=19)	7 (37)
Place of first fit	
Home[1]	25 (35)
Hospital[2]	47 (65)
Total number of fits	
One fit	29 (40)
Two fits	25 (35)
Three or more fits	18 (25)
Recurrent fit in hospital	33 (46)
Women who had first fit at home (n=25)	10 (40)
Women who had first fit in hospital (n=47)	23 (49)
Diagnosis of HDP / chronic HT prior to admission	12 (17)
Signs or symptoms (n=69)	
No signs recorded	26 (38)
Headache	33 (48)
Visual disturbances	14 (20)
Abdominal tenderness	4 (6)
Hyperreflexia	3 (4)
Highest blood pressure recorded (n=69)	
Hypertension ≥ 140/90 mmHg	65 (94)
Severe hypertension ≥ 160/110 mmHg	50 (72)
Systolic, median [Q1, Q3]	180 [160, 190]
Diastolic, median [Q1, Q3]	110 [100, 120]
Laboratory values (n=70)	
Proteinuria present (≥ 0.3 g/L or dipstick 1+) (n=48)	37 (77)
HELLP	8 (11)
Thrombocytopenia below 100	10 (14)
Elevated liver enzymes (2x normal value)	13 (19)
WHO maternal near-miss	22 (31)
ICU-admission	36 (50)
Any adverse outcome	22 (31)
Placental abruption	6 (9)
Cerebral vascular incident	4 (6)
Maternal deaths	2 (3)
Stillbirths	9 (13)
Neonatal deaths <28 days after birth	2 (3)

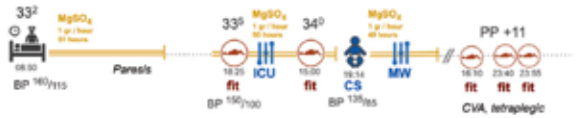
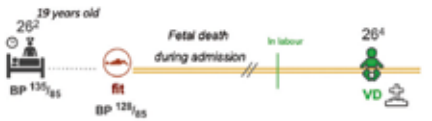
Legend: [1]First fit at home was antepartum in 92% (n=23/25) and postpartum in 8% (n=2/25); [2]First fit in hospital was antepartum in 36% (n=17/47), intrapartum in 32% (n=15/47) and postpartum in 32% (n=15/47)

Table 4 Audit of management in women with eclampsia

	Eclampsia n=70[1] (100%)
Prevention	
Aspirin prophylaxis, gestation 12-36w in women with history of HDP (n=13)	0 (0)
Prophylactic $MgSO_4$ in women who experienced first fit in the hospital (n=47)	8 (17)
Management of hypertension	
Antihypertensive medication, in women with BP >160/110 mmHg (n=60)	59 (98)
▪ Parenteral therapy in women with BP >160/110 mmHg (n=59)	35 (59)
▪ Parenteral therapy in women with BP >180/120 mmHg (n=37)	22 (59)
Therapeutic magnesium sulfate[2]	69 (99)
Regimen according to national guideline[2] (n=65, missing n=7)	28 (43)
▪ Loading dose 4-6 grams in 5-30 minutes (n=65)	48 (74)
▪ Maintenance 1-2 grams per hour (n=69)	69 (100)
▪ Total duration of $MgSO_4$ therapy at least 24 hours (n=69)	54 (78)
▪ Bolus during recurrent fit while on magnesium sulfate (n=16)	4 (25)
▪ Continuation of $MgSO_4$ therapy during caesarean section (n=40)	0 (0)
Stabilization for caesarean section in women with ante or intrapartum eclampsia (n=40)	
Patient received $MgSO_4$ before CS and had stable BP during CS (n=37)	16 (43)
▪ Blood pressure stable during CS (<160/110 mmHg) (n=37)	17 (46)
▪ Received $MgSO_4$ before CS	39 (98)
Interval eclampsia and delivery, hh:mm, median [IQR]	
Antepartum (n=39)	27:35 [15:20 - 40:51]
▪ < 34 weeks (n=16)	36:00 [27:00 - 42:45]
▪ 34-36 weeks (n=15)	22:42 [17:19 - 48:25]
▪ $\geq$ 37 weeks (n=8)	3:46 [03:03 - 11:03]
Antepartum or intrapartum (n=53)	16:33 [03:17 - 36:00]
Intrapartum (n=14)	1:30 [00:33 - 02:15]
Interval more than 24 hours (n=53)	20 (38)
Interval more than 48 hours (n=53)	9 (17)
Other	
Benzodiazepines, total (n=61)	27 (44)
Benzodiazepines, prior to or simultaneously with $MgSO_4$ (n=61)	21 (34)

Legend [1]One medical file could not be found and one woman died at home**;** [2] MgSO4 regimen according to guideline entails loading dose of 4-6 grams in 5-30 minutes, followed by 1 gram per hour during at least 24 hours and a bolus of 2 grams in 5 minutes in recurrent fit under $MgSO_4$.

Figure 1 Summary of problems identified and recommendations of the quality-of-care audits

Problem	Clinical case example	Numbers	Recommendation
Magnesium sulfate given, however not according to protocol (no loading dose, short duration, stopped before CS)		MgSO4 administered in **99% (n=69/70),** yet according to protocol **43% (n=28/65)**	Dichtomous MgSO4 coverage is not a good indicator for quality-of-care
Magnesium sulfate ceased during CS due to concerns of *hypotension, risk of PPH and possible adverse effects on baby*		Eclampsia occurred during C-section in **27% (n=12/45)**	MgSO4 needs to be continued during CS / labor (not mentioned in international guidelines)
Stabilization BP not achieved during CS		BP adequate during CS **in 46% (n=17/37)**	Define stabilization and recommend target BP during CS
Long interval between seizure and delivery, especially in preterm eclampsia. This ultimately leads to more / severe complications		Interval median <34 weeks: **36 hours** 34-36 weeks: **22 hours** ≥ 37 weeks: 3.5 hours	Determine of a time frame in which delivery should ideally be achieved, especially at gestational age below 34 and 37 weeks
Magnesium sulfate not iniated immediately upon arrival leading to recurrent fit in emergency room		Recurrent hospital fit in women who presented with eclampsia in **40% (n=10/25)**	Prompt diagnosis and treatment of eclamptic women with immediate MgSO4 administration upon arrival to hospital.
Adolescents are more prone to eclampsia and experience eclampsia with lower blood pressures		Adolescents with eclampsia had no hypertension in **18% (n=4/22)** and mild hypertension in **59% (n=13/22)**	Consider lowering the threshold of initiating MgSO4 in adolescents

Legend: Hospital bed sign (black) is admission, pregnant woman sign (red) is eclampsia seizure, number above is gestational age in weeks and days, number below is blood pressure (BP), yellow line is magnesium sulfate therapy, the baby sign is the delivery (green: vaginal, blue: cesarean section (CS) epidural anesthesia, purple: cesarean section general anesthesia), ICU is intensive care unit admission, MW is transfer to maternity ward, NICU is neonatal intensive care unit admission.

Eclampsia is more common among adolescents than in other age groups.[7,31-33] The prevalence of adolescent pregnancy in women with eclampsia was 31% in Suriname, compared to 26-55% in Latin American countries.[28] A hypothesis is that the lower socioeconomic status within populations with high adolescent birth rates, such as Indigenous and African-descendant women, contribute to this higher prevalence.[3,30,31] Another hypothesis for the high proportion of adolescents with eclampsia is that young women generally have lower median BPs than older women, leading to diagnostic delay or failure of pre-eclampsia and the possible sequelae of eclampsia.[32]

A Columbian study demonstrated that adolescents with eclampsia had normal BPs in almost half of the cases[33], similar to our results in Suriname. Before 2000, International guidelines for HDP included a relative increase in BP (30 mmHg systolic and 15 mmHg diastolic).[34] This criterion was removed, based on findings from two studies, conducted in New Zealand[35] and the USA[36], where the rise of basal BP (first BP at booking) >30/15 mmHg in healthy nulliparous women was not associated with complicated pregnancies. However, these studies reported no cases of eclampsia and did not analyse adolescents separately. Revising diagnostic HDP criteria by including the relative increase of BP in high-risk populations at risk of underdiagnosis with absolute BP criteria (adolescents), may help reduce the prevalence and burden of eclampsia.[33]

The WHO near-miss tool currently does not consider eclampsia a 'near-miss'[13], averting attention from one of the primary causes of preventable maternal and perinatal deaths.[1] With the global increase of maternal deaths due to non-communicable diseases and the evidence of underreporting eclampsia with organ-dysfunction[28,37,38], the WHO may need to reconsider including eclampsia as a separate criterion. The WHO tool provides certain process indicators to address quality-of-care.[13] However, 'magnesium sulfate coverage' (i.e., the proportion of women with eclampsia who received $MgSO_4$) is a poor indicator of the quality-of-care as different LMIC have reported a high prevalence of eclampsia despite the majority of women receiving $MgSO_4$.[25-27] Our study complements these findings by demonstrating that $MgSO_4$ coverage conceals inadequate quality of $MgSO_4$

provision according to evidence-based recommendations. Specifically, reduction of eclampsia and recurrent fits will not be established if factors such as lower dosage $MgSO_4$ regimens, no bolus administration in recurrent seizures, and the temporary discontinuation of $MgSO_4$ during labour and CS are not revealed. Recent studies in low-income countries have been experimenting with a lower dosage and shorter duration $MgSO_4$ regimens, howbeit, available evidence does not justify introduction in global clinical practice beyond research settings.[39-41]

Audits are necessary to reveal shortfalls in prevention and management and develop targeted strategies to improve quality-of-care within countries and between countries. For example, a comparative analysis of two high-income countries (2006) showed that the Netherlands had twice the prevalence (5.4/10,000 deliveries) of eclampsia compared to the United Kingdom (2.7/10,000 deliveries).[42] Following these results, the Netherlands improved hypertension management and achieved a 70% reduction of eclampsia prevalence (1.8/10,000 deliveries) in ten years.[10] While $MgSO_4$ halves the risk of eclampsia[9], prompt management of severe hypertension is also key in preventing eclampsia and other severe outcomes. In a large three-way randomized controlled trial, three oral antihypertensives were compared in 894 women with severe hypertension.[43] Despite the lack of $MgSO_4$ prevention (12% total, 4% before enrolment), only one woman (0.1%) with severe hypertension developed seizures. Therefore, more emphasis is necessary on the role of timely and tight blood pressure control next to $MgSO_4$ prevention strategies to optimize maternal outcomes.[43] The abovementioned studies are illustrative examples of the value of international comparison. A vital condition for international comparisons is to have well-established definitions, and similar core outcome measures.[6,44]

Implementing continuous audit of maternal mortality and severe morbidity is crucial in improving the quality of maternal health care.[10,12,13] While the maternal mortality committee in Suriname (MaMS) achieved to conduct national maternal death audits continuously since 2015[45], severe maternal morbidity and perinatal mortality is audited only periodically, and guidelines are re-evaluated and renewed by the committee every three years. Similar to many other low- and middle-

income countries, the lack of financial and human resources is the main challenge in the implementation of continuous audit. The facilitators, which make periodic audits and guideline renewal possible in Suriname, are durable commitment, local ownership and involvement of many local health care providers and national policymakers.

To eliminate preventable maternal deaths, we need to reduce the prevalence and burden of eclampsia. Suggestions include to

(1) develop well-established disease-based criteria and a HDP core outcome set;

(2) establish international recommendations concerning $MgSO_4$ dosage regimen, blood pressure control, eclampsia stabilization and seizure-to-delivery interval;

(3) consider adding eclampsia as a near-miss criterion, and;

(4) re-evaluate diagnostic criteria for HDPs in adolescents (i.e., increase of basal BP)

Local recommendations to reduce the burden of eclampsia in Suriname include to

(1) improve adherence to local evidence-based HDP guidelines;

(2) perform facility-based eclampsia audits to improve quality-of-care;

(3) establish a national perinatal data registry to monitor trends and disaggregate data, and;

(4) target inequity by ensuring universal access to quality care and preventing adolescent pregnancies by providing free contraception and safe abortion services.

Strengths and limitations

Our study's strength includes its prospective, nationwide population-based design and the rigorous method of data acquisition, which minimized underreporting. One of the limitations was that we did not study women with pre-eclampsia, who ultimately did not develop eclampsia. As a result, we could not address quality-of-care for women with pre-eclampsia or study which women developed eclampsia. Further, the reference group was limited to one year, and potential explanatory factors (such as socioeconomic status, body mass index, or pre-existing disease) were not available.

CONCLUSION

The prevalence of eclampsia and recurrent seizures in Suriname is high. Eclampsia is most common in nulliparous, African-descent adolescents. Adolescents with eclampsia had lower blood pressures than adults, and the increase in basal blood pressure needs to be considered to prevent diagnostic delay. The '$MgSO_4$ coverage' was high (99%) and could not explain the high prevalence of eclampsia and the rate of recurrent seizures. Solely '$MgSO_4$ coverage' is not a reliable quality-of-care indicator, as it conceals more important indicators of quality of care, such as $MgSO_4$ dosage, duration and continuation, stabilization before Caesarean section and seizure-to-delivery interval. These quality-of-care indicators need more international attention in order to reduce the prevalence of eclampsia and recurrent seizures.

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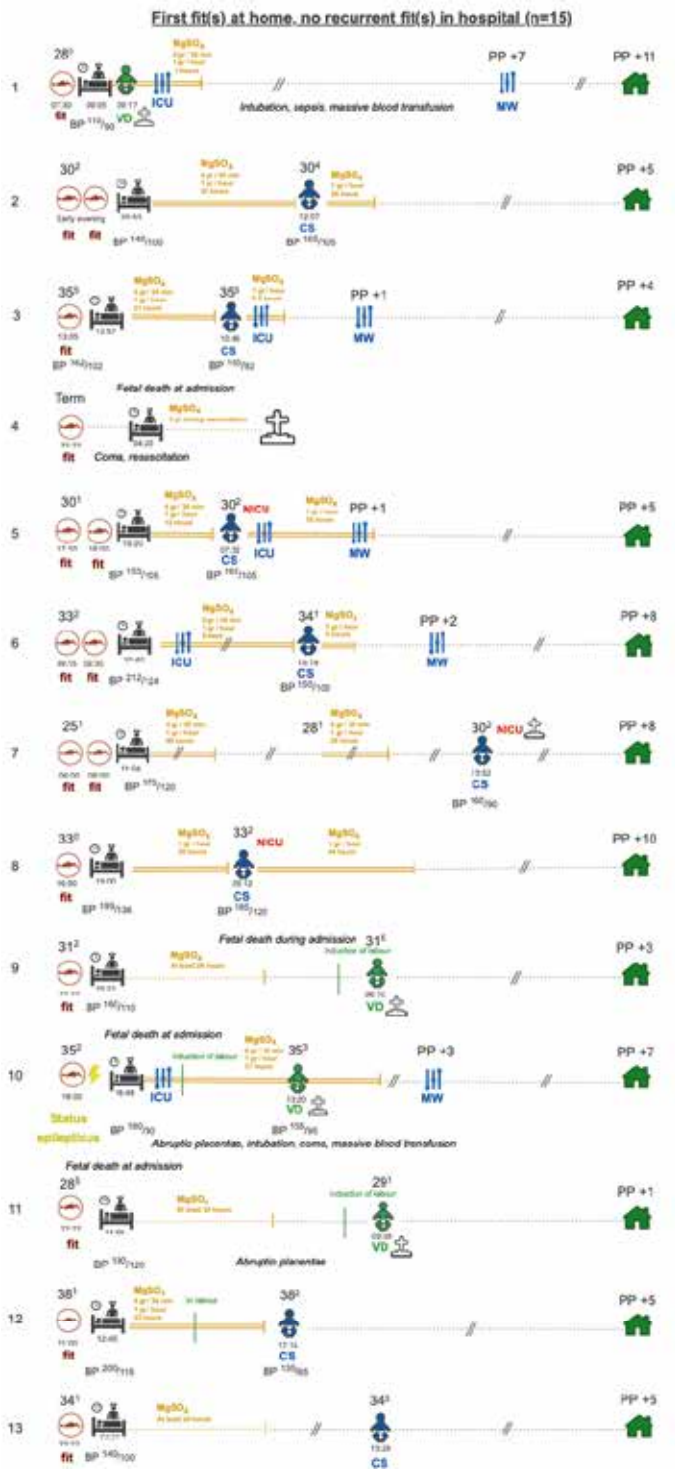
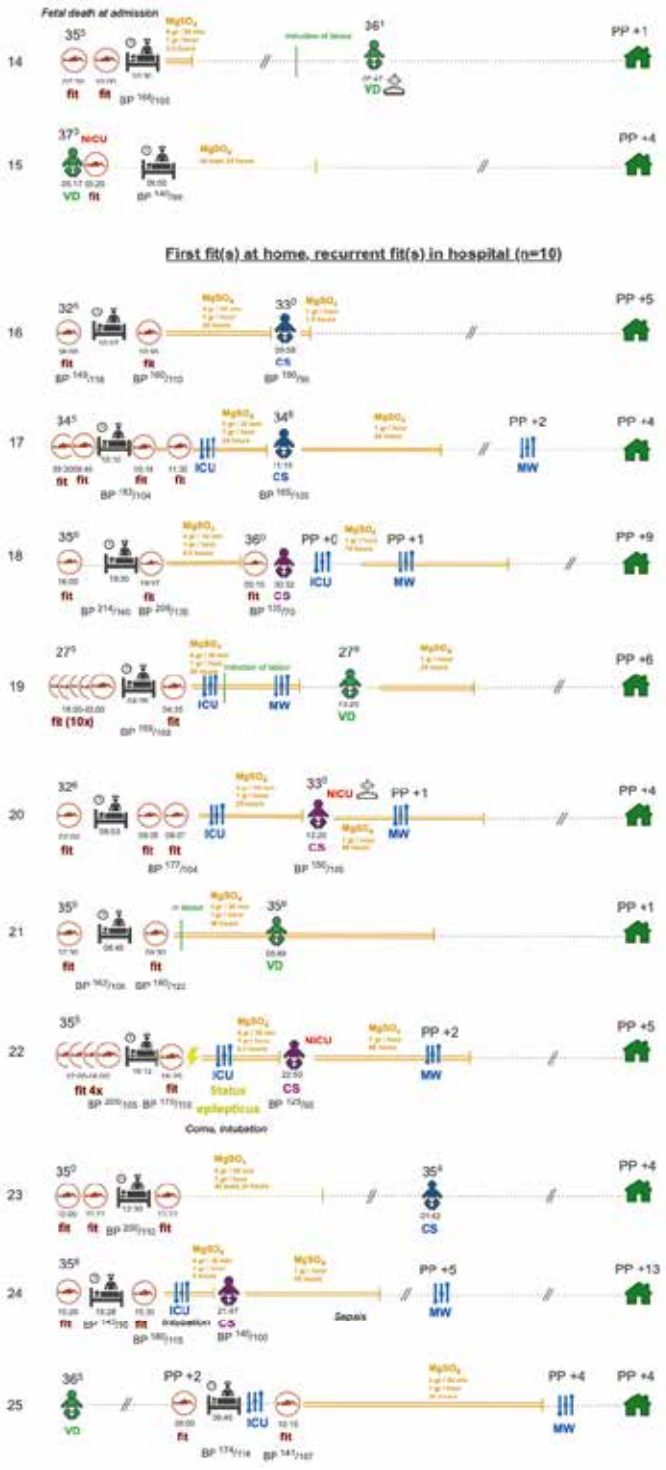


Supplementary file 1. Visual case summaries of women with eclampsia in Suriname, 2017-2019



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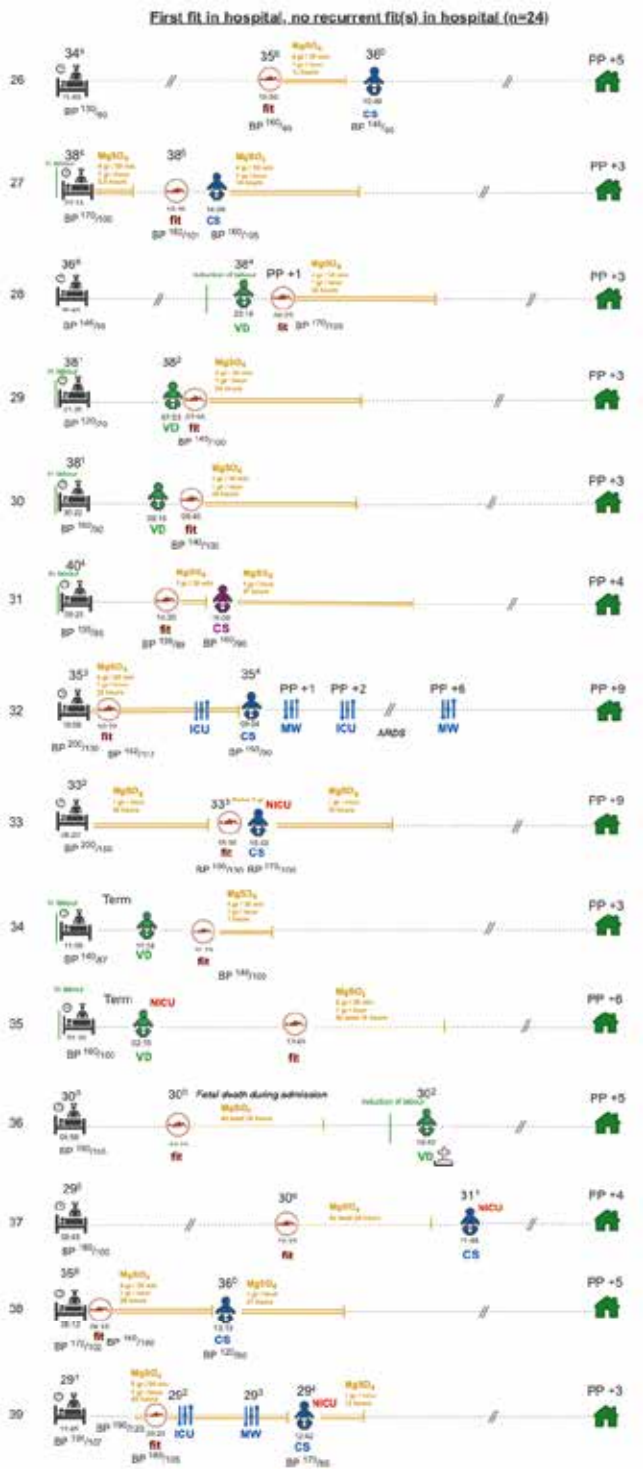

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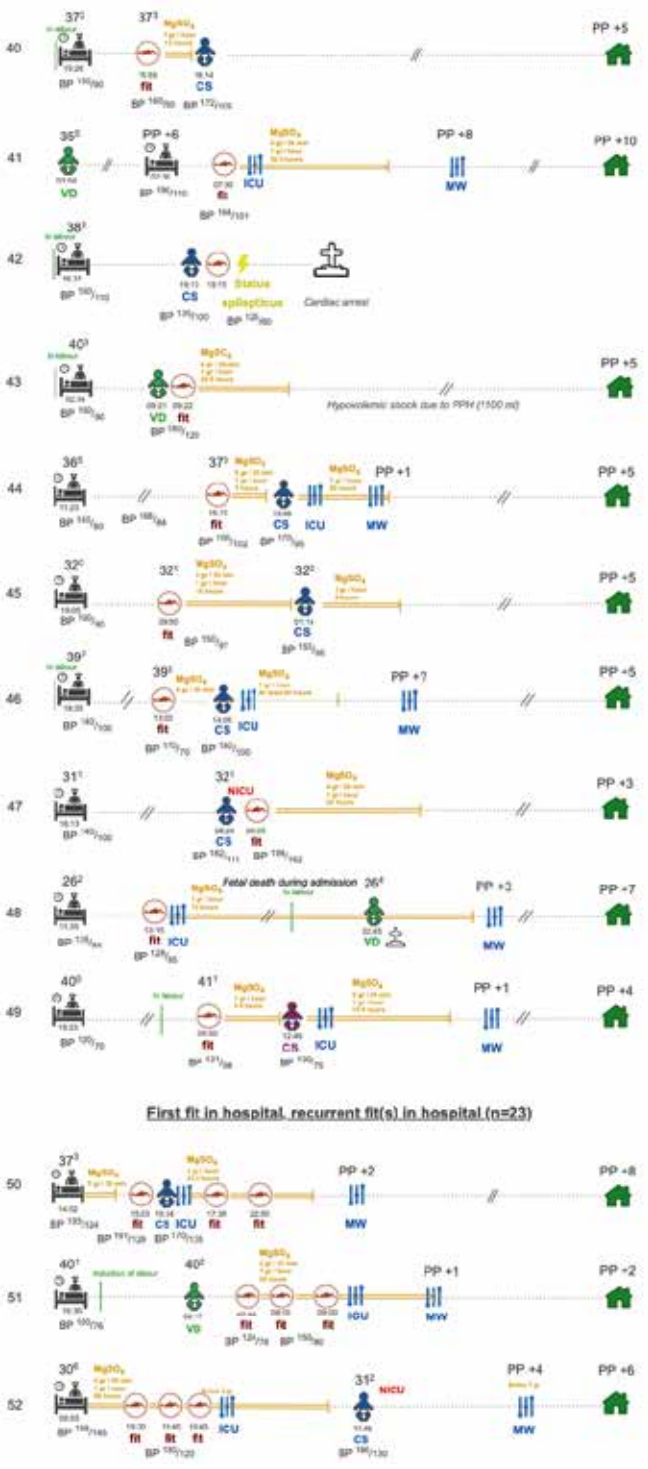

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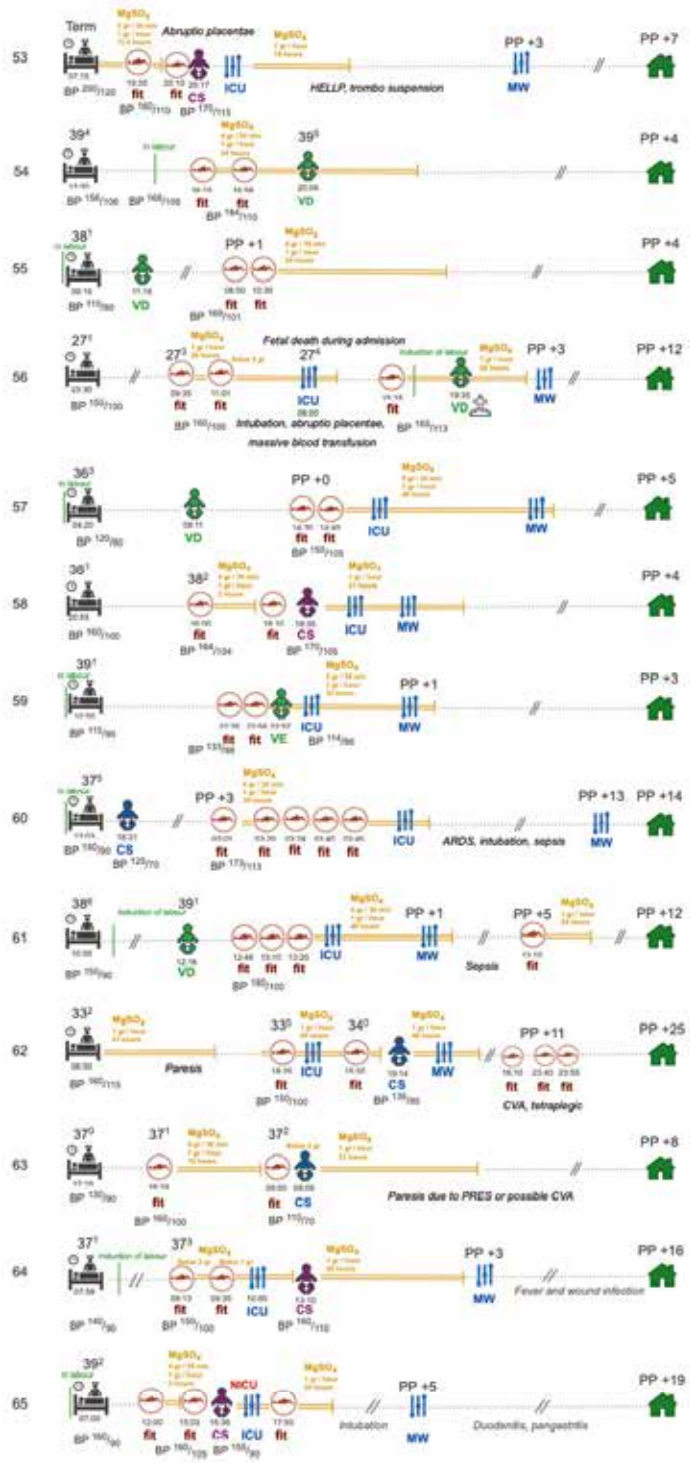

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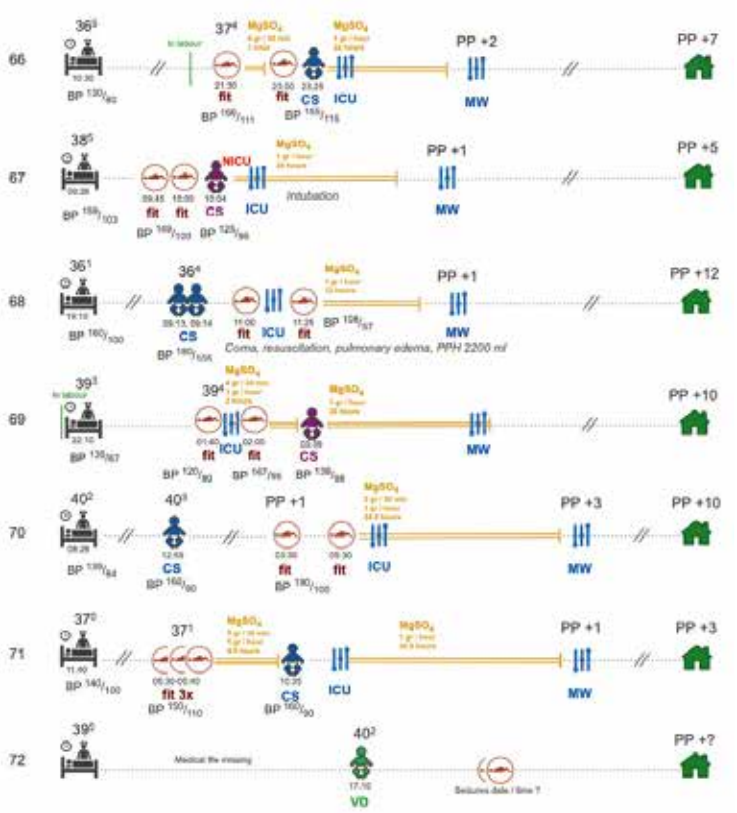

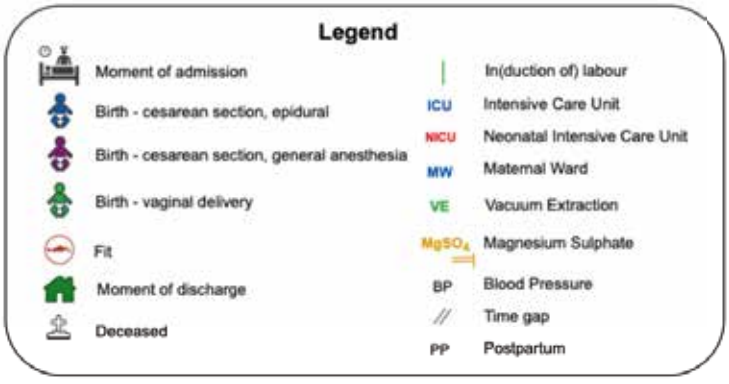

Postpartum haemorrhage in Suriname: a national descriptive study of hospital births and an audit of case management

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Lachmi R. Kodan
Kim J. C. Verschueren
Zita D. Prüst
Nicolaas P.A. Zuithoff
Marcus J. Rijken
Joyce L. Browne
Kerstin Klipstein-Grobusch
Kitty W.M. Bloemenkamp
Antoon W. Grunberg

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ABSTRACT

Background: Postpartum haemorrhage (PPH) is the leading cause of direct maternal mortality globally and in Suriname. We aimed to study the prevalence, risk indicators, causes, and management of PPH to identify opportunities for PPH reduction.

Methods: A nationwide retrospective descriptive study of all hospital deliveries in Suriname in 2017 was performed. Logistic regression analysis was applied to identify risk indicators for PPH (≥500ml blood loss). Management of severe PPH (blood loss ≥1000ml or ≥500ml with hypotension or at least three transfusions) was evaluated via a criteria-based audit using the national guideline.

Results: In 2017, the prevalence of PPH and severe PPH in Suriname was 9.2% (n=808/8747) and 2.5% (n=220/8747), respectively. PPH varied from 5.8% to 15.8% across the hospitals. Risk indicators associated with severe PPH included being of African descent (Maroon aOR 2.1, 95% CI 1.3-3.3), Creole aOR 1.8, 95%CI 1.1-3.0), multiple pregnancy (aOR 3.4, 95% CI 1.7-7.1), delivery in Hospital D (aOR 2.4, 95% CI 1.7-3.4), caesarean section (aOR 3.9, 95% CI 2.9-5.3), stillbirth (aOR 6.4, 95% CI 3.4-12.2), preterm birth (aOR 2.1, 95% CI 1.3-3.2), and macrosomia (aOR 2.8, 95% CI 1.5-5.0). Uterine atony (56.7%, n=102/180, missing 40) and retained placenta (19.4%, n=35/180, missing 40), were the main causes of severe PPH.
Criteria-based audit revealed that women with severe PPH received prophylactic oxytocin in 61.3% (n=95/155, missing 65), oxytocin treatment in 68.8% (n=106/154, missing 66), and tranexamic acid in 4.9% (n=5/103, missing 117).

Conclusions: PPH prevalence and risk indicators in Suriname were similar to international and regional reports. Inconsistent blood loss measurement, varied maternal and perinatal characteristics, and variable guideline adherence contributed to inter-hospital prevalence variation. PPH reduction in Suriname can be achieved through prevention by practicing active management of the third stage of labour in every birth and considering risk factors, early recognition by objective

and consistent blood loss measurement, and prompt treatment by adequate administration of oxytocin and tranexamic acid according to national guidelines.

BACKGROUND

Postpartum haemorrhage (PPH) remains the most frequent cause of maternal mortality, accounting for 27% of maternal deaths worldwide.[1] Most of these deaths occur in low- and middle-income countries (LMIC) and are associated with limited access to timely and quality care and inadequate availability of resources such as blood products.[2,3] PPH has become more prevalent due to increasing rates of advanced maternal age, obesity, preeclampsia, prolonged labour, caesarean delivery, and multiple pregnancies.[4-7] Besides, PPH contributes to severe maternal morbidity and permanent disability worldwide.[8] Global PPH prevalence ranges from 6 to 10% but varies widely between and within countries.[9-11] In Latin America and the Caribbean (LAC), the estimated prevalence of PPH is between 8.2% and 8.9%, and severe PPH (defined as blood loss ≥ 1,000 ml) occurred between 3.3% and 5.3% of births.[10,11]

The main causes of PPH are the "4 T's": uterine atony (tone, 80%), genital tract laceration (trauma, 13%), retained placenta or placental tissue (tissue, 5%), and coagulopathy (thrombin, 2%).[8,12,13] While risk indicators are associated with various socio-demographics, pregnancy complications, and delivery characteristics, many women experience PPH without exhibiting any specific risk indicator.[12,14,15] Therefore, prevention, early recognition, and prompt PPH treatment for each woman remain the cornerstone to avoid maternal morbidity and mortality.[13,17,18]

In Suriname, PPH was the leading direct cause of maternal mortality responsible for 20% (n = 13/65) of deaths from 2010 to 2014. Delays in diagnosis, monitoring, and treatment were critical factors contributing to these deaths.[18] However, no detailed information on PPH prevalence, causes, and risk indicators were available for Suriname.

Therefore, this study aimed to (1) assess the prevalence of PPH, (2) identify risk indicators and underlying causes of PPH, and (3) evaluate the management of severe PPH by performing a criteria-based audit. Specific identified gaps provide

evidence to guide further efforts to reduce PPH-related maternal mortality and morbidity.

METHODS

Study design and setting: A nationwide retrospective descriptive study of all hospital deliveries was conducted in Suriname between January 1 and December 31, 2017. In addition, a criteria-based audit was performed to analyse case management of severe PPH. Suriname is a middle-income country on the northern coast of South America with the lowest population density on the continent. More than 80% of the estimated population of 583,200 lives in the urban and rural coastal lowlands.[19] The ethnic distribution includes Hindustani (27%), Maroon (22%), Creole (16%), Javanese (14%), mixed (combination of ethnicities – 13%), Indigenous (4%), and others (Chinese, Brazilian, Caucasian, and unknown – 4%).[20] Maroons and Creoles are of African ancestry, while Hindustani and Javanese are of Asian descent. Of the approximately 10,000 deliveries per year, 92% are institutional (86% hospital, 6% primary care).[20,21] Four out of five major hospitals are in the capital Paramaribo; one is located at the western border of Suriname (Nickerie). All complicated pregnancies and births in primary care, including women with ongoing or severe PPH, are transferred to the nearest hospital. Every hospital has an intensive care unit (ICU). A national PPH guideline developed in 2016 incorporates international recommendations for prevention (screening for and treating anaemia and active management of the third stage of labour (AMTSL)), early recognition (measurement or visual estimation of the amount of blood loss and clinical signs), and management (oxytocin prevention and therapy and tranexamic acid use).[21]

Data collection and variables: Birth attendants documented each birth with a gestational age ≥ 22 weeks and a birth weight of ≥ 500 grams in a parturition book. The blood loss amount was usually visually estimated. In case of estimated high blood loss, the measurement was taken using a measuring jug. However, in two hospitals, only blood clots were measured.[21] Hospital administrative personnel anonymously entered data from the paper parturition books into a password-

secured digital database on a daily basis. The datasets from the five hospitals were merged, yielding one national delivery database for 2017. Missing and incorrect data were crosschecked with the original parturition books and medical files. The Surinamese Obstetric Surveillance System (SurOSS) identified all women with potentially life-threatening disorders in pregnancy between March 2017 and February 2018.[22] Study data for the criteria-based audit were derived from this database. The primary outcome variable of our study was PPH, which was defined as a blood loss of at least 500 mL within 24 hours postpartum. Moderate PPH was defined as blood loss between 500 and 999mL. Severe PPH was defined as blood loss of at least 1000mL bleeding associated with hypotension (systolic blood pressure below 90 mmHg with a pulse rate higher than 90 beats per minute), or transfusion of at least three units of blood products based on the criteria of SurOSS.[22] The available independent variables (maternal, pregnancy, and delivery characteristics) were categorized according to international classifications (supplementary file 1). The criteria-based audit was confined to severe PPH. Prevention and management of severe PPH were audited using the national PPH guideline.[21,22] Detailed information on the cause, course, and management of severe PPH was not always available (supplementary file 2). This manuscript was written in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology Guidelines.[23]

Statistical analysis: Data were analysed using IBM SPSS version 24.0 (Armonk, New York, USA) and SAS v9.4 (SAS Institute, Gary Indiana). Frequencies of maternal, delivery, and perinatal characteristics were calculated in women with and without PPH. Logistic regression was used to investigate the independent association of risk indicators with moderate and severe PPH. Univariate regression analysis generated odds ratios (ORs) with 95% confidence interval (CI). The multivariable regression analysis included all variables with a p-value <0.10 from the univariate analysis and variables reported by the literature as important risk indicators (e.g., multiple gestations, parity). These were presented as adjusted OR (aOR) with 95% confidence interval (CI). A Pareto chart was used to prioritize areas for quality of care

improvement, applying the "80-20 rule" of the Pareto principle, which suggests that most problems (80%) are due to a few key causes (20%).[24] Clinical management of PPH was reported as frequencies and percentages after applying the audit criteria. Pearson correlation was used to evaluate the association between blood loss, units of blood transfused, and ICU admission.

Ethical considerations: This research was performed according to the Declaration of Helsinki. The ethical review board of the Surinamese Committee on Research Involving Human Subjects approved the study on maternal morbidity on October 4th, 2016 (VG21-16) and the study on postpartum haemorrhage on September 8th, 2018 (VG11-18). The registry data was anonymous and aggregated, and the need for individual consent was waived.

RESULTS

Blood loss was documented in 96.4% (n=8747/9071) of the hospital deliveries in 2017 (table 1). The median blood loss of all included women who gave birth was 150 ml (range 0-4620). PPH occurred in 9.2% (n=808/8747) of the deliveries, with 6.7% (n=588/8747) being moderate and 2.5% (n=220/8747) severe PPH. The diagnosis of severe PPH was based on blood loss of more than 1000 ml in 82.7% (n=182/220) of women, and in 17.3% (n=38/220) blood loss was moderate, but at least three units of blood products were transfused, or there was hemodynamic instability. In table 1, the maternal, perinatal and delivery characteristics of the births with and without PPH are compared. Pre-delivery anaemia occurred in 34.9% (n=65/186, missing 622) of women with PPH. Women of African descent were more frequently anaemic antepartum (63.0%, n=677/1074) than women from other ethnicities were (based on data availability of only two hospitals). The prevalence of PPH was higher in women delivered by caesarean section (CS) than those delivered by a vaginal birth (20.8%, n=400/1924 vs. 6.0%, n=408/6823, respectively, $p<0.01$). There were nine maternal deaths, three of which were complicated by PPH.

Information on blood loss was most frequently missing in CS (65.7%, n=213/324), low birth weight (29.1%, n=94/324), and preterm births (25.7%, n=81/324).

The prevalence of moderate and severe PPH in the hospitals varied significantly between 4.5 to 11.8% (p<0.001) and 1.3 to 4.0% (p<0.001), respectively, with the highest prevalence in Hospital D and the lowest in Hospital E (figure 1). CS prevalence was highest in Hospitals D (24.6%, n=604/2456) and E (37.8%, n=564/1493) and lowest in Hospital C (14.4%, n=53/367) (supplementary file 1). PPH after CS was more common in Hospital D than in other hospitals (48.4% vs 6.9-13.9%, p < 0.001). In Hospitals A, B, and D, women giving birth were more often of African descent (68.0% vs. 51.8% vs. 55.5%) compared to Hospitals C (5.8%) and E (26.6%). AMTSL (by administration of oxytocin for PPH prevention) was applied less frequently for severe PPH cases in Hospital D than in the other hospitals (46% (n=29/155) vs. 67.9-77.8%) (supplementary file 3).

Figure 1. Prevalence of PPH per hospital in Suriname, 2017

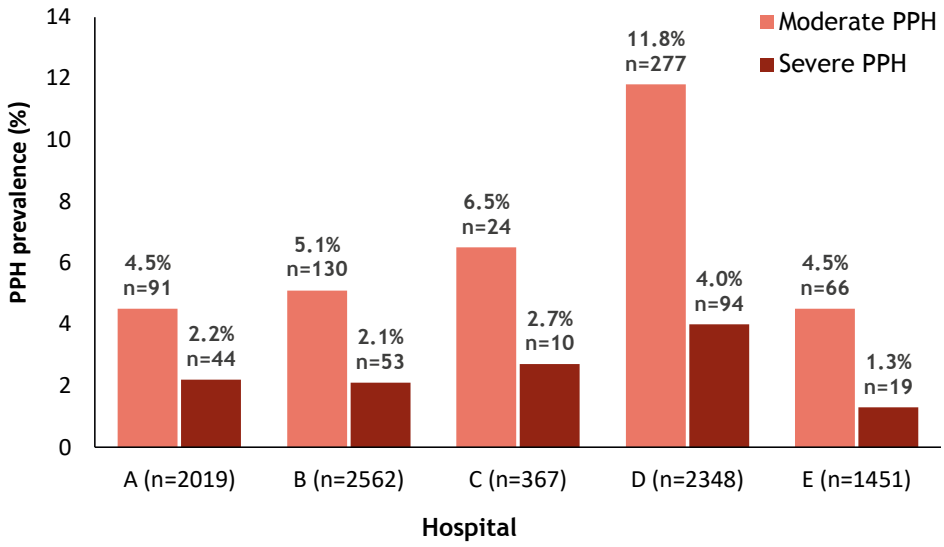


Table 1. Maternal, perinatal, and delivery characteristics of births in Suriname in 2017 with and without postpartum haemorrhage and undocumented blood loss

	No PPH	Moderate[1]	Severe PPH[2]	Undocumented blood loss
Total, n= (100%)	7939	588	220	324
Live births	7811 (98.4)	577 (98.1)	200 (91.9)	301 (92.9)
Stillbirths	128 (1.6)	11 (1.9)	20 (9.1)	23 (7.1)
Maternal characteristics				
Age (years)				
12–19	1164 (14.7)	64 (10.9)	24 (10.9)	37 (11.5)
20–34	5678 (71.6)	421 (71.6)	147 (66.8)	228 (70.8)
≥ 35	1087 (13.7)	103 (17.5)	49 (22.3)	57 (17.7)
Missing	*10*	*0*	*0*	*2*
Ethnicity				
Maroon	2271 (28.8)	151 (25.9)	80 (36.4)	82 (26.0)
Creole	1709 (21.7)	124 (21.2)	52 (23.6)	85 (27.0)
Hindustani	1469 (18.6)	88 (15.0)	27 (12.3)	71 (22.5)
Other[3]	1301 (16.5)	118 (20.2)	29 (13.2)	46 (14.6)
Javanese	835 (10.6)	76 (13)	21 (9.5)	22 (7.0)
Indigenous	295 (3.7)	27 (4.6)	11 (5.0)	9 (2.9)
Missing	*59*	*4*	*0*	*9*
Maternal HIV status				
Positive	58 (0.8)	5 (0.9)	2 (1.0)	3 (0.9)
Missing	*333*	*24*	*11*	*0*
Pregnancy characteristics				
Parity				
0	2729 (34.5)	205 (35)	65 (29.5)	113 (36.1)
1–4	4579 (57.8)	334 (57)	125 (56.8)	174 (55.6)
≥ 5	612 (7.7)	47 (8)	30 (13.6)	26 (8.3)
Missing	*19*	*2*	*0*	*11*
Gestational age				
< 32 weeks	231 (2.9)	12 (2)	17 (7.8)	34 (10.8)
32–36 weeks	806 (10.2)	79 (13.5)	45 (20.5)	47 (14.9)
≥ 37 weeks	6863(86.4)	495 (84.5)	157 (71.7)	234 (74.3)
Missing	*39*	*2*	*1*	*9*
Anaemia[4]	990 (37.6)	46 (34.3)	19 (36.5)	30 (36.6)
Missing	*5307*	*454*	*168*	*242*
Multiple pregnancy	88 (1.1)	9 (1.5)	10 (4.5)	9 (2.8)

Table 1. Continued

	No PPH	Moderate[1]	Severe PPH[2]	Undocumented blood loss
Delivery characteristics				
Hospital of delivery				
A	1884 (23.7)	91 (15.5)	44 (20.0)	82 (25.3)
B	2379 (30.0)	130 (22.1)	53 (24.1)	92 (28.4)
C	333 (4.2)	24 (4.1)	10 (4.5)	24 (4.1)
D	1977 (24.9)	277 (47.1)	94 (42.7)	108 (33.3)
E	1366 (17.2)	66 (11.2)	19 (8.6)	42 (13.0)
Onset of labour				
Augmentation	1771 (47.4)	86 (45.7)	38 (48.1)	32 (33.0)
Missing	*4202*	*400*	*141*	*227*
Mode of delivery				
Spontaneous	689 (79.2)	267 (45.4)	127 (57.7)	107 (33)
Caesarean section	1524 (19.2)	311 (52.9)	89 (40.5)	213 (65.7)
Instrumental	126 (1.6)	10 (1.7)	4 (1.8)	4 (1.2)
Vaginal laceration				
2nd grade or higher	1644 (50.6)	86 (55.8)	26 (41.9)	19 (29.7)
Missing	*4961*	*434*	*158*	*260*
Birth weight (grams)				
< 2,500	1115 (14.1)	69 (11.7)	48 (22.2)	94 (29.1)
2,500–3,999	6582 (83.2)	483 (82.6)	154 (71.3)	219 (67.8)
≥ 4,000	211 (2.7)	33 (5.6)	14 (6.5)	10 (3.1)
Missing	*31*	*3*	*4*	*1*

Legend [1]Blood loss 500–999mL; [2]Blood loss ≥1000mL or blood loss <1000mL with hemodynamic instability or ≥ 3 units blood transfusion**;** [3]Ethnicity other: Mixed, Chinese, Brazilian, Caucasian, or unknown; [4]Haemoglobin ≤100 g/L or ≤6.1 mmol/L

The logistic regression analysis for moderate and severe PPH is presented in table 2. Women of Creole and Maroon ethnicity had significantly higher odds of developing severe PPH than Hindustani women did (aOR 1.8, 95% CI 1.1–3.0 vs 2.1, 95% CI 1.3–3.3, respectively). Women delivering in Hospital D were more likely to experience moderate (aOR 2.7, 95% CI 2.2–3.4) and severe PPH (aOR 2.4, 95% CI 1.7–3.4) compared to Hospital B. Also, the risk of both moderate and severe PPH was significantly higher in women delivering by CS (aOR 5.4, 95% CI 4.5–6.6 vs aOR 3.9, 95% CI 2.9–5.3) compared to vaginal delivery.

Table 2. Univariate and multivariate logistic regression for moderate and severe postpartum haemorrhage (PPH)

	Moderate PPH[1]		Severe PPH[2]	
	cOR (95% CI)	**aOR[3] (95% CI)**	**cOR (95% CI)**	**aOR[3] (95% CI)**
		p = 0.003	p < 0.001	p < 0.001
Live birth	Reference	Reference	Reference	Reference
Stillbirth	1.2 (0.6–2.2)	**2.9 (1.4–6.0)**	**6.1 (3.7–10.0)**	**6.4 (3.4–12.2)**
Maternal characteristics				
Age (years)	p = 0.004		p = 0.001	
12–19	0.7 (0.6–1.0)	0.8 (0.6–1.1)	0.8 (0.5–1.2)	0.8 (0.5–1.3)
20–34	Reference	Reference	Reference	Reference
≥ 35	**1.3 (1.2–1.7)**	1.1 (0.9–1.4)	**1.7 (1.3–2.4)**	1.4 (0.9–2.0)
Ethnicity	p = 0.02	p = 0.001	p = 0.04	p = 0.07
Maroon	1.1 (0.9–1.5)	**1.5 (1.1–2.0)**	**1.9 (1.2–3.0)**	**2.1 (1.3–3.3)**
Creole	1.2 (0.9–1.6)	**1.5 (1.1–2.0)**	1.7 (1.0–2.7)	**1.8 (1.1–3.0)**
Hindustani	Reference	Reference	Reference	Reference
Other[4]	1.5 (1.1–2.0)	**1.8 (1.3–2.4)**	1.2 (0.7–2.1)	1.3 (0.8–2.3)
Javanese	1.5 (1.1–2.1)	**2.0 (1.4–2.8)**	1.4 (0.8–2.4)	1.9 (1.0–3.4)
Indigenous	1.5 (1.0–2.4)	1.5 (0.9–2.5)	2.0 (1.0–4.1)	2.0 (0.9–4.1)
HIV status				
Positive	1.2 (0.5–2.9)		1.3 (0.3–5.2)	
Negative	Reference		Reference	
Pregnancy characteristics				
Parity			p = 0.005	
0	1.0 (0.7–1.2)	1.1 (0.9–1.3)	0.9 (0.6–1.2)	1.1 (0.8–1.5)
1–4	Reference	Reference	Reference	Reference
≥ 5	1.1 (0.8–1.5)	1.1 (0.8–1.6)	**1.8 (1.2–2.7)**	1.2 (0.8–1.9)
Gestational age	p = 0.03	p = 0.05	p < 0.001	p = 0.004
< 32 weeks	0.7 (0.4–1.3)	1.2 (0.6–2.4)	**3.2 (1.9–5.4)**	**2.3 (1.1–4.9)**
32–36 weeks	**1.4 (1.1–1.7)**	**1.5 (1.1–2.0)**	**2.4 (1.7–3.4)**	**2.1 (1.3–3.2)**
≥ 37 weeks	Reference	Reference	Reference	Reference
Antepartum anaemia				
No anaemia	Reference		Reference	
Anaemia[5]	0.9 (0.6–1.3)		1.0 (0.5–1.8)	
Type of pregnancy			p < 0.001	p < 0.001
Singleton	Reference	Reference	Reference	Reference
Multiple	1.4 (0.7–2.8)	1.4 (0.6–3.0)	**4.3 (2.2–8.3)**	**3.4 (1.7–7.1)**

Table 2. Continued

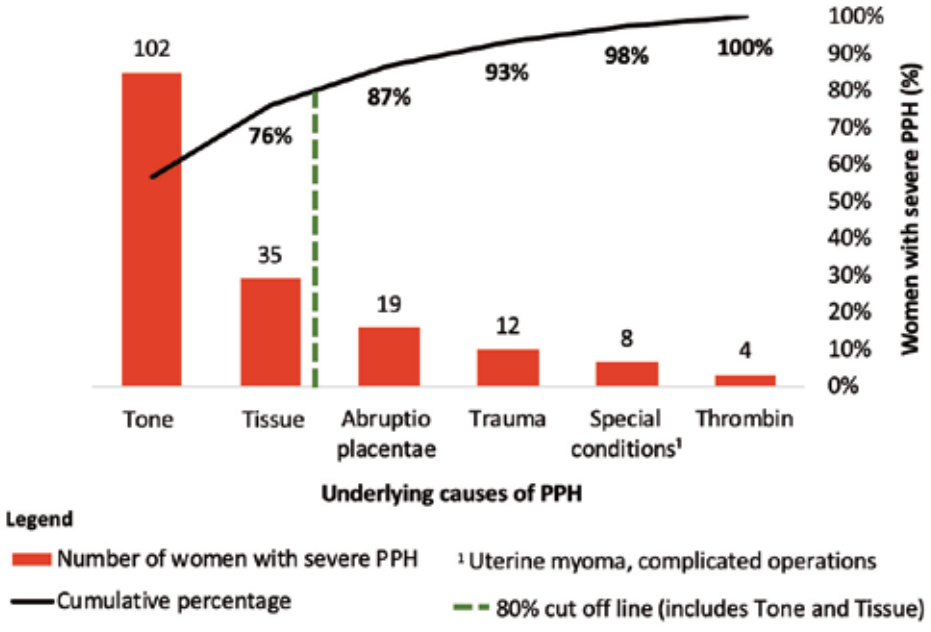
	Moderate PPH[1]		Severe PPH[2]	
	cOR (95% CI)	**aOR[3] (95% CI)**	**cOR (95% CI)**	**aOR[3] (95% CI)**
Delivery characteristics				
Hospitals	p < 0.001	p < 0.001	p < 0.001	p < 0.001
A	0.9 (0.7–1.2)	1.0 (0.7–1.3)	1.1 (0.7–1.6)	1.0 (0.6–1.5)
B	Reference	Reference	Reference	Reference
C	1.3 (0.8–2.1)	1.7 (1.0–2.8)	1.4 (0.7–2.7)	2.1 (1.0–4.4)
D	**2.6 (2.1–3.2)**	**2.7 (2.2–3.4)**	**2.1 (1.5–3.0)**	**2.4 (1.7–3.4)**
E	0.9 (0.7–1.2)	0.6 (0.4–0.8)	0.6 (0.4–1.1)	0.5 (0.3–0.9)
Onset of labour				
Spontaneous	Reference		Reference	
Augmentation	0.9 (0.7–1.3)		1.0 (0.7–1.6)	
Mode of delivery	p < 0.001	p < 0.001	p < 0.001	
Spontaneous	Reference	Reference	Reference	Reference
Instrumental	1.9 (1.0–3.6)	**2.1 (1.1–4.1)**	1.6 (0.6–4.3)	2.1 (0.9–6.1)
Caesarean section	**4.8 (4.0–5.7)**	**5.4 (4.5–6.6)**	**2.9 (2.2–3.8)**	**3.9 (2.9–5.3)**
Vaginal laceration				
None or 1st grade	Reference		Reference	
2nd grade or higher	0.8 (0.6–1.1)		1.4 (0.9–2.4)	
Birth weight (grams)	p < 0.001	p < 0.001	p < 0.001	p = 0.001
< 2500	0.8 (0.7–1.1)	0.2 (0.4–0.9)	**1.8 (1.3–2.6)**	0.7 (0.4–1.1)
2500–3999	Reference	Reference	Reference	Reference
≥ 4000	**2.1 (1.5–3.1)**	**1.9 (1.3–2.9)**	**2.8 (1.6–5.0)**	**2.8 (1.5–5.0)**

Legend [1]Blood loss 500–999 mL; [2]Blood loss ≥1000mL, or blood loss <1000mL with hemodynamic instability or ≥3 units blood transfusion; [3]Adjusted: multivariate analysis of risk factors with p < 0.10 in univariate analysis and a priori risk factors (multiple gestations, parity); [4]Ethnicity other: mixed, Chinese, Brazilian, Caucasian, or unknown; [5]Haemoglobin ≤100 g/L or ≤6.1 mmol/L

Other strongly associated risk indicators for severe PPH were stillbirths (aOR 6.4, 95% CI 3.4–12.2), multiple pregnancy (aOR 3.4, 95% CI 1.7–7.1), very preterm birth (aOR 2.3, 95% CI 1.1–4.9), preterm birth (aOR 2.1, 95% CI 1.3–3.2), and neonatal macrosomia (aOR 2.8, 95% CI 1.5–5.0). At least one risk indicator was present in 70.1% (n=6130/8747) of the births without PPH and in 80.8% (n=653/808) of births complicated by PPH.

The Pareto chart shows that uterine atony (56.7%, n=102/180, missing 40) and retained placenta (19.4%, n=35/180, missing 40) caused almost 80% of severe PPH (figure 2). Severe PPH occurred among women with preeclampsia in 23.2% (n=45/194, missing 26) and eclampsia in 2.6% (n=5/194) of cases. Of the women with severe PPH, 17.1% (n=33/193, missing 27) were admitted to the ICU. Among women with a CS and severe PPH (n=89), the CS was considered elective for 53.9% (n=48), emergency for 32.6% (n=29), and unclassified for 13% (n=12). Women with severe PPH had a stillbirth in 9.1% of cases (n=20/220) in contrast to 1.6% (n=128/7939) stillbirth prevalence in women without PPH. Women with severe PPH and stillbirth were often diagnosed with placental abruption (85%, n=17/20) [concomitant pre-eclampsia existed in 70.6% (n=12/17) of women with placental abruption].

Figure 2. Pareto chart of the specific underlying causes of PPH in Suriname, 2017

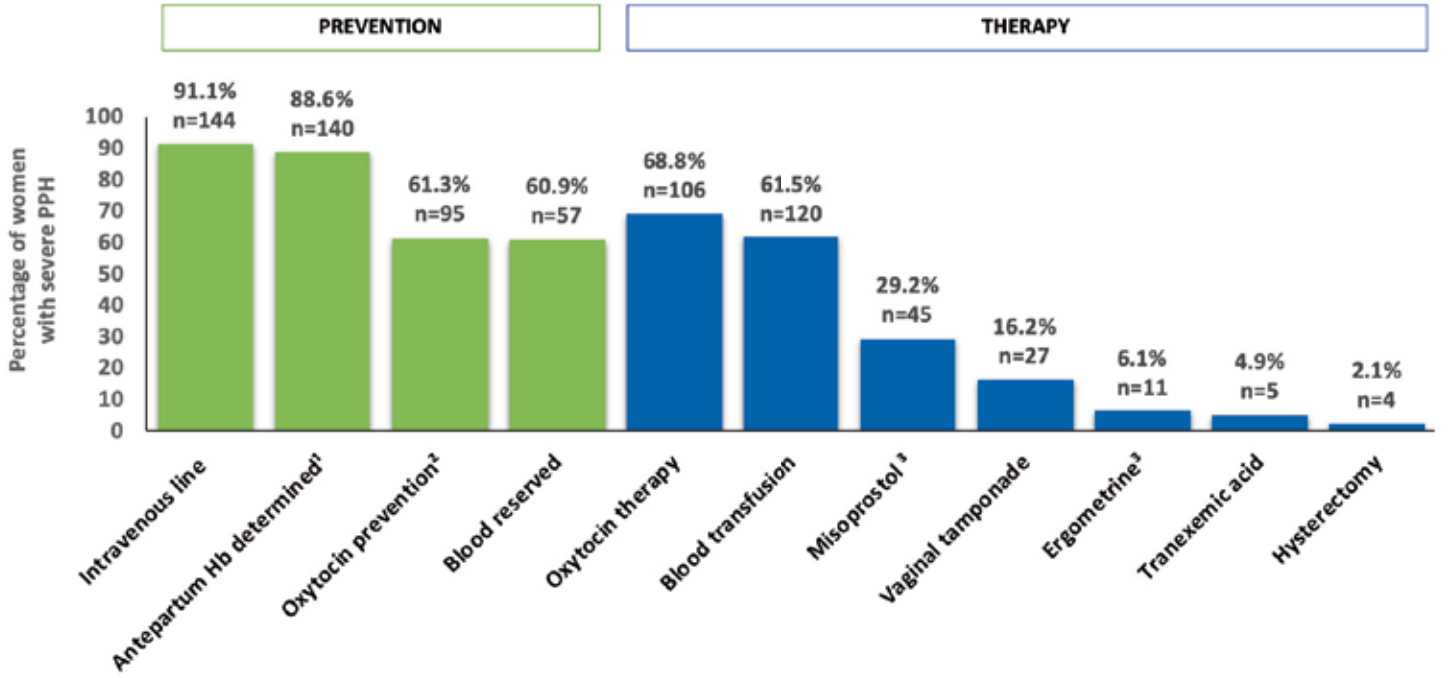


The management of PPH was evaluated using the criteria of the national guideline (figure 3). AMTSL by administering oxytocin immediately after delivery was applied in 61.3% (n=95/155, missing 65) of women with severe PPH. When a CS was performed, fewer women (55.3%, n=26/47, missing 42) received prophylactic oxytocin compared to vaginal births (65.1%, n=69/106, missing 25). Two of the three cases of severe PPH received oxytocin treatment (68.8%, n= 106/154, missing 66). Tranexamic acid was administered to 4.9% (n=5/103, missing 117) of women with severe PPH. While five women with blood loss below 1 litre received 6 to 10 units of blood products, eight women with blood loss ≥1500 ml (17.4%, n=46) received no blood products. These eight women had haemoglobin levels of at least 100 g/l and were hemodynamically stable. Blood loss was weakly to moderately correlated with the number of blood units transfused (Pearson's coefficient 0.47, $p<0.01$) but not with ICU admission (Pearson's coefficient 0.05, $p=0.46$).

DISCUSSION

Based on national registry data in 2017, the prevalence rates of PPH and severe PPH in Suriname were 9.2% and 2.5%, respectively, with substantial variation across the different hospitals. Risk indicators associated with severe PPH were (1) being of African descent, (2) having a multiple pregnancy, (3) delivery in Hospital D, (4) CS, (5) stillbirth, (6) preterm birth, and (7) macrosomia. At least one risk indicator was present in 80% of women with PPH but also in 70.1% of those without PPH. Severe PPH was mainly due to uterine atony and retained placental tissue. The criteria-based audit identified inadequate administration of oxytocin for PPH prevention (AMTSL) and therapy and infrequent use of tranexamic acid for treatment. While CS was a major risk factor, fewer women who delivered by CS received prophylactic oxytocin than women delivering vaginally did. Worldwide and in Latin America and the Caribbean (including Suriname), PPH was the most frequent direct underlying cause of maternal deaths in 2010.[1,18] To reduce preventable maternal mortality from PPH in the Americas The Pan-American Health Organization (PAHO) and its Latin American Centre for Perinatology, Women and Reproductive Health launched the "Zero Maternal Mortality from Haemorrhage" initiative in 2015.[2]

Figure 3. Criteria-based audit of the management of severe PPH in Suriname, 2017, conform national standards (guidelines)



Legend ¹ Recent antepartum haemoglobin (Hb) level determined; ² Oxytocin prevention, defined as active management of the third stage of labor (AMTSL); ³ Misoprostol a synthetic prostaglandin analog and ergometrine is a potent uterotonic drug

Following the designation of Suriname as one of 10 priority countries for reducing maternal mortality, PAHO implemented this project in Suriname in 2018.[25] In Suriname, efforts to reduce preventable maternal deaths from PPH resulted in national PPH guideline development and obstetric emergency training in 2016 and 2019.[27]

The prevalence of (severe) PPH in Suriname in this study was consistent with global and regional prevalence.[10,11] Interhospital prevalence varied significantly despite the close geographic vicinity of four hospitals in the capital city. One explanation for this variation could be the differences in maternal, perinatal, and delivery characteristics among the hospitals as reported in this study. In Hospital D, for example, PPH prevalence was the highest, with the second-highest CS rate and higher prevalence of preterm delivery and multiparity. Another explanation for the varied interhospital PPH prevalence was the inconsistent and subjective way of obtaining information on blood loss postpartum as described in the methods of this study.[21] Subjective determination of the quantity of blood loss was inaccurate since blood loss was often underestimated at large volumes and overestimated at lower volumes.[17,21,27] The inaccurate estimation could also explain the weak or moderate correlation between blood loss volume and PPH severity in this study. Finally, interhospital differences in PPH could result from the unequal availability of or adherence to local and national protocols and consequently, different PPH management.[21] For example, AMTSL for PPH prevention was applied less frequently in Hospital D (studied only for severe PPH). We, therefore, recommend consistent and accurate blood loss quantification and adherence to PPH national guidelines.

The risk indicators found in this study (ethnicity, premature delivery, stillbirth, multiple gestations, CS, and macrosomia) were congruent with those reported elsewhere.[27,29-31] African descendants have higher risks of developing PPH compared to women of other ethnicities.[32-34] Additionally, women of African origin were more commonly anaemic antepartum[28], putting them at higher risk of adverse clinical outcome when PPH develops.[17] Our study shows that women with

higher antepartum haemoglobin levels stayed hemodynamically stable despite severe blood loss. This highlights the importance of prevention and treatment of antenatal anaemia by routine iron and folate supplementation, especially in women of African descent.[21,35]

We found a strong association between severe PPH and stillbirths, which is most likely attributable to a high frequency of placental abruption among these women. A recent stillbirth study in Suriname (2016–2017) reported that placental abruption contributed to 23% of stillbirths.[36] This indicates that placental abruption and maternal conditions such as preeclampsia could be confounders in the association of stillbirth with PPH. As such, improved management of preeclampsia should reduce the risk of PPH from placental abruption.

Most healthcare workers were familiar with grand multiparity as a risk indicator and anticipated accordingly, which may explain the non-significant result found in our study. At least one risk indicator was present in most deliveries complicated by PPH but also in two thirds of uncomplicated pregnancies without PPH. This weak discriminative ability of risk indicators to identify women who could develop PPH was also reported elsewhere.[12,14,15] Therefore, although risk indicator analysis should be considered to anticipate PPH occurrence, PPH can occur unforeseen, and other approaches are also needed for appropriate management.

Extrapolating the Pareto principle to our study (the "80-20 rule"), a focus on prevention of uterine atony and retained placental tissue could significantly reduce severe PPH. In AMTSL, the best preventive measure for PPH was the administration of uterotonics (oxytocin) immediately after every birth.[8,37] The criteria-based audit showed inadequate use of prophylactic oxytocin in severe PPH, especially among women delivering by CS. In contrast, according to previous interviews with healthcare providers in Suriname AMTSL was applied in all births by CS.[21] This indicates that AMTSL was not yet routine practice in Suriname in 2017 despite advice from World Health Organization (WHO) and national guidelines.[8,21] Tranexamic acid is an antifibrinolytic agent widely used to prevent and treat haemorrhages.[38,39] While sporadically used to treat severe PPH in Suriname in

2017, it is now routine practice in the first response to PPH.[38] In 2017, the WHO updated the PPH guidelines by adding the use of tranexamic acid in early PPH as advised by the World Maternal Antifibrinolytic (WOMAN) trial, which was a large multi-country randomized control trial.[40,41] We recommend the application of AMTSL in every delivery and integration of tranexamic acid as a component of the primary treatment of PPH consistent with recent international guidelines.[38,41]

Strengths and limitations

The strengths of this study included its national coverage. Information was obtained on the prevalence of PPH in Suriname for the first time by incorporating routinely available information from the parturition book. Application of the criteria-based audit based on national guidelines allowed for in-depth analysis of specific gaps in care to guide the prioritization of actions to reduce PPH. This study had several limitations. First, parturition books only include facility-based deliveries or postpartum referrals, and the inclusion of primary care and home births could have resulted in lower PPH prevalence rates since the 14% primary care and home births were excluded from the analysis. The second limitation was the higher percentage of missing data for women who delivered by CS or preterm, which are two significant risk indicators for PPH. The third limitation is that only postpartum haemorrhage was evaluated, while obstetric haemorrhage leading to mortality and severe morbidity could also result from antepartum, post-abortion, and late miscarriages. The fourth limitation was that several known risk factors (such as socioeconomic status, body mass index, medical history, complications in the current pregnancy, anaemia, CS indication, and labour duration) could not be included in the regression analysis since these data were not available. This may explain certain observations, such as why Hospital E with the highest CS prevalence had the lowest prevalence of PPH. Finally, missing information on the causes and management of PPH impacted the criteria-based audit analysis, such as undocumented information on PPH prevention (AMTSL) among births without PPH.

CONCLUSION

Although PPH prevalence and risk indicators for Suriname are consistent with global and regional figures, wide interhospital variations exist. Since uterine atony and retained placenta are associated with almost 80% of severe PPH, intervention efforts should focus on adequate prevention, anticipation, early recognition, and prompt treatment. PPH in Suriname can be reduced by (1) prevention of PPH by applying AMTSL in every delivery and anticipating risk factors, (2) early recognition of PPH by precisely and consistently measuring blood loss, and (3) adequate therapy conforming to national guidelines. Accurate, relevant, and comprehensive data collection is essential to identify specific risk indicators and evaluate guideline implementation in the future. To gain precise insight into the gaps in PPH management, we suggest that countries focus on disaggregated data analysis and criteria-based audits.

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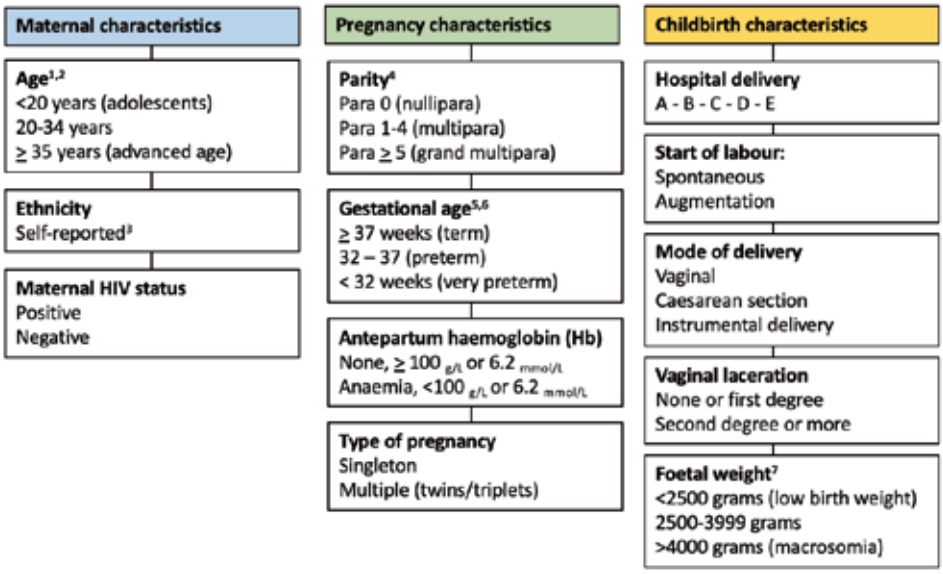
42. World Health Organization. Recommendation on Tranexamic Acid for the Treatment of Postpartum Haemorrhage. 2017. Accessed July, 2020..

Supplementary file 1. Categories of available maternal characteristics, pregnancy and delivery outcomes based on international classification



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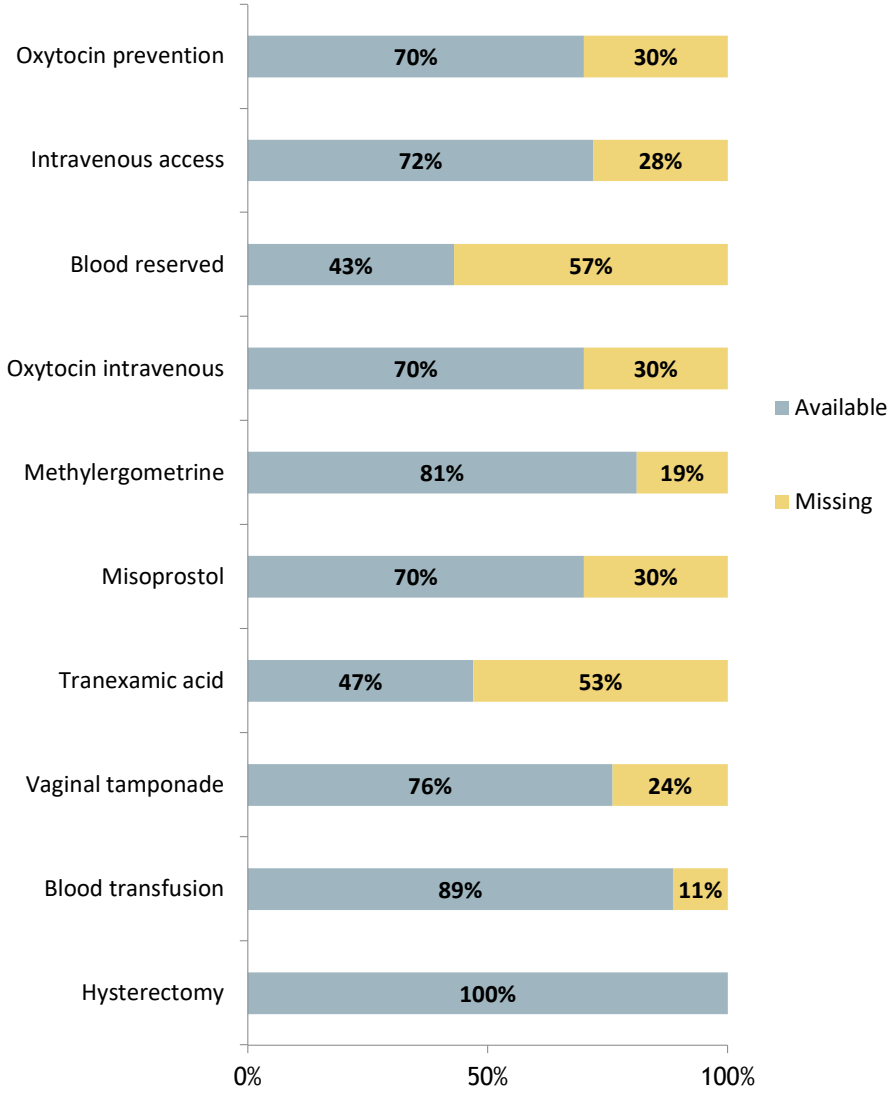
Supplementary file 2. Availability of data on causes and management of postpartum haemorrhage (PPH) to perform a criteria-based audit



Supplementary file 3. Maternal and perinatal characteristics of the hospital deliveries in Suriname, 2017

Hospital	A	B	C	D	E
Total, n= (100%)	**2101**	**2654**	**367**	**2456**	**1493**
Live births	2018 (96.0)	2616(98.6)	361 (98.4)	2416 (98.4)	1478 (99.0)
Stillbirths	83 (4.0)	38 (1.4)	6 (1.6)	40 (1.6)	15 (1.0)
Maternal Characteristics					
Age (years)					
12 – 19	382 (18.2)	355 (13.4)	67 (18.3)	384 (15.7)	101(6.8)
20 - 34	1465 (69.9)	1851 (69.8)	264 (71.9)	1724 (70.4)	1170 (78.4)
≥ 35	250 (11.9)	447 (16.8)	36 (9.8)	342 (14)	221 (14.8)
Missing	4	1	0	6	1
Ethnicity					
Maroon	863 (41.8)	785 (29.6)	2 (0.6)	844 (34.4)	90 (6.1)
Creole	541 (26.2)	589 (22.2)	18 (5.2)	517 (21.1)	305 (20.5)
Hindustani	328 (15.9)	477 (18.0)	196 (56.6)	382 (15.6)	272 (18.3)
Other[1]	155 (7.5)	381 (14.4)	66 (19.1)	394 (16.0)	498 (33.5)
Javanese	102 (4.9)	324 (12.2)	40 (11.6)	198 (8.1)	290 (19.5)
Indigenous	74 (3.6)	93 (3.5)	24 (6.9)	120 (4.9)	31 (2.1)
Missing	*38*	*5*	*21*	*1*	*7*
Maternal HIV status					
Positive	39 (1.9)	14 (0.5)	N/A	1 (0)	14 (0.9)
Missing	*1*	*0*		*1*	*0*
Pregnancy characteristics					
Parity					
0	601 (28.7)	1000 (38.0)	147 (40.2)	721 (29.4)	643 (43.1)
1 – 4	1265 (60.4)	1423 (54.0)	206 (56.3)	1495 (60.9)	823 (55.2)
≥ 5	227 (10.8)	210 (8.0)	13 (3.6)	240 (9.8)	25 (1.7)
Missing	*8*	*21*	*1*	*0*	*2*
Anaemia[2]	731 (50.4)	N/A	N/A	N/A	347 (24.2)
Missing	*652*				*58*
Twin / triplet	30 (1.4)	41 (1.5)	1 (0.3)	29 (1.2)	15 (1)

Supplementary file 3. Continued

Hospital	A	B	C	D	E
Delivery characteristics					
Onset of labour					
Augmentation	781 (37.2)	781 (37.2)	101 (27.5)	N/A	445 (34.2)
Missing	*1*	*2054*	*266*		*193*
Mode of delivery					
Spontaneous	1725 (82.1)	2026 (76.3)	285 (77.7)	1827 (74.4)	927 (62.1)
Caesarean Section	364 (17.3)	552 (20.8)	53 (14.4)	604 (24.6)	564 (37.8)
Instrumental	12 (0.6)	76 (2.9)	29 (7.9)	25 (1.0)	2 (0.1)
AMTSL severe PPH[3], n=155 (100%)					
Oxytocin prevention	19 (67.9)	30 (75.0)	7 (77.8)	29 (46.0)	11 (73.3)
Missing	*16*	*13*	*1*	*31*	*4*
Vaginal laceration					
2nd grade or higher	434 (27.8)	771 (72.7)	101 (95.3)	N/A	469 (58.6)
Missing	541	1593	261		1692
Birthweight (grams)					
< 2500	435 (20.9)	318 (12.0)	55 (15.1)	354 (14.4)	164 (11.0)
2500 – 3999	1599 (76.7)	2234 (84.6)	293 (80.3)	2054 (83.7)	1258 (84.6)
≥ 4000	52 (2.5)	88 (3.3)	17 (4.7)	46 (1.9)	65 (4.4)
Missing	*15*	*14*	*2*	*2*	*6*

Legend [1]Ethnicity other: Mixed, Chinese, Brazilian, Caucasian, unknown; [2]Haemoglobin ≤ 100 g/l or 6.1 mmol/l; [3]AMTSL: Active Management of the Third Stage of Labour; N/A = not available

The golden hour of sepsis: an in-depth analysis of sepsis-related maternal mortality in middle-income country Suriname

9

Lachmi R. Kodan
Kim J. C. Verschueren
Humphrey H.H. Kanhai
Jos J.M. van Roosmalen
Kitty W. M. Bloemenkamp
Marcus J. Rijken

PLoS ONE. 2018:13(7):e0200281

ABSTRACT

Background: Sepsis was the main cause of maternal mortality in Suriname, a middle-income country. Objective of this study was to perform a qualitative analysis of the clinical and management aspects of sepsis-related maternal deaths with a focus on the 'golden hour' principle of anti- biotic therapy.

Methods: A nationwide reproductive age mortality survey was performed from 2010 to 2014 to identify and audit all maternal deaths in Suriname. All sepsis-related deaths were reviewed by a local expert committee to assess socio-demographic characteristics, clinical aspects and substandard care.

Results: Of all 65 maternal deaths in Suriname 29 (45%) were sepsis-related. These women were mostly of low socio-economic class (n=23, 82%), of Maroon ethnicity (n=14, 48%) and most deaths occurred postpartum (n=21, 72%). Underlying causes were pneumonia (n=14, 48%), wound infections (n=3, 10%) and endometritis (n = 3, 10%). Bacterial growth was detected in 10 (50%) of the 20 available blood cultures. None of the women with sepsis as underlying cause of death received antibiotic treatment within the first hour, although most women fulfilled the diagnostic criteria of sepsis upon admission. In 27 (93%) of the 29 women from which sufficient information was available, substandard care factors were identified: delay in monitoring in 16 (59%) women, in diagnosis in 17 (63%) and in treatment in 21 (78%).

Conclusion: In Suriname, a middle-income country, maternal mortality could be reduced by improving early recognition and timely diagnosis of sepsis, vital signs monitoring and immediate antibiotic infusion (within the golden hour).

BACKGROUND

Sepsis is a major cause of severe maternal morbidity and mortality, especially in low- and middle- income countries. Early recognition of sepsis is crucial and sepsis should be treated by resuscitation with fluids and effective intravenous antibiotics should be given within one hour of the diagnosis.[1] The "golden hour of sepsis" stresses the relationship between timely initiation of antibiotic treatment and outcome: each hour delay in treatment reduces sepsis survival by 7.6%.[2] Pregnancy and delivery predispose women to infectious complications due to immunological and physiological alterations or from tissue damage during delivery. Recognition of sepsis during pregnancy, delivery and postpartum is difficult because of physiological adaptations to pregnancy, blood loss and increased maternal activity during labour.[3] WHO recently launched a new consensus defining maternal sepsis: a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or postpartum period.[4]

Although the 'golden hour of sepsis' principle is not validated for women with pregnancy or in the puerperium due to a lack of studies, the principle is assumedly even more important in pregnant, predisposed women where recognition is more difficult. Globally, maternal sepsis (10%) is the third most frequent cause of direct maternal deaths, preceded by haemorrhage (27%) and hypertension (14%).[5-7] In low- and middle-income countries (LMIC) maternal sepsis is a larger contributor to maternal mortality than in high- income countries (10.7% vs. 4.7% respectively).[5,8] In high-income countries, however, maternal morbidity and mortality due to sepsis is increasing.[9,10]

Suriname is an upper middle-income country in South America with a maternal mortality ratio of approximately 130 per 100.000 live births between 2010 and 2014.[11] A confidential enquiry in Suriname in 1991 reported sepsis to be the third most frequent underlying cause of maternal death (n = 10/64, 16%).[12] We recently published an increase in maternal deaths from sepsis, with sepsis as the most frequent cause (n=17/65, 27%).[11] This is poorly under- stood; therefore, an in-depth case analysis was considered necessary.

Classification of maternal deaths into direct (obstetric) and indirect (non-obstetric) causes has given the impression that direct maternal deaths should receive greater attention than indirect deaths. However, since the focus is on the reduction of all preventable deaths, division between direct and indirect maternal deaths can be seen as arbitrary and counterproductive.[13] In this study, we therefore choose for a more theme-based approach by analysis of all sepsis-related deaths.

Primary objective of this study was to perform a qualitative analysis of the clinical aspects and management (based on the golden hour principle) of sepsis-related maternal deaths in Suriname. Secondary objectives were first to describe incidence and characteristics, second to analyse underlying causes, and third to evaluate quality of care and finally substandard care identification with audit to improve sepsis prevention, recognition and treatment strategies.

METHODS

Suriname is multi-ethnical with 541.638 inhabitants and one of the smallest populated countries in South America, with a density of 3,3 inhabitants per square kilometre. There are approximately 10.000 deliveries annually of which most in hospitals led by midwives and obstetricians (82%).[11] Women with high-risk pregnancies are referred by the primary health services, which can take more than two hours, as some rural areas are only accessible by boat or airplane. Postpartum, women are usually discharged from hospital six hours after an uncomplicated delivery. They are seen at outpatient clinics or hospitals once, seven days after discharge. Postnatal care home visits are not done.

In 2015 a reproductive age mortality survey (RAMoS) was performed to identify maternal deaths in Suriname between 2010 and 2014.[11] Medical records were collected of pregnancy related deaths identified by vital registration, or by screening of medical archives of all hospitals and primary care facilities. An anonymous case summary was made conform the FIGO-LOGIC *MDR clinical summary form* tool.[14] A local expert committee consisting of obstetricians,

midwives, internal medicine specialists or anaesthetists reviewed each case summary. The committee agreed on the underlying causes and classified the cases.[11] To analyse substandard care factors an adapted version of the FIGO-LOGIC MDR *Grid analysis of clinical case management* form was used.[14] For this study specifically, medical records of all maternal deaths related to sepsis, were scrutinised for signs of sepsis, clinical management, primary sources of infection and causative pathogens. Data were manually entered into IBM SPSS version 21.0 (Armonk, New York, USA) for analysis. Descriptive statistics and frequencies were used to describe patient demographics, clinical and pregnancy characteristics and substandard care factors. Graphs were manually made in IBM SPSS version 21.0 and Microsoft Excel 2016 to demonstrate qualitative information on sepsis diagnosis and management.

Definitions: Sepsis-related maternal deaths included deaths with sepsis as the underlying cause, sepsis as the mode of death and sepsis as a contributing factor. The underlying death cause was defined as the disease or condition that initiated the chain of events leading to death.[15] The mode of death was the disease or condition ultimately leading to death.[15] A contributing factor was defined as a condition existing before or developed during the chain of events leading to death, that predisposed the woman to death but was not causing death.[15]

Clinical diagnosis of severe maternal sepsis was made by using the UK Obstetric Surveillance System definition, which is an adapted version of the systemic inflammatory response syndrome (SIRS) criteria: an assumed or proved infection with at least two of the four criteria (temperature of > 38 ℃ or < 36 ℃, heart rate of > 100 beats per minute, respiratory rate of > 20 per minute, white blood cell count of > 17 x 10^9 cells/L or < 4 x 10^9 cells/L) measured on two occasions at least four hours apart.[9,10] Severe sepsis was associated with organ dysfunction (i.e. cardiovascular, respiratory, renal, coagulation, hepatic, neurological and uterine), hypoperfusion or hypotension.[16,17] Organ dysfunction was determined with the WHO near-miss tool.[18] In depth analysis of the maternal deaths with sepsis as underlying cause was performed in this study by determining when the first

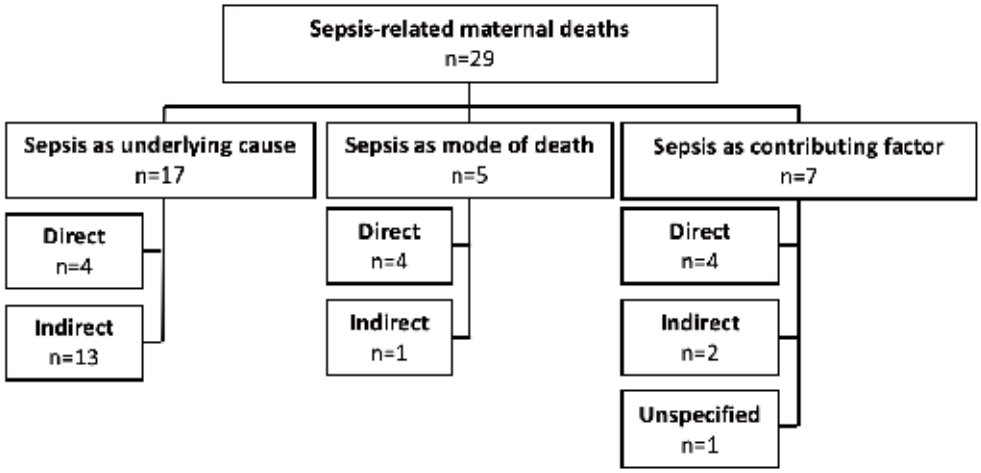
clinical signs of sepsis were manifested. The 'golden hour' principle (intravenous antibiotics given within an hour of severe sepsis diagnosis) was then evaluated.[1] Substandard care was defined as care below expected standards in the specific setting the woman was treated. The local expert committee evaluated substandard care in the absence of guidelines on sepsis in Suriname. Assessment of delay in receiving care was made by evaluating vital signs monitoring, diagnosing sepsis and initiation of antibiotic treatment. Other sub- standard care factors such as miscommunication, availability and patient-associated factors were also evaluated.

Ethical considerations: The medical ethical review board of the Surinamese Central Committee on Research Involving Human Subjects and the Ministry of Health of Suriname approved the study [VG 006–15]. Patient's names, hospitals and health care workers information remained confidential. No informed consent was required as only retrospective anonymised information from medical records of deceased women was used.

RESULTS

In the previously reported study on maternal mortality in Suriname between 2010 and 2014 sepsis was the most frequent underlying cause of death occurring in 17 of the 65 maternal deaths.[11] Of the women who died of other underlying causes, in five sepsis was the mode of death and in seven women sepsis was contributing to the death. Hence, in total 29 (45%) of the 65 maternal deaths were sepsis-related (figure 1). Medical records of two sepsis-related deaths (classified as indirect deaths with sepsis as underlying cause) were missing, therefore in-depth analysis of clinical aspects and substandard care was performed in 27 (93%) of sepsis-related maternal deaths. All the sepsis-related cases defined by the expert committee were also diagnosed by the clinicians who were in charge of the patients.

Figure 1. Overview of the sepsis-related maternal deaths in Suriname, 2010-14



Characteristics: In fourteen (48%) of the twenty-nine sepsis-related maternal deaths women were from maroon ethnicity, of which 13 (93%) had social insurance (insurance paid by the government for people of low socio-economic status) (table 1). Death occurred postpartum in 21 women (72%), mostly within one week (n=13, 62%). Two of the HIV-positive deceased women also had sickle cell (type SS) disease. Eighteen women (62%) died in the intensive care or coronary care unit, while nine (31%) died on the ward where critically ill women could not be monitored adequately. One woman died in the emergency department and one at home. Caesarean section was performed in eight (38%) of the 21 postpartum, sepsis-related deaths. All were elective caesarean sections; in two of these eight women the death was classified as a direct maternal death (table 2). In four women a caesarean section was performed because of pre- eclampsia, in one case because of foetal distress, one woman had a sickle cell crisis, and two women were in a critical condition due to heart failure and Shigella sepsis.

Sepsis as the underlying cause: Four women with sepsis as underlying cause were classified as direct maternal deaths (table 2). Underlying causes were endometritis in three women and wound infection in one woman.

Table 1. Characteristics of the sepsis-related maternal deaths (n=29)

	n=29 (100%)
Age	
< 20	7 (24)
20-35	18 (62)
> 35	4 (14)
Ethnicity	
Hindu	5 (17)
Creole	6 (21)
Maroon	14 (48)
Javanese	3 (10)
Indigenous	0 (0)
Mixed	1 (4)
Insurance (n=28)	
Social insurance	23 (82)
State health	4 (14)
Private	1 (4)
Not insured	0 (0)
Parity (n=27)	
< 3	18 (67)
≥ 3	9 (33)
Antenatal care[1] (n=23)	
None	4 (19)
< 4	6 (29)
≥ 4	11(52)
Sickle cell disease (n=19)	
SS	4 (21)
Negative	15 (79)
HIV (n=23)	
Positive	6 (26)
Negative	17 (74)
Anaemia in mmol/L (n=23)	
Severe anaemia (Hb ≤ 4.5)	6 (26)
Moderate anaemia (Hb 4.6 – 6.5)	8 (35)
Mode of delivery (n=21)	
Spontaneous	13 (62)
Caesarean section	8 (38)
Twins (n=23)	
Yes	3 (13)
No	20 (87)

Table 1. continued

	n=29 (100%)
Stillbirth[2] (n=27)	
Yes	13 (48)
No	14 (52)
ICU-admission	
Yes	18 (62)
No	11 (38)
Gestation at death	
Early pregnancy	2 (7)
Antepartum (n=6)	
< 34 weeks	*4 (14)*
≥ 34 weeks	*1 (3)*
GA unknown	*1(3)*
Postpartum (n=21)	
≤ 48 hours	*4 (14)*
2 – 7 days	*9 (31)*
1 – 6 weeks	*8 (28)*

Legend [1] Antenatal care starting from gestation of 16 weeks; [2] Stillbirth of a gestation of more than 22 weeks or 500 grams.

All women had term or near-term pregnancies and died within the first week postpartum. They had ruptured membranes less than 12 hours before delivery and none of the neonates died or showed signs of infection. The remaining 13 deaths were classified as indirect maternal deaths: pneumonia (n=7, 54%), meningitis (n=2), gastro-enteritis (n=2), urosepsis (n=1) and HIV therapy-induced hepatitis (n=1).

Sepsis as the mode of death: These five cases included death from 1) a bowel perforation following a mechanically induced abortion; 2) a central venous line sepsis in a woman in the ICU with bleeding from coagulation disorders following foetal death syndrome; 3) a craniotomy wound infection in a hypertensive woman with intracranial bleeding and eclampsia; 4) severe sepsis following multi-organ failure after iatrogenic hypote;nsion due to overdose of antihypertensive medication in severe pre-eclampsia and 5) endocarditis in a woman with aortic valve prosthesis.

Table 2. Case description of direct maternal deaths with sepsis as underlying cause

Case	Diagnosis	Culture	Time Death	Time to death	ICU	Antibiotics
Teenager Term pregnancy	Endometritis after manual placenta removal	Not performed	PP 3 days	3 days	No	Amoxicillin orally
40+ years Near term pregnancy	Caesarean due to pre-eclampsia, complicated by endometritis and pneumonia	Blood culture: no growth	PP 6 days	7 days	Yes	Initially amoxicillin orally. After 2 days intravenous amoxicillin, gentamycin and metronidazole
Term pregnancy HIV +	Vacuum extraction and episiotomy complicated by endometritis and pneumonia	Blood culture: P. aeruginosa (no suscep-tibility done)	PP 7 days	2 days	No	Initially ciprofloxacine orally profylactic. 5 days later intravenous cefotaxime, metro-nidazole, cotrimoxazole
Near term pregnancy HIV + HbSS	Caesarean due to pre-eclampsia, complicated by a wound infection	Blood culture: no growth	PP 7 days	2 days	Yes	Initially amoxicillin orally. After 5 days amoxicillin intravenously + metro-nidazole, gentamycin and ciprofloxacine

Sepsis as a contributing factor

In seven cases sepsis was a contributing factor; underlying causes were severe pre-eclampsia and/or eclampsia (n=4), diabetic kidney failure with an infected diabetic foot and osteomyelitis (n=1), heart failure in a woman with mitral valve prostheses and endocarditis (n=1) and one case where sepsis contributed to the death but with the cause remaining unclear. The main cause of infection was pneumonia, which affected 14 women (48%), followed by wound infections (n=3, 10%) and endometritis (n=3, 10%). Blood, urine and/or sputum cultures or vaginal swabs were obtained in 23 cases (85%).

Table 3. Micro-organisms isolated from the cultures performed

Blood cultures n=10/20 (50%)	**Urine cultures** n=3/13 (23%)	**Sputum cultures** n=4/6 (66%)
P. aeruginosa[n=2]	Actinobacter	P. aeruginosa [n=2]
Enterobacter [n=2]	K. pneumoniae	K. pneumoniae [n=2]
Gram negative rods [n=2]	E. Coli	
E. Coli		
Shigella flexneri		
β-hemolytic strept.group A		
Enterococcus faecalis		

No culture was done in four cases because of temperature below 38 degrees (n=2), very rapid deterioration of the condition of the patient (n=1) and loss of blood sample before reaching the laboratory (n=1). Results of the cultures were available in 20 cases and not traceable in the remaining three cases. Either one of the cultures were positive in 15 cases (75%). Blood culture showed growth of pathogens in 10 cases (50%) (table 3).

Clinical aspects: Figure 2 demonstrates the number of cases per dysfunction organ system. At least two organ dysfunctions were present in 20 (74%) cases. The respiratory system was the most frequently documented organ dysfunction in 17 cases (63%), followed by the renal (n=14, 52%) and hepatic system (n=12, 44%).
Substandard care factors which contributed to death were identified in 25 of 27 women (93%) with a sepsis related death. Two medical files were not reviewed for substandard care as they were missing. Delay in reaching care occurred in four women (15%), while delay in receiving care in the hospital occurred in 24 women (89%) (table 4).

Delay in monitoring & diagnosis: The expert committee identified delay in the diagnosis of sepsis in 17 women (63%). Inadequate monitoring occurred in 16 women (59%). In Figure 3 the adapted SIRS-criteria that were used and reported by clinicians in the 27 cases are shown. Respiratory rate was the most poorly reported vital sign, reported in only 13 women (52%).

Figure 2. Sepsis-related maternal deaths with organ dysfunction (n=27)

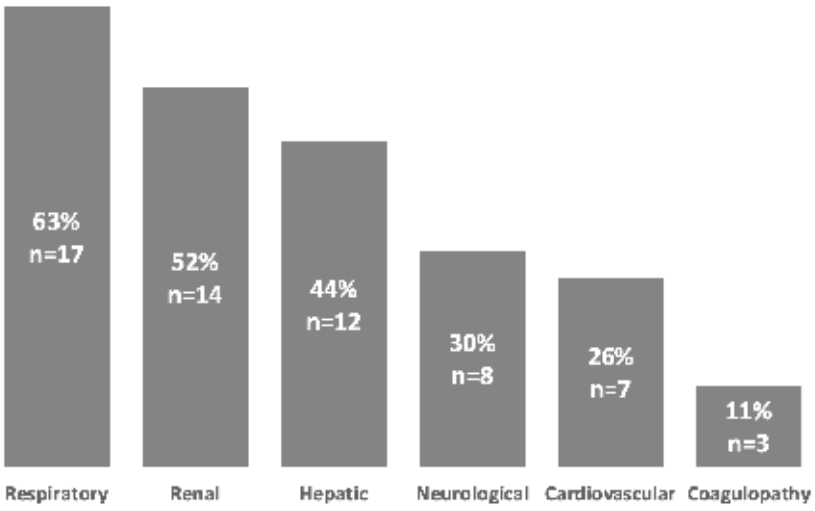
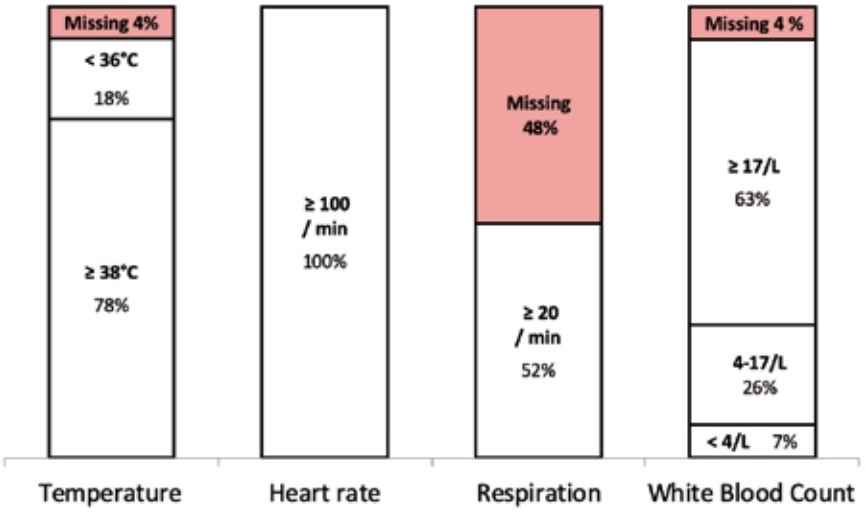


Figure 3. Clinical signs when sepsis was diagnosed in the sepsis-related maternal deaths in Suriname between 2010 and 2014 (n=27)



Temperature was below 36 degrees in five women (18%) and white blood cell count was nor- mal in seven women (26%). Information on mental state was missing in 19 women (70%). In-depth analysis of the maternal deaths with sepsis as the underlying cause (n=17) is provided in Figure 4. Vital signs were taken upon admission in all cases, though any of the vital signs were rechecked within 24 hours in only seven septic women. According to documentation temperature, pulse and blood pressure were rechecked within 24 hours in respectively four (24%), five (30%), and six (35%) women. Organ dysfunction was already present when initial signs of sepsis were manifest in 15 of the 17 women. In two women no information was available because no laboratory tests were done at the time sepsis was diagnosed.

Delay in treatment and the golden hour principle: The committee agreed that there was delay in treatment in 22 women (81%). Intravenous antibiotic treatment was given in 25 of the 27 women (93%). In 12 women (44%) empiric antibiotic treatment appeared to be right according to the culture sensitivity profiles. In eight women (30%) frequent switch in antibiotics, with more than three different regimes, was given within three days, without sensitivity profiles known. In-depth analysis of the maternal deaths with sepsis as the underlying cause (n=17) illustrated that 15 women (88%) had already signs of severe sepsis when admitted in the hospital. In none of those women antibiotics were administered within the first hour of diagnosis of sepsis (Figure 4). Mean (SD) time between the first sign of sepsis and initiation of intravenous antibiotic treatment was 12.5 hours (SD 5, range 2–48 hours). In five (29%) women intravenous antibiotics were administered more than 24 hours after the onset of sepsis. No intravenous antibiotics were administered in two women: in one case the woman died within two hours after the diagnosis and in the other woman antibiotics were given orally.

Other substandard care factors: Delay due to miscommunication between health care professionals occurred in ten cases (37%) (table 4). An example where miscommunication occurred is the case of direct maternal death from sepsis after

manual placenta removal: one gynaecologist prescribed primperan (a gastrointestinal stimulant) for vomiting in this woman with a bumped and shiny belly and another stopped it the next day considering primperan to be contra-indicated when an intestinal obstruction is suspected. In three cases (11%) an Intensive Care bed was requested but not available. In one case (4%) blood was not available for transfusion. The expert committee agreed that substandard care factors definitely or most probably led to death in 10 of the 27 women (37%).

Discussion

This is the first detailed clinical study of pregnant and postpartum women dying of sepsis in Suriname. Of all 65 maternal deaths from 2010–2014 in Suriname 29 (45%) were sepsis related and in 17 of these women (27%) sepsis was the leading underlying cause of death. The attribution of sepsis to maternal deaths in Suriname was much higher than the 8.3% reported in Latin America and Caribbean or the 10.7% worldwide.[5] In Brazil, however, infection was responsible for nearly half (46%) of all facility-based maternal deaths, much higher than previously thought.[19] While various high-income countries performed extensive qualitative studies on sepsis-related maternal mortality and morbidity, there is scarce data from middle- or low- income countries.[9,10,19-22]

Three major findings of our study were identified: first, most sepsis-related maternal deaths occurred in women with low economic status and postpartum, within one week after delivery; second, the most common identified source of sepsis causing maternal deaths in Suriname was pneumonia; and finally, there was a major delay in monitoring, diagnosis and prompt treatment with regards to the golden hour principle.

Classifying the cause of maternal death is a complex matter with great classification differences between countries.[23] WHO guideline for ICD-MM classification states that the underlying cause of maternal death is where the chain of events leading to death starts. The ICD-MM classification system, however, impedes for example “a death with an abortive outcome” to be classified as a “pregnancy-related infection”.

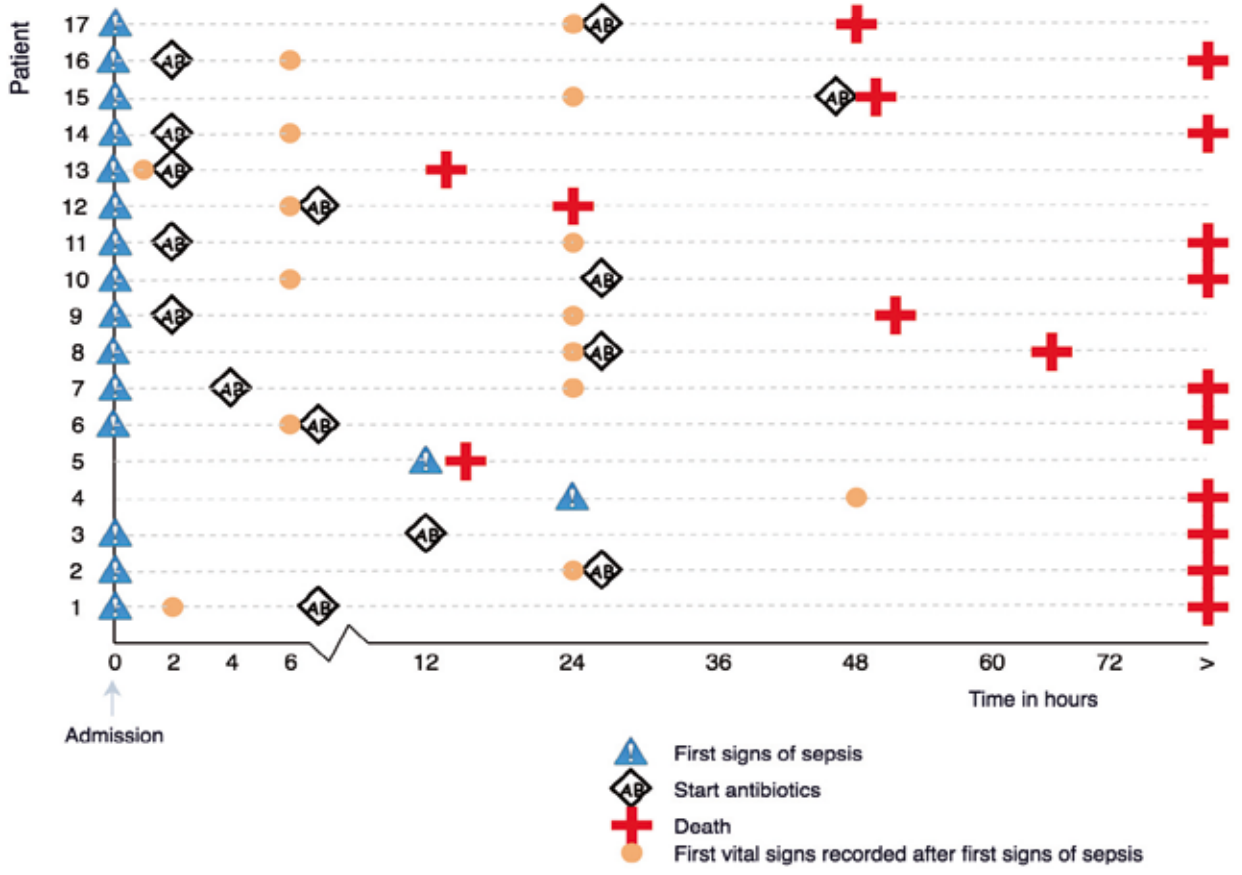
Table 4. Substandard care of sepsis-related maternal deaths (n=27)

	n=27 (100%)
Delay in reaching care	4 (15)
Delay in receiving care	24 (89)
Health care provider factors	
Insufficient quality of care	21 (77)
Inadequate monitoring	16 (59)
Poor Communication	10 (37)
Delay in diagnosis	17 (63)
Delay in treatment	21 (78)
Unavailability	
Intensive Care Unit Bed	3 (11)
Staff	2 (7)
Medication	4 (15)
Blood	1 (4)
Patient factor	
Poor adherence to medication	7 (26)
Substandard factors leading directly to maternal death	
Definitely / most probably	10 (37)
Possibly	13 (48)
Unable to determine	2 (7)

Also, a woman can only have one underlying cause of death for classification purposes. One of the cases in our study, a woman who died due to com- plications (sepsis) of a mechanically-induced abortion, was classified as "a death with an abortive outcome", would not be included in this study if only underlying causes were studied. Similarly, another case of a woman with cerebral bleeding due to hypertensive disorder who died due to a sepsis caused by the craniotomy wound, would not have been included (sepsis as mode of death).

While malaria in pregnancy caused maternal mortality in the nineties in Suriname (4,7%, n=3/64), no maternal deaths due to malaria have been diagnosed between 2010 and 2014.[11,12] This is in line with the numbers in the general population: deaths from malaria have declined with 92% since 1990.[24] Pneumonia was the most common source of sepsis in Suriname.

Figure 4. Overview of the time between admission, first signs of sepsis, first vital signs after admission, the initiation of antibiotic treatment and death per patient with sepsis as the underlying cause of death (n = 17)



Accordingly, as in the UK, not only genital tract sepsis but more importantly non-obstetric causes as especially pneumonia, but also urosepsis were reasons for maternal mortality.[22] The attribution of indirect causes has been increasing globally.[5] An improved enquiry and registration of deceased women on non-obstetric wards, as done in this study, can also be the result of the relative increase of indirect maternal deaths in middle-income countries. Because a RAMoS was done nationwide, also indirect deaths at other wards than the maternity ward were included, leading to more non-obstetric cases as pneumonia.[11]

Delays in reaching health care facilities were not a major problem (n=4/27, 15%). Each year only 5% (n=500/10.000) of deliveries take place in the rural interior and these are mainly low risk pregnancies. However, delays in receiving quality care in health facilities occurred more frequently (n=24/27, 89%): there was delay in monitoring, diagnosis and treatment of sepsis- related deaths.[25] Suriname, with an MMR of 130, could be classified as stage III in the WHO model of "obstetric transition", which describes the shift of countries from high MMR to low ratios.[25] In this stage of transition indirect causes such as non-obstetric sepsis, are becoming important contributors to maternal deaths, whereas direct maternal deaths still remain significant. In this model essential recommendations to reduce maternal mortality for stage III include improvement of quality of intra-hospital care (third delay), with skilled birth attendance and appropriate management of complications.[25,26] Therefore, we focus on these delays in health facilities in greater detail.

Adequate monitoring of pregnant women for clinical signs of infection in early stages is crucial.[27,28] To identify critically ill pregnant women a modified early obstetric warning score (MEOWS) could be used.[29] To perform MEOWS systolic blood pressure, diastolic blood pressure, respiration rate, heart rate, oxygen saturation, temperature and con- science level should be assessed repeatedly. Recognition of predetermined abnormal values of these vital signs should lead to an adequate medical response.[29]

In this study substandard care by poor monitoring occurred in 16 of 27 women (59%) and there had been inadequate recognition of early warning signs. No

structural scoring of vital parameters as the MEOWS was used. In all sepsis-related cases initially there was a tachypnoea of >20 per minute (documented in 48% of the records) and/or a tachycardia of more than 100 per minute indicating first signs of severe sepsis.[20] However, these early signs of sepsis were not recognised in nine women (32%) as they died on the ward without receiving adequate monitoring and treatment.

Clinical characterization of sepsis may be achieved by performing a SOFA (sepsis-related or sequential organ failure assessment) score, which determines the extent of organ dysfunction.[30,31] Though SOFA is not validated in pregnant women, a simplified form of SOFA, the quick SOFA or qSOFA (respiration rate $\geq$22 per minute, altered mentation and systolic blood pressure <90 mmHg) can be used as a simple bedside test to identify women with suspected infection associated with poor outcome. Respiratory rate also seems to correlate with severity of sepsis.[27] In this study we did not use qSOFA as diagnostic or prognostic criterium as it is not validated in pregnant women. More importantly information on respiration rate (n=13, 48%) and mentation (n=19, 70%) were often missing in our population and it was therefore not possible to assess qSOFA scores.

This study illustrated that delay in monitoring led to delay in diagnosis and treatment of sepsis. Even when sepsis was recognised, in none of the cases antibiotic treatment was started within one hour. According to the Surviving Sepsis Campaign guidelines any sign of infection should promptly be recognised and treated.[1] Aggressive fluid resuscitation and early and appropriate antibiotic treatment is the best way to manage sepsis.[1,3] Antibiotic treatment should be started within one hour (golden hour principle).[1]

Recommendations to prevent maternal deaths from sepsis in Suriname

From this maternal death from sepsis analysis we could distillate three major recommendations for maternal care in Suriname:

1) improve postpartum care;
2) introduce a maternal sepsis bundle for diagnosis;

3) early treatment of pregnant and postpartum women in close collaboration with other medical disciplines;

4) improve postpartum care by improving the information given to patients and a structured care system after delivery;

5) introduction of standard recording of vital signs (as MEOWS) is strongly recommended in order to identify critically ill septic patients.[29]

Sepsis performance improvement programs which includes guidelines on monitoring, prevention and early treatment of sepsis are necessary.[1] Introduction, implementation and adherence to Surviving Sepsis Campaign (SSC) bundles (a set of recommendations for sepsis screening and treatment) could enhance the care for septic pregnant and postpartum women in hospitals. Selection of an optimal intra- venous empiric antimicrobial regimen is the cornerstone of the treatment of sepsis.[1] A nationwide guideline should be developed and implemented in Suriname. As non-obstetric causes of sepsis are becoming more important, a multidisciplinary approach in treatment of sepsis is essential.[1,22] Collaboration of obstetricians with other physicians as internal medicine specialists, microbiologists, nurses, and pharmacists is mandatory.

Strengths and limitations

Regarding the difficulties collecting clinical data from medical records in a middle-income country, this extensive dataset is unique and valuable. There are, however, some limitations. Cases were analysed and classified by the expert committee based on information of medical records, in which documentation was not always sufficient and sometimes information was missing. However, the local team was accustomed to these records and scrutinised all medical information for signs of recognised medical comorbidities predisposing pregnant and postpartum women to infection including obesity, diabetes mellitus, HIV / AIDS, hepatitis, sickle cell disease, malaria, malnutrition, multiple gestations and severe anaemia.[1,21,32] Unfortunately, in this study information on weight and nutrition of the women was not available. At the moment we are prospectively collecting morbidity data for all pregnant women in Suriname. Finally, while WHO launched the new definition of

maternal sepsis, it remains difficult to compare data between countries because various criteria and definitions are used.[4] The WHO GLOSS, the Global Maternal Sepsis Study, in more than 500 healthcare facilities in 53 countries will address these issues.[4]

CONCLUSION

Sepsis was the leading cause of maternal death in Suriname, with most deaths occurring after delivery. Non-obstetric causes (as pneumonia) were the most important primary contributors to sepsis. Monitoring of critically ill septic patients was inadequate and antibiotics were not started within the "golden hour". A uniform international definition of sepsis in pregnancy / postpartum with clear criteria is mandatory for early recognition of sepsis. Close monitoring and prompt treatment of patients with sepsis is essential. Introduction of early sepsis warning signs, guidelines on postpartum care and introduction and implementation of SSC bundles for pregnant and postpartum women could prevent maternal deaths from sepsis.

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Part IV

Response

If you can't fly, then run,
If you can't run, then walk,
If you can't walk, then crawl,
But whatever you do,
You have to keep moving forward
~ Martin Luther King Jr.

Bottom-up development of national obstetric guidelines in middle-income country Suriname

10

Kim J.C. Verschueren
Lachmi R. Kodan
Tom K. Brinkman
Raëz R. Paidin
Sheran S. Henar
Humphrey H.H. Kanhai
Joyce L. Browne
Marcus J. Rijken
Kitty W.M. Bloemenkamp

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ABSTRACT

Background: Obstetric guidelines are useful to improve the quality of care. Availability of international guidelines has rapidly increased, however the contextualization to enhance feasibility of implementation in health facilities in low and middle-income settings has barely been studied. This study describes the approach and lessons learned from the 'bottom-up' development process of context-tailored national obstetric guidelines in middle-income country Suriname.

Methods: Local obstetric health care providers initiated the guideline development process in Suriname in August 2016 for two common obstetric conditions: hypertensive disorders of pregnancy (HDP) and post-partum haemorrhage (PPH).

Results: The process consisted of six steps: (1) determination of how and why women died, (2) interviews and observations of local clinical practice, (3) review of international guidelines, (4) development of a primary set of guidelines, (5) initiation of a national discussion on the guidelines content and (6) establishment of the final guidelines based on consensus. Maternal enquiry of HDP- and PPH-related maternal deaths revealed substandard care in 90 and 95% of cases, respectively. An assessment of the management through interviews and labour observations identified gaps in quality of care and large discrepancies in the management of HDP and PPH between the hospitals. International recommendations were considered unfeasible and were inconsistent when compared to each other. Local health care providers and stakeholders convened to create national context- tailored guidelines based on adapted international recommendations. The guidelines were developed within four months and locally implemented.

Conclusion: Development of national context-tailored guidelines is achievable in a middle-income country when using a 'bottom-up' approach that involves all obstetric health care providers and stakeholders in the earliest phase. We hope the

descriptive process of guideline development is helpful for other countries in need of nationwide guidelines.

BACKGROUND

Reducing maternal mortality remains a universal priority for clinicians, researchers and policymakers. The obstetric transition model describes five stages in which countries move, from high to low maternal mortality.[1] Phase three is considered a tipping point, in which pre- dominantly direct causes of mortality persist, but as most women reach hospitals, improving the quality of care (skilled birth attendance, appropriate management of complications) becomes essential to further reduce mortality.[1] In low- and middle-income countries (LMIC), where informal sharing of knowledge and experience-based decision-making often dominates, the development and implementation of feasible clinical guidelines are key to improve quality of evidence-based, respectful maternity care.[2]

Evidence about guideline implementation strategies in low- and middle-income countries has increased in the past years and a number of enablers of effective implementation have been identified.[3,4] The most import- ant known enabler is to use a multi-facetted strategy (i.e. combining different methods of implementation) instead of a single intervention (e.g. providing health care workers with existing guidelines).[3-7] Positive health care providers' attitude towards the guidelines is strongly associated with adherence to the guidelines. The process of guideline development before implementation is critical. By creating appropriate guidelines tailored to the context, use in local reality is ensured and sustainable adherence is created.[7-9]

Suriname is an example of a country in obstetric transition phase three with a fairly high maternal mortality ratio (MMR) of 130 per 100.000 live births compared to other countries in Central and South America.[10-12] Similar to most LMICs, the primary causes of maternal deaths in Suriname are postpartum haemorrhage (PPH) and hypertensive disorders of pregnancy (HDP).[11] The majority of these deaths are due to 'third delay' factors linked to the quality of care, such as in-hospital delay of diagnosis and treatment.[11,13] The introduction of nationwide guidelines for the

clinical management of these complications is therefore a promising strategy to improve health outcomes.

The aim of this article is to describe the approach and lessons learnt from our 'bottom-up' strategy to develop national guidelines tailored to the context of middle-in- come country Suriname for post-partum haemorrhage and hypertensive disorders of pregnancy. These lessons can inform and support the guideline development processes in other settings.

METHODS

Suriname is a middle-income country on the northeastern coast of South-America with 550.000 inhabitants in 2016 and almost 10.000 deliveries annually. Of all deliveries, 92% of women give childbirth in the five hospitals in the country, while 8% deliver in primary health care centres and 2% at home. Four hospitals are located in capital city Paramaribo and one smaller hospital is located on the far West-coast, Nickerie.[14,15] In 2016, fifteen obstetricians, eight residents and approximately fifty midwives provided maternal care in the hospitals in Suriname. Obstetric care provision in Suriname is mainly influenced by Dutch guidelines (Nederlandse Vereniging van Obstetrie en Gynaecologie, NVOG) as residents follow two years of their training in the Netherlands.[16,17] In addition, the American College of Obstetrics and Gynecology (ACOG) and the World Health Organization (WHO) guidelines are used.[18-21] In 2015 and 2016 a national maternal death review committee was established, consisting of local obstetric health care providers. This committee audits all pregnancy-related deaths in the country. Among the recommendations are the implementation of national guidelines on the most important causes of maternal mortality and training emergency (obstetric) skills. Subsequently, the maternal death committee members initiated the bottom-up guideline development consisting of six-steps, as described below.

I. Determine how and why women died: A Reproductive Age Mortality Survey was initiated by a local obstetrician (LK) and the principle investigator (KV) to audit all maternal deaths between 2010 to 2014. The study revealed a maternal mortality

ratio of 130 per 100.000 live births with many preventable deaths due to post partum haemorrhage and hypertensive disorders.[11] The maternal deaths due to, or aggravated by HDP and PPH were further analyzed for substandard care factors and the three-delay model was applied to establish why women died and what could have prevented the death.[22]

II. Interviews and observations of local clinical practice: First, to determine the standard of care for HDP and PPH management, the obstetric departments of the five hospitals were asked to share their local protocols. Second, interviews on practice were performed with forty-three obstetric health care providers from all hospitals: 13 obstetricians, 8 residents, and 24 midwives. An anonymous national questionnaire was completed. The questionnaire was developed for the purpose of this study. The structure of the interview was based on international consensus on HDP and PPH prevention, diagnosis and treatment (adapted ACOG checklists).[19,23] Questions were also asked on encountered barriers and enablers in the current system. Semi-structured one-on-one interviews, conducted by the principle investigator (KV), were held with the gynaecologists and head of midwives of each hospital to assess their opinions and wishes with regard to the new guidelines.
Third, clinical observations were performed by four medical doctors working in the hospitals and four medical students conducting their rotations. The principle investigator provided the observers a summary of the abovementioned findings per hospital. During a two-month period (250 deliveries) observations were performed in all hospitals on whether the answers in the surveys matched reality. The medical students used the ACOG-adapted checklists for HDP and PPH during the observations.

III: Review international guidelines: The four international guidelines on HDP and PPH used most by local health care providers were compared for similarities and differences in definition, causes and recommendations in diagnosis and treatment. Both the HDP and PPH guidelines from the WHO, ACOG and NVOG were assessed. Additionally, the PPH guideline of the British Royal College of Obstetrics and

Gynaecology (RCOG) and HDP guideline of Australian Queensland Brisbane (QB) were assessed.

IV: Develop a primary set of guidelines: In August and September 2016 the initial version of the guidelines were drafted by four members of the study team and one nurse-midwife of each hospital. The above mentioned guidelines were used as a template. The drafted guidelines were reviewed by external (four international experts from the Netherlands) and internal reviewers (eighteen local obstetricians and nurse-midwives). The reviewers independently discussed the guidelines with the principle investigator. During a three-hour meeting with all the reviewers the 'key discussion points' were established and simulation-based trainings were prepared. A literature search was conducted on the 'key discussion points' by five of the authors (KV, TB, RP, LK, KB) for evidence-based answers and considerations.

V: Initiate national discussion about content of guidelines: Two hundred and one obstetric health care providers (obstetricians, paediatricians, anesthesiologists, residents, doctors, midwives, nurses, trainees) and policy makers (Ministry of Health and Pan-American Health Organization (PAHO)) attended a four-day conference (November 10-13, 2016) to discuss the recommendations in two new national obstetric guidelines. The meeting was moderated by one local and one international obstetrician. The two guidelines were adapted during the conference. A two-hour simulation-based training was held on each day to practise and evaluate the content of the guidelines. These trainings were based on maternal deaths of the previous years and led by a team existing of one international expert, two local obstetricians, an anesthesiologist and two midwives. The participants completed an evaluation survey (5-point Likert scale, from unsatisfied to extremely satisfied) about the different components of the conference.

VI: Final guideline development and evaluation

The last drafts of the guidelines were distributed digitally and on paper. All obstetric health care providers (including those who did not attend the meeting)

were requested to provide feedback within six weeks. The local obstetricians (n=13) and chief midwives of each hospital (n=5) were personally visited for the final feedback and their formal approval.

Ethical approval was obtained from the Surinamese Central Committee on Researching Human Subjects for the study of maternal deaths [Reference number VG 006-15] in March 2015.[11] The Surinamese Central Committee on Researching Human Subjects waived the need for approval for the remainder of the project.

RESULTS

The six phases of the guideline development process were executed in a period of four months (figure 1).

I: Determine how and why women died

The substandard care analysis of the extracted maternal deaths related to HDP (n=19) and PPH (n=21) in Suriname reveals that most substandard care factors are *third delay* factors due t a lack of quality of care (see table 1).[11]

The substandard quality in care seen in the maternal deaths was mostly due to the lack of anticipation, delay in recognition of seriously ill women, delay in providing available treatment and a lack of supportive treatment (e.g. oxygen, uterine massage). In three (15%) of the maternal deaths blood products were not available within 60 minutes. Medication (oxytocin, misoprostol or magnesium sulfate) was not available in two women who died of PPH during transportation to the hospital.

II. Interviews and observations of local clinical practice: Two of the five hospitals used short local protocols for HDP and PPH. These protocols were available both digitally and on paper. The other three hospitals did not have protocols. Fourty-three interviews were conducted with obstetric health care providers and showed differences in perception of optimal HDP and PPH-care (table 2 and 3). The interviewees indicated that the guidelines most frequently used by local staff were from WHO, NVOG and ACOG, though only 60% (n=26/43) said to actually use

them.[16-21] A frequent mentioned arguments of the health care providers was that the international guidelines were *"complex, not applicable, not achievable, unclear and/or not practical in its use"*. Doctors mentioned that *"there are discrepancies between international guidelines leading to discrepancies in regimens between gynaecologists in daily practice"*. Lastly, midwives mentioned that they *"miss easy-to-use checklists or flowcharts which we can adapt to our situation"*. The 'standard care' regarding HDP and PPH per hospital can be found in supplementary file 1 and 2. Noteworthy, are differences in daily regimen between hospitals within five kilometers distance of each other.

Figure 1. National obstetric guideline development strategy in Suriname

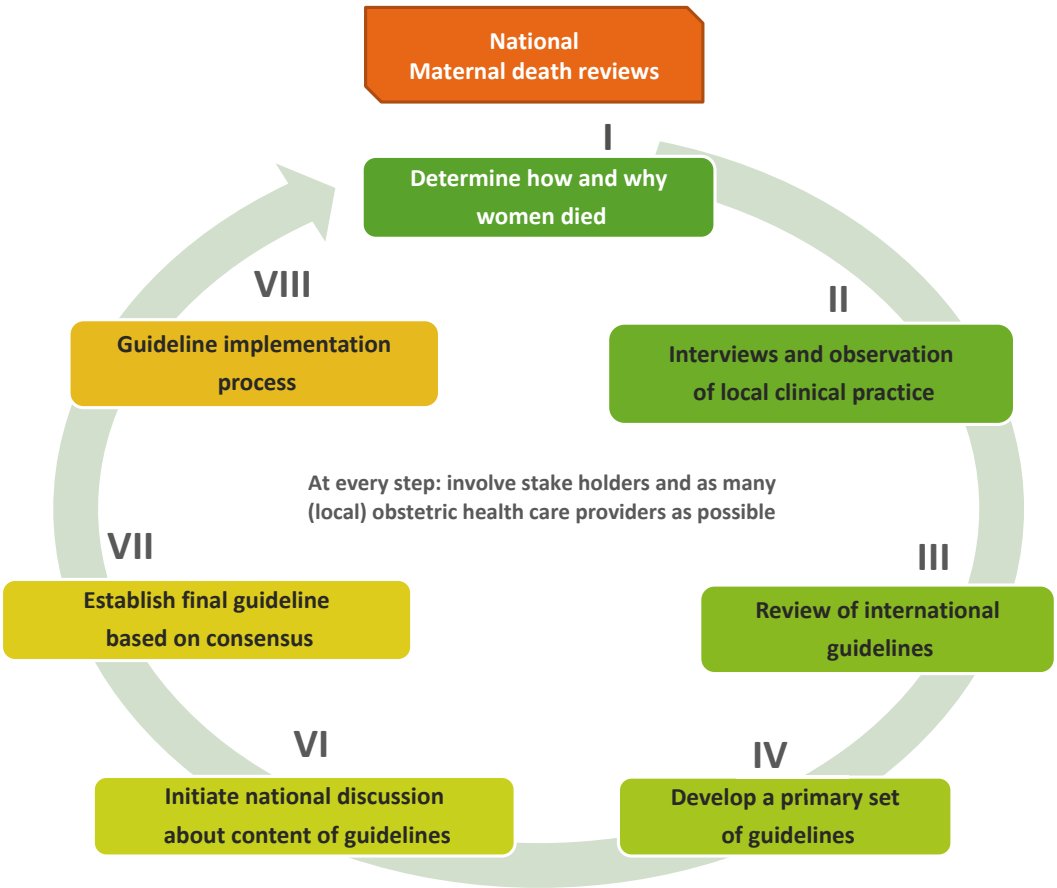

Table 1. Three-delay model of maternal deaths related to HDP and PPH

	HDP deaths n= 19 (%)	PPH deaths n = 21 (%)
1st delay (patients do not seek care)	1 (5.3)	1 (4.8)
2nd delay (patients do not reach care)	1 (5.3)	4 (19.0)
3rd delay (no adequate care in hospital), reasons:	17 (89.5)	20 (95.2)
i. Essential medications unavailable	-	2 (10.0)
ii. Blood products unavailable	N/A	3 (15.0)
iii. Necessary staff unavailable	1 (5.9)	2 (10.0)
iv. Lack of quality of care (significant delay in diagnosis and treatment, inadequate monitoring, poor supportive treatment)	16 (94.1)	19 (95.0)
Death most likely preventable	9 (47.4)	16 76.2)

Clinical observations revealed that the management of HDP and PPH was found to differ between obstetricians within the same hospital. We did not observe that the international guidelines were consulted by nurses or midwives in any of the hospitals. When asked for, the digitally available protocols could not be localised by the staff on duty in two of the hospitals. In PPH management, we observed blood loss estimation was often inadequately (text box 1).

III: Review international guidelines: A summary of similarities and differences between the four international guidelines used most frequently by local health care providers is presented in supplementary file 3 and 4. The four HDP guidelines (WHO, ACOG, QB, NVOG) differed from each other in the following major recommendations: diagnosis of severe pre-eclampsia, timing of aspirin prevention, antihypertensive therapy choices and dose, magnesium sulfate dose and therapy duration, recommendations on fluid restriction, vital sign monitoring and timing of delivery.[17,18,21,25] The four PPH guidelines (WHO, ACOG, RCOG, NVOG) differed from each other in the following major recommendations: active management in the third stage of labour (AMTSL), dose of uterotonics, oxygen therapy initiation, uterine massage, blood transfusion ratio, tranexamic acid, balloon tamponade, embolization, vessel ligation and hysterectomy.[16,19,20,24]

IV. Development of the two national guidelines: The first drafts of the guidelines were created in September 2016. International reviewers added specific recommendations, e.g. the use of tranexamic acid in PPH, the necessity of a blood transfusion protocol, restricting fluids in pre-eclampsia and aspirin prevention of pre-eclampsia. The local reviewers (all gynecologists and head nurses) requested for the guidelines to be more practical with flowcharts and checklists and with more specific recommendations, e.g. the frequency of vital sign monitoring in HDP or PPH. The 'key discussion points' were summarised and attached to the draft guidelines as an appendix.

V: Initiate national discussion about content of guidelines: The four-day meeting was attended by 201 health care providers, including all obstetricians (n=15), residents (n=4), the majority of midwives and nurses (-in training) (80%, n=161)) and different stakeholders, i.e. representatives of the Ministry of Health and the Pan-American Health Organization. Key discussion points were presented and discussed for final consensus on the HDP and PPH guideline (table 4 and 5). This discussions was facilitated by the local and international moderators who were prepared with evidence-based background information.

Text box 1. Example of revelations during clinical labour observations

Blood loss measurement
Perception of staff
"Measurement of blood loss is very accurate as we always use a measuring cup" - explained by midwives and confirmed by obstetricians.

Reality
Delivery room
Blood loss measurement included only the blood clots (blood poured through a sieve, removing the plasma/fluids before pouring clots in a measuring cup) in 3 of 4 hospitals.

Operating theatre (caesarean)
Blood loss measurement included only the blood loss by suction, in a measuring cup (not gauzes / clots) in 2 of 4 hospitals.

Table 2. Interviews with obstetric health care providers on HDP care provision

	n = 43 (100%)
Definitions clear	
Pre-eclampsia	38 (88)
Severe pre-eclampsia	22 (51)
Eclampsia	34 (79)
Anticipation / prevention	
Risk factors known	36 (84)
Aspirine	10 (23)
Calcium	22 (51)
Oral medical treatment (1st line)	
1. Methyldopa	43 (100)
2. Hydralazine	43 (100)
3. Nifidipine (antepartum)	5 (12)
4. Labetalol	21 (48)
Parenteral medical treatment (2nd line)	
1. Hydralazine (direct shots)	43 (100)
2. Hydralazine (perfussor)	25 (58)
3. Labetalol	15 (35)
4. Ketanserin	5 (12)
Magnesium sulfate	
Loading dose (4-6 g/30 min)	26 (60)
Maintanance dose (1 g/hr)	43 (100)
Duration: 24 – 48 hours	43 (100)
Repeat (2 g/5 min) in seizure	6 (14)
Diazepam before $MgSO_4$	38 (88)
Stabilization of severe PE / eclampsia	
Minimum 48 hr before termination of pregnancy	8 (19)
Earliest termination in severe PE	
GA ≥27 weeks	23 (53)
GA ≥30 weeks	15 (35)
GA ≥32 weeks	5 (12)
Other	
Eclampsia box available [1]	9 (21)
Oxygen during eclampsia	12 (28)
Restrict fluids to < 2 L / 24 hrs	0 (0)
Early warning score (MEOWS)	7 (16)

Legend [1] Eclamspia kit includes magnesium sulfate, calciumgluconate, labetalol, hydralazin, sodium choloride ampoule, fluids (ringers lactate and sodium chloride), blood sample bottles, tourniquet, syringes, plaster to fix cannula, guedel aiways, bag and mask, oxygen, reflex hammer.

Table 3. Interviews with obstetric health care providers on PPH care provision

	n = 43 (100%)
Definitions clear	
PPH	38 (88)
Severe PPH	19 (44)
Clear when to alarm doctor	24 (56)
Anticipation / prevention	
Uterotonics in caesarean section	43 (100)
Uterotonics in all vaginal births	14 (33)
Controlled cord traction	19 (44)
Measuring blood	
Measuring by cup	18 (42)
Only clots measured	16 (37)
Medical treatment (1st line)	
Oxytocin i.m. or i.v. (2nd shot)	16 (37)
Oxytocin infusion (10IU/4 hrs)	43 (100)
Misoprostol 400mcg supp	41 (95)
Methergine 0.2mg i.m.	11 (26)
Resuscitation	
Always place 2nd i.v. line	11 (26)
Fluids: Crystalloids	43 (100)
Fluids: Colloids	16 (37)
Oxygen	20 (47)
Tranexamic acid (1 gr i.v.)	10 (23)
Blood transfusion	
Clear guidelines available	0 (0)
Indication: Hb <4 mmol/L	37 (86)
Indication: Hb <3.5 + Ht <0.20	6 (14)
Ratio: 1 PC : 2 FFP	9 (21)
Ratio: 2 PC : 1 FFP	34 (79)
Other	
PPH box available[1]	19 (44)
Balloon / B-Lynch / uterine pack	0 (0)
Hysterectomy if necessary	43 (100)
Early warning score (MEOWS)	9 (21)

Legend [1] PPH box includes oxytocin, Methergin, misoprostol, different IV cannulas, blood sample bottles, tourniquet, syringes, plaster to fix cannula, catheter size 16 with urobag, infusion set, blood set, sterile gloves, cotton swabs, scissors, fluids (ringers lactate and sodiumchloride), 3-way connectors, oxygen face mask, spculums, sponge holding forceps, condom tamponade and catheter, uterine pack

The simulation trainings in smaller groups were well-received as the local health care providers felt they *"could practice"* and felt *"safe to ask remaining questions"*. The evaluation survey revealed that the majority (93%, n=186/201) of the health care providers were 'very satisfied' (4 or 5 points on scale of Likert) with the guideline development proces. There was a high rate of agreement on the content of the guidelines and commitment to implementation (82%, n=164/201). The participants mentioned that they felt important to the development process. One fifth of the participants (18%, n=37) commented that they would have liked more training opportunities and a better location for the four-day meeting.

VI: Final guideline development and evaluation

The obstetric health care providers had no further comments six weeks after guideline distribution. The final versions of both guidelines were approved by all obstetricians, head midwives and participating stakeholders. The final guidelines were distributed four months after the initiation of the project and further implementation followed in the hospitals. The Ministry of Health technically supported the abovementioned development process and accepted the guidelines as national guidelines. The guidelines were reviewed by health providers two years after initial implementation during a second national conference, and were adapted with new recommendations accordingly.

DISCUSSION

We have presented the participatory approach of the development process of context-tailored national obstetric guidelines on HDP and PPH in Suriname. The process consisted of six steps: (1) determination of how and why women died, (2) interviews and observations of local clincal practice, (3) review of international guidelines, (4) development of a primary set of guidelines, (5) initiation of a national discussion about the guideline content and (6) consensus-based finalization of both guidelines. The most important enabler of succesful guideline development was the bottom-up approach with early involvement of local, intrinsically motivated, health care providers. Important barriers were the

inconsistencies between international recommendations, the unavailability of easily adaptable guidelines and the use of several different international guidelines by health care providers which differed among each other.

In the assessment of causes of maternal deaths due to HDP and PPH in Suriname, we found that insufficient quality of care played the most important role. This led to the development of the guidelines. Our approach is aligned with the recommendations from the obstetric transition model, in which evidence-based guideline implementation is a key intervention to further reduce maternal mortality in countries in the third stage of transition.[26,27] Contrary to the more common maternal health guideline development approach (with a top-down mentality, in which experts distribute knowledge or guidelines without involvement of target users), our guideline development approach demonstrates how to succesfully bridge the gap between evidence-based international recommendations and local realities by involving end users from the earliest phases of guideline development to enhance final guideline use.[3,4,8,27] This is crucial, as merely the existence of (international) guidelines does not guarantee implementation. Our assessment of practice in the hospitals in Suriname showed that guidelines for HDP and PPH were not routinely used and quality of decision-making was based on experience rather than evidence, as often reported from similar settings.[5,7,8,28] Local health professions often considered the international guidelines unfeasible and impractical. Next to this, similar to other studies, we found that well-established international guidelines on HDP and PPH differ significantly in their recommendations and interpretation of underlying evidence that resulted in these recommendations.[29-31] This suggests that a critical evaluation is necessary of how available evidence is used to develop global obstetric guidelines. There were substantial differences in the management of HDP and PPH between hospitals. This is in part a reflection of the various clinical practices that influence care in Suriname with influences from Europe, the United States and the WHO. Yet, even in high-income countries with national guidelines endorsed by professional organizations, inter-hospital differences in management of HDP and PPH are reported.[32,33]

Table 4. 'Key discussion points' during the HDP guideline development process

	Discussion points	Evidence-based consensus
Definition		
1	Can you diagnose severe pre-eclampsia without proteinuria?	Yes, if severe hypertension is accompanied by hematologic, renal, neurological, hepatic or pulmonary complications.
Prevention		
2	Which women should receive aspirin therapy for the prevention of pre-eclampsia?	All women with an obstetric history of pre-eclampsia should be administered 100mg of aspirin during their 16th and 37th week. Women with cardiovascular risk factors may be counselled for its use as well.
Therapy		
3	Which antihypertensive therapy is preffered?	Methyldopa is first choice, followed by hydralazine or labetalol. Nifedipine is first choice postpartum.
4	In severe HDP, what should be given first: antihypertensives or magnesiumsulfate?	Magnesium sulfate (4 gram in 30 minutes, followed by 1 gram per hour) is initiated immediately; hypertensive medication will be added depending on the blood pressures.
5	Can magnesium sulfate be administered by nurses or midwives prior to consultation with a doctor?	In emergency situations nurses or midwives can administer magnesium sulfate before or during consultation with a doctor. It should never be administered over the same tap as oxytocin.
6	Is magnesium sulfate therapy without a loading dose an option when severe pre-eclampsia presents without clinical symptoms?	International evidence and recommendations suggest always using a loading dose, as the maintenance dose does not give the magnesium plasma rise that is necessary to prevent a seizure. When magnesium sulfate is given, it should be given adequately and not stopped during (caesarean) delivery.
7	Should magnesium sulfate therapy be continued in caesarean section with spinal analgesia?	Magnesium sulfate should be continued during the delivery or caesarean section, as the intra partum risk of eclampsia is highest.
8	Can nifedipine and magnesium sulfate therapy be combined?	There is a potential theoretical interaction between the two, leading to hypotension and neuromuscular blockade effects, although this is seldom reported. Regular monitoring is recommended.

Table 4. Continued

	Discussion points	Evidence-based consensus
9	Should a fluid preload be administration before intravenous antihypertensive or magnesium sulfate therapy?	No, because the risk of fluid overload (and subsequent pulmonary oedema) is high in severe pre-eclampsia. Fluid preloading is acceptable in hypovolemia. Early consultation of an anaesthesiologist is advised.
10	Is diazepam of added value to magnesium sulfate in the treatment of eclampsia?	Magnesium sulfate is the drug of choice for treating eclamptic seizures. Diazepam is not advised by international guidelines. During the discussion it was decided upon that diazepam use should be limited to unremitting seizures.
Other		
12	How can we define "stabilization" in eclampsia or severe pre-eclampsia?	The definition of stabilization of pre-eclampsia and eclampsia is: (1) stable blood pressure (RR 130-150 / 70-100); (2) adequate magnesium sulfate (loading dose must be administered); (3) platelets of >80); (4) fluid restriction of <1.5 liters. Stabilization is not time-dependent and can be reached even within an hour if management is adequate.
13	When and how should the pregnancy be terminated in eclampsia or severe pre-eclampsia?	The delivery should not be terminated until the mother is stable (see point 13). The termination of pregnancy is on maternal indication. Vaginal delivery should be strived for whenever feasible without foetal compromise.
13	How often should vital signs be checked and what should be checked?	Every 15 minutes (4 times), every 30 minutes (4 times), every hour (4 times), every two hours (4 times), followed by regular checks in case of normal blood pressures.
14	When is admission to the Intensive Care Unit indicated?	In any case of organ dysfunction, such as pulmonary oedema, neurological complications, HELLP, etc.

Table 5. 'Key discussion points' during the PPH guideline development process

	Discussion points	Consensus
Definition		
1	Should the threshold for PPH be blood loss of 500mL (WHO) or 1000mL (Netherlands)?	Blood loss after vaginal delivery is often underestimated. Therefore, blood loss of 500mL will be considered PPH.
2	How should the blood loss be measured, by a measuring cup, by weight or estimation)	Blood loss needs to be measured by measuring cup or by weight (minus the pad). To be precise, it is advised to exchange the pads just after childbirth to subtract the amniotic fluid loss.
Prevention		
3	Should oxytocin prevention after childbirth always be available and given, including in rural areas?	The cost-efficacy was discussed and health care workers of the interior (n=12) and the different stake holders agreed that oxytocin should be made available in the interior. Misoprostol use in the interior is avoided as much as possible to avoid unsafe abortion.
4	Can the oxytocin-infusion used for uterine stimulation be used as preventive measure for PPH?	A calculation of the blood oxytocin concentration after bolus or infusion revealed that an extra (intravenous or intramuscular) 5-10 units of oxytocin bolus is necessary for adequate prevention op PPH based on international recommendation.
5	Which health care providers should be permitted to perform controlled cord traction?	Midwives should all be competent in performing controlled cord traction. If they do not feel competent to do so, they should be trained by more experienced personnel.
Therapy		
6	Misoprostol is frequently used in PPH in Suriname, what is the additional value on top of adequate oxytocin infusion?	If oxytocin is adequately administered (an extra shot of 5 units plus continuous infusion of 10 units in maximum four hours), misoprostol has no additional value. If oxytocin is not available, or the uterus does not contract sufficiently, misoprostol can be given.
7	What should the oxytocin regimen be in caesarean section?	Oxytocin 5 units slowly intravenously, followed by an infusion (10 units in four hours) is advised in all caesarean sections.

Table 5. Continued

	Discussion points	Consensus
Fluids and blood products		
8	In severe PPH should crystalloids or colloids be used?	International recommendations show no better outcome when using colloids.[d] Colloids are more expensive, adverse effects have been reported and there is no decrease in the risk of respiratory problems due to pulmonary oedema.[e] The preference is to use crystalloids.
9	What is the ideal ratio for the transfusion of packed cells, fresh frozen plasma and platelets?	Ratio 1 : 1 : 0. For every packed cell also fresh frozen plasma. In acute severe blood loss it is advised to initiate the fresh frozen plasma transfusion, as it is generally available more rapidly than packed cells. Platelet transfusion is given for specific indications (coagulopathy).
Other		
10	Should a parthograph always be used?	The partograph is an important tool to assess the progress of labour. Induction or slow progress of labour and oxytocin-stimulation are merely a few examples of PPH risk factors.
11	When is tranexamic acid recommended and what is the risk for a subsequent thrombo-embolism?	Tranexamic acid (1 gram in 10 minutes) is recommended in cases of 1000 mL blood loss or more. In ongoing blood loss, it is advised to repeat this after 30 minutes. It should not be administered to women with a contra-indication for antifibrinolytic therapy (e.g. thrombosis in pregnancy). The results of the WOMAN trial are to be published.
12	What are more affordable options for an intra-uterine tamponade balloon such as the Rush or Bakri?	Intra-uterine balloon can be made with condoms and a urinary catheter. Recommendations were to insert a large vaginal tampon after the balloon insertion to prevent displacement.
13	How often should vital signs be monitored after severe PPH?	Every 5 to 10 minutes during blood loss. After PPH vitals should be recorded after 30 minutes, one hour, 2 hours, 4 hours and 8 hours.

These findings underline the importance of involving also the end users in the guideline development process (i.e. health care providers and stakeholders involved in pregnancy, delivery and postpartum care).

Important barriers of guideline development that need to be elaborated upon is that some recommendations are not immediately accepted. In Suriname, for example, the use of magnesium sulfate for prevention of eclampsia was initially not accepted by all as healthcare workers were not yet familiar with this.

Another barrier for Suriname is the fact that there is currently no regulatory framework for health professionals. We believe such framework would be relevant to reduce maternal deaths, especially by helping health care workers to monitor their delivered quality of care. A general barrier for the development of context-tailored obstetric guidelines is the fact that it is time consuming and resource demanding. We noticed that early involvement of end users, understanding their barriers and engaging all health care professionals are essential to ensure a fast guideline development process. If more global consensus on the most important obstetric complications would be attained, with recommendations tailored at region or health care system resources and include easily-adaptable flowcharts or checklists, the local guideline development would be much more feasible. The WHO Handbook for Guideline Development is an example of a comprehensive tool for evidence-based guideline development, but also a very large document and it uses a time-consuming process that seems not readily achievable for most LMIC.[34]

The recently published PartoMa study from in a low-resource referral hospital in Zanzibar, Tanzania, is one of the few examples of a systematic approach to evidence-based international recommendations adaptation to local reality and evaluation of it's impact on health outcomes. Their 'bottom up' approach was similar to ours and appeared to be associated with significant reductions in stillbirths and improvement of treatment of hypertensive disorders of pregnancy.[6,7,35] The PartoMa Guideline Development in Zanzibar and our strategy in Suriname were both achievable due to the smaller size of the island or country.[6,7,35]

However, when healthcare workers are fully engaged in the quality cycle of plan-do-check-act, nationwide improvement can also be made in larger countries.[36]

Strengths and limitations

This is the first evaluation of the development of national obstetric guidelines in a middle-income country, and can serve as an example for low and middle-income countries in the process of developing contextually-tailored guidelines. There was a high rate of agreement and the guideline development process was completed very steadily, in only four months. A limitation to consider is that our guideline development process was conducted in a small country and thus, for larger countries this might not be applicable directly. Another limitation is that qualitative data on maternal mortality most likely did not reflect 'standard' management of HDP and PPH before the guideline development proces.

We therefore recommend others to perform a study before guideline development to better assess the current situation and be able to do a before-after analysis. We also acknowledge that the evaluation surveys were not conducted by an independent party and may not have captured all the dimensions of the development process. Nevertheless, if the incidence of maternal mortality and severe morbidity declines, the awareness created among healthcare providers by recent publications on local maternal mortality in Suriname together with the development of the guidelines will likely have contibuted, especially as no other major interventions related to HDP and PPH have taken place the past decade.[11,13] In the context of research, we are evaluating implementation of the guidelines by criteria-based audits embedded in a prospective cohort study on severe maternal morbidity and mortality due to HDP and PPH, currently ongoing in Suriname. Yet, it remains a recommendation to independently evaluate the impact on core outcomes in order to evaluate actual quality improvement.

CONCLUSION

Bottom-up development of context-tailored guidelines are achievable within a reasonably short timeframe. Important barriers for the guideline development process are the discrepancies between international recommendations, which require local consensus to be reached on key issues, and the unavailability of easily adaptable guidelines. The main enabler for both development and implementation is the involvement of local birth attendents from the early phases onwards to ensure use in local reality, drive change and create sustainable adherence. We recommend bottom-up context-tailored guideline development with early involvement of the end users.

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Supplementary file 1. Comparison of HDP practice in Suriname

Hypertensive disorders in pregnancy – The variation in practice between the four hospitals in Paramaribo - Suriname

		Hospital A (2016)	Hospital B (2016)	Hospital C (2016)	Hospital D (2016)	The final national guideline
Definitions	Pre-eclampsia	*BPs ≥ 140 mm Hg **AND/OR** BPd ≥ 90 mm Hg (measured twice at least 4 hours apart) **OR** BPd ≥ 110 mm Hg; all after GA 20 weeks; **with** proteinuria*	BPd ≥90 (measured twice at least 4 hours apart) **OR** BPds≥ 110 **OR** increase of BP 15-20 compared to pre-pregnancy BP; all after GA 20 weeks; **with** proteinuria **OR** clinical symptoms	*BPs ≥ 140 **AND/OR** BPd ≥ 90 (twice; interval 4h) **OR** BPd ≥ 110; all after GA 20 weeks; **with** proteinuria*	BPs ≥ 140 **AND/OR** BPd ≥ 90 mm Hg (twice; interval 4h) **OR** BPd ≥ 110 mm Hg; all after GA 20 weeks; **with** proteinuria	BPs ≥ 140 mm Hg **AND/OR** BPd ≥ 90 (2x, interval 4 –6h) OR increase BPs >30 **OR** BPd >15 mmHg **with** proteinuria OR clinical symptoms
	Severe pre-eclampsia	*Pre-eclampsia with BP diastolic ≥ 110 mm Hg with clinical symptoms*	Not specified	*Pre-eclampsia with BP diastolic ≥ 110 mm Hg **OR** clinical symptoms*	Not specified	BPd ≥ 110 mmHg (once) **with** proteinuria **OR** organ dysfunction (renal, liver, hematological, neurological, pulmonal)
	Eclampsia	*Generalized tonic-clonic seizures, with no other cause than pre-existent pre-eclampsia*	Convulsion in a pre-eclamptic patient with no other cause	Convulsion in a pre-eclamptic patient with no other cause	Convulsion in a pre-eclamptic patient with no other cause	Tonic-clonic seizures with no other attributable cause than pre-eclampsia
Hypertensive	Calcium	*No*	History of IUGR or pre-eclampsia	No	No	Low intake → 2 grams in 2-3 trimester
	Aspirine	*Chronic hypertension or medical history of IUFD or IUGR due to pre-eclampsia*	History of IUGR or pre-eclampsia	No	No	High risk → 100mg in GA 16-37
	Admission criteria	BPs ≥ 160 **AND/OR** BPd ≥ 110 **AND/OR** clinical symptoms	Not specified	Not specified	Not specified	Severe PIH (persistent BPs ≥ 150/100), pre-eclampsia / HELLP / eclampsia, foetal indication
	Oral initiation	*BPd ≥ 100*	Not specified	BPd ≥ 100 mm Hg (twice)	BPd ≥ 100 **OR** BP increase >20	BPs ≥ 150 **OR** BPd ≥ 100
	Parenteral initiation	*BPd ≥ 110*	Not specified	BPd ≥ 110 mm Hg	BP diastolic ≥ 110 mmHg > once	BPd ≥ 110
	Oral drug choice *Antepartum* *Postpartum*	*1. methyldopa 250-750mg 2-3* *2. hydralazine 25-50 2-3dd* *nifedipine 20mg 2dd*	1. methyldopa 250-500mg 2-3 2. hydralazine 25-50 2-3dd nifedipine 20mg 2dd	1. methyldopa 250-500mg 2-3 2. hydralazine 25-50 2-3dd 3. labetalol 100-200mg 2dd nifedipine 20mg 2dd	1. methyldopa 250-500mg 2-3 2. hydralazine 25-50 2-3dd nifedipine 20mg 2dd	1. methyldopa 250-1000mg 3-4dd 2. hydralazine 25-75mg 3dd 3. labetalol 50-200mg 3dd nifedipine 5-40mg 3dd
	Parenteral drug choice	*1. hydrolazine via perfusor* *2. hydralazine 5mg i.v.* *3. ketanserine or labetalol* *Perfusor available*	1. hydralazine via perfusor 2. hydralazine 5mg i.v. 3. labetalol Perfusor available only in ICU	1. hydralazine via perfusor 2. hydralazine 5mg i.v. Perfusor available	hydralazine 5mg i.v. Perfusor not available	1. hydralazine 5-10mg à 20-40 min. **OR** by infusion system 2. labetalol 1-2 mg/kg in 20 min. Continue 20-70mg/hr
$MgSO_4$	Indication	*Eclampsia; severe pre-eclampsia; neuroprotection*	Eclampsia; pre-eclampsia	Eclampsia; severe pre-eclampsia	Eclampsia; severe pre-eclampsia; pre-eclampsia with symptoms	Eclampsia; severe pre-eclampsia (BPd ≥ 110 OR clinical symptoms); neuroprotection
	Loading dose	*4 grams / 30 minutes*	2 grams / 30 minutes	4-6 grams / 30 minutes	1 gram / 30 minutes	4-6 grams / 30 minutes
	Maintenance dose	*1 gram / hour*	1 gram / hour	1 gram / hour	1 gram / hour	1 gram / hour
	Dose repeated seizure	*2 grams / 5 minutes*	None (diazepam)	None (diazepam)	None (diazepam)	2 grams / 5 minutes
	Stop treatment	After 48 hours	After 24 hours and stable	After 48 hours	After 48 hours and stable	24 – 48 hours (max 7 days; measure plasma $MgSO_4$)
	Diazepam indication	If no iv-access	If no iv-access or in repeated seizure	If no iv-access or in repeated seizure	In seizures (whether or not on $MgSO_4$)	If no iv-access; when $MgSO_4$ shot given twice
Fluids	Oxygen	*Eclampsia: 10 L NRM*	No	Eclampsia: 5-10 L NRM	No	Eclampsia: 15 L NRM
	Intravenous access	*1 in pre-eclampsia; 2 in eclampsia*	1 in pre-eclampsia and eclampsia	1 in pre-eclampsia; 2 in eclampsia	1 in pre-eclampsia and eclampsia	2
	Before i.v. drugs	500ml NaCl 0.9% quick	1000mL gelofusine quick	500mL Ringers **OR** gelofusine	No fluids	No fluids
	Maintenance	500mL Ringers à 8 hours (no gelofusine, glucose/NaCl 0.9%, glucose 5%)	500mL glucose/NaCl 0.9% à 6 hours	First 1000mL Ringers in 6 hours, then 500mL gluc/NaCl 0.9% à 8 hours	500mL Ringers **OR** NaCl 0.9% à 8 hours	Max. 1500mL in 24 hours. Preference for Ringer's Lactate or NaCl 0.9%
Monitoring	Vital signs: Rr <12/6 Rr >12/6 **OR** $MgSO_4$	Every 3 hours At once per hour, then every 4 hours	Every 4 hours Every 2-3 hours	Every 2-3 hours At every 30 min, At every hour	Every 6 hours Every 4 hours	Every 4 hours (intrapartum every ½ hour) Every ½ hr (4x), 1hr (4x), 2 hrs (4x), 4 hrs (4x)
	Fluid balance	Pre-eclampsia	Pre-eclampsia / HELLP	Severe pre-eclampsia	Pre-eclampsia	Every admission of hypertensive disorders
	Blood tap	2x per week	2x per week	2x per week	3-4x per week	2x per week
	Doppler	GA >24	GA >24	GA >30	GA >30	GA >27
	CTG	GA >27	GA >24	GA >30	GA >30	GA >27
Delivery	Corticosteroids	GA 26[0] – 34 Dexamethasone 24mg /day; 12hrs	Severe pre-eclampsia and GA 28-34 Dexamethasone 12mg, twice, 12hrs	Delivery expected in: GA 27-34 Dexamethasone 12mg bi-en; 12hrs	Severe pre-eclampsia and GA 28-34 Dexamethasone 12mg twice, 12hrs	GA 24 – 34 Dexamethasone 4 x 6mg; 12 hours apart (total 48 hours)
	Eclampsia loc	In non-delivery rooms	Not present	In non-delivery room	Not present	In non-delivery room
	Timing mild PE	GA 37 Induction (balloon, misoprostol)	Dependent on gynaecologist Induction (misoprostol) or C-section	GA 37, induction Induction (misoprostol) or C-section	GA 37 Induction (misoprostol) or C-section	GA 37: preference for vaginal birth with induction (depending on BS=0? → balloon/misoprostol/oxytocin) GA <37 induction, GA > 37: preference for induction
	Timing severe PE	GA >33 C-section / induction after stabilisation	GA >34 C-section for stabilisation	GA >30 C-section / induction after stabilisation	GA >33 C-section after stabilisation	GA <34 in case of failed induction or failed induction
Postpartum	Duration of admission	At least 24 hours post partum	At least 24 hours post partum	At least 24 hours post partum	At least 24 hours post partum	At least 24 hours post partum and stable (BP normalized, urine output normal, lab results improved)
	Antihypertensives	No target BP, switch to nifedipine	No target BP, switch to nifedipine	No target BP, switch to nifedipine	No target BP, switch to nifedipine	BPs 120-150 and BPd 80-100 (switch to nifedipine)
	Blood tap	If necessary	One day post partum	If necessary	Two days post partum	One day post partum
	Postnatal clinic visit	7 days	7-10 days	7 days	7 days	7-10 days and 6 weeks

Supplementary file 2. Comparison of PPH practice in Suriname

Postpartum hemorrhage – The variation in practice between the four hospitals in Paramaribo - Suriname

		Hospital A (2016)	Hospital B (2016)	Hospital C (2016)	Hospital D (2016)	The final national guideline
	Definition PPH	500mL blood loss or more after vaginal delivery	500mL blood loss or more after vaginal delivery	500mL blood loss or more after vaginal delivery	500mL blood loss or more after vaginal delivery	500mL blood loss or more during and after childbirth
	Definition severe PPH	1000mL blood loss or more	Not specified	Not specified	Not specified	1000mL blood loss or more or blood loss with clinical hypovolemia during and after child birth
	Call for help (supervisor)	500mL blood loss or more (general doctor) 1000mL blood loss or more (gynaecologist)	Not specified	500mL blood loss or more	500mL blood loss or more	500mL blood loss or more (call general doctor) 1000mL blood loss or more (call gynaecologist)
	Risk factors	Not specified	Prolonged labor, twin pregnancy, macrosomia, high parity, uterus myomatosis	Not specified	Not specified	Risk factors grouped (see guideline for elaboration): - General (e.g. age >40, BMI >35, uterus myomatosis) - Obstetric history (e.g. grande mult, caesarean, etc) - Current pregnancy (macrosomia, pre-eclampsia, etc) - During delivery (prolonged labor, etc) - Post partum (full bladder, retained placenta, etc).
Prevention	**Partograph**	On indication (prolonged labor, caesarean in history, on request of physician)	Sometimes	Never	Never	Always recommended
	Oxytocin in the 3rd stage of labor	Caesarean – always Vaginal birth – always (before delivery of placenta) 5-10 IU i.m. or slowly i.v. (2 minutes)	Caesarean – always Vaginal birth – in patients with high-risk for PPH (done after delivery of placenta) 5-10 IU i.m. or slowly i.v. (2 minutes)	Caesarean – always Vaginal birth – in patients with high-risk for PPH (done after delivery of placenta) 5-10 IU i.m. or slowly i.v. (2 minutes)	Caesarean – always Vaginal birth – in patients with high-risk for PPH (done after delivery of placenta) 5-10 IU i.m. or slowly i.v. (2 minutes)	Caesarean – always Vaginal birth – always (before delivery of placenta) 5-10 IU i.m. or slowly i.v. (2 minutes)
Management	**Measurement of blood**	- Measurement cup (mL) - Liquid (blood) removed from blood clots with a sve. Measurement done of only the blood clots.	- Measurement cup (mL) - Liquid (blood) removed from blood clots with a sieve. Measurement done of only the blood clots.	- Measurement cup (mL) and / or scale (kg) - Liquid (blood) and blood clots measured	- Measurement cup (mL) - Liquid (blood) removed from blood clots with a sieve. Measurement done of only the blood clots.	- Measurement cup (mL) and / one scale (kg) - Measure liquid (blood) and bloodclots all together. Subtract the estimated amniotic fluid.
	Oxytocin i.m. / i.v.	Repeat 5-10 IU shot i.m. or i.v.	5 IU shot i.m. or i.v.	5 IU shot i.m. or i.v.	10 IU shot i.m. or 5 IU shot i.v.	10 IU shot i.m. or i.v.
	Oxytocin infusion	10 IU in 500mL / 4-6 hours During at least 24 hours	5 IU in 500mL / 6 hours Until bleeding stops	10-20 IU in 500mL / 4 hours During at least 24 hours	10 IU in 500mL / 4-6 hours Until bleeding stops	10 IU in 500mL / 4 hours
	Misoprostol	400 – 800 micrograms rectal	400 – 800 micrograms rectal	400 micrograms rectal	400 – 800 micrograms rectal	Not first choice, as misoprostol is not beneficiary when adequate oxycitin dosis is given.
	Methergin	Not prescribed	0.2 mg i.m. if bleeding persists	Not prescribed	Not prescribed	0.2 mg i.m.
	Tranexamic acid (Cyclokapron)	1 gr i.v. slowly in persistent bleeding	2 gr i.v. slowly in severe and persistent bleeding	2 gr i.v. slowly in severe and persistent bleeding	Not prescribed	1 gram i.v. slowely when 1000mL blood loss or more
	Calcium gluconate	1 gram i.v. After transfusion of 4 blood products	1 gram i.v. After transfusion of 6 blood products	1 gram i.v. After transfusion of 4 blood products	Not prescribed	1 gram i.v. After transfusion of 4 blood products
	I.V. access	2 i.v. access lines (> 1000 mL blood loss)	Not specified	Not specified	Not specified	2 x intravenous access (preferably green or grey)
Resuscitation	**Infusion**	Ringer's Lactate or Sodium Cloride 0.9%	Ringer's Lactate or Glucose 5%	Sodium Cloride 0.9%, Glucose 5% or Gelofusine	Ringer's Lactate or Sodium Cloride 0.9%	Ringer's Lactate or Sodium Cloride 0.9% Infuse 1 : 1 (blood loss : infusion), max 3 liters
	Oxygen	10 L / min in 1000 mL blood loss or more	Sometimes in severe blood loss	10 L / min in 2000 mL blood loss or more	Sometimes in severe blood loss	10 – 15 L / min in 1000 mL blood loss or more
	Transfusion indication	Hb < 4 mmol/L	Hb < 5 mmol/L	Hb < 3.5 mmol/L or Ht < 0.20	Hb < 4.5 mmol/L and complaints	Hb < 4.0 mmol/L or Ht < 0.20, 1000 mL blood loss or more and persistent or with symptoms of hypovolemic shock
	Blood products ratio	2 PC : 1 FF	2 PC : 1 FFP	1 PC : 2 FFP	2 PC : 1 FFP	1 PC : 2 FFP (in massa transfusion 4 PC : 4 FFP : 1 TC)
	Surgical and other	Vaginal tampon; Hysterectomy	Vaginal tampon; Hysterectomy	Vaginal tampon; Hysterectomy	Vaginal tampon; Hysterectomy	Vaginal and uterine packing (gauzes); balloon tamponade (Bakri, Foley, condom); B-lynch; bilateral ligation of uterine (or internal iliac) arteries; hysterectomy (rather sooner than later)
Vital signs	**Measurements of**	Blood pressure, pulse, temperature , blood loss, tone of uterus	Blood pressure, pulse, temperature, blood loss, tone of uterus	Blood pressure, pulse, temperature. blood loss, tone of uterus	Blood pressure, pulse, temperature. blood loss, tone of uterus	Blood pressure, pulse, respiratory rate, saturation, temperature, blood loss, tone of uterus, urinary output
	Timing of monitoring - after a normal delivery - during hemorrhage - after hemorrhage	Directly; after 1 hour; after 8 hours Not specified Directly; after 1 hour; after 4 hours	Directly; after 1 hour; after 8 hours Not specified Directly; after 1 hour; after 8 hours	Directly; after 1 hour; after 8 hours Not specified Directly; after 1 hour; after 2 hours	Directly; after 1 hour; after 8 hours Not specified Directly; after 1 hour; after 8 hours	Directly; after 1 hour; after 8 hours Every 10 minutes Directly; after 30 minutes; 1 hour; 2 hours; 8 hours
	MEOWS score performed	Yes	No	No	No	Not specified
	Follow up in severe PPH	- Blood exam (Hb, Ht, Tr, INR, fibrinogen) - Performed a day later - Discharge not specified	- Blood exam (not specified) - Performed same day - Discharge not specified	- Blood exam (not specified) - Performed a day later - Discharge not specified	- Blood exam (not specified) - Performed same day - Discharge not specified	- Blood exam (Hb, Ht, Tr, INR, APTT, PT fibrinogen, electrolytes, creatinine and liver enzymes) - Performed 4 hours later and 24 hours later - Discharge (by doctor) after at least 24 hours
	PPH-box in delivery room	Yes	No	Yes	No	Yes, should always be
	PPH-checklists or flow charts in delivery rooms	Yes	No	Yes	No	Yes, should always be

Supplementary file 3. Comparison of international HDP guidelines

	WHO (2011)	ACOG (2013)	Queensland Brisbane (2016)	NVOG (2011)
Definition				
Pre-eclampsia	Onset of new episode of hypertension during pregnancy (persistent diastolic BP ≥ 90 mm Hg) with substandial proteinuria (>0.3 g/day)	BP systolic ≥ 140 and/or diastolic ≥ 90 mm Hg (measured twice at least 4 hours apart) after GA20 OR BP systolic ≥ 160 and/or diastolic ≥ 110 mm with either proteinuria OR with severity symptoms	Hypertension (BPs≥ 140 OR BPd ≥ 90) after 20 weeks of gestation on 2 or more occassions accompanied by one of the following: proteinuria (>30mg/mmol), creat >90, oliguria, thrombopenia (<100), hemolysis, raised transaminases, DIC, neurological symptoms, pulmonary oedema or foetal growth restriction.	Pregnancy induced hypertension (BP systolic ≥ 140 and/or diastolic ≥ 90 mm Hg after GA 20, meassured twice in women with normal previous BP. BP should be normal within 3 months post partum) with proteïnuria (>0.3g/day)
Severe PE	Severe hypertension (not defined), heavy proteinuria or substantial maternal organ dysfunction. Early onset (before 32-34 weeks) and foetal morbidity are used as independent severity criteria in some countries	Systolic ≥ 160 or diastolic ≥ 110 mm Hg (measured twice at least 4 hours apart while patient is on bed) AND thrombopenia <100 OR impaired liverfunction or epigastric pain OR impaired renal function (creatinine 2x normal) OR pulmonary oedema OR cerebral/ visual disturbances.	[Magpie Trial] BPs ≥ 170 or BPd≥ 110 mm Hg AND 3+ proteinuria OR BPs ≥ 150 or BPd≥ 100 mm Hg AND 2+ proteinuria AND 2 severity symptoms OR pre-eclampsia with at least one sign of central nervous system irritability	Systolic ≥ 160 or diastolic ≥ 110 mm Hg OR clinical symptoms of pre-eclampsia (headache, upper-abdominal pain, nausea) OR proteïnuria >5 g / 24 hours. [Proteinuria can remain absent]
Eclampsia	Generalised seizures in addition to pre-eclampsia criteria	New-onset grand mal seizures in a woman with pre-eclampia	One or more seizures superimposed on PE (HT/proteinuria may be absent)	Not specified
Prevention				
Calcium	When low calcium intake (<900mg/ day)	In populations with low calcium intake	In high risk women with low calcium intake	Not specified
Aspirin	75mg/ day in high risk women, initiate GA<20 weeks	In high risk women, start 60-80 mg daily in late first trimester	Moderate to high risk of PE; 100mg/day , initiate <16 weeks. Until 37 weeks or birth of baby (NNT 42)	Not specified
Antihypertensive				
Initiation	Not specified	Persistent BP systolic ≥ 160 mm Hg OR diastolic ≥ 110 mm Hg	BP systolic ≥ 160 OR diastolic ≥ 100 mm Hg	Systolic ≥ 160 OR diastolic ≥ 110 mm
Drug choice	Hydralazine, methyldopa, labetalol, nifedipine, ketanserin, and others are compared.	Labetalol, nifedipine, methyldopa	Oral: methyldopa, labetalol, oxyprenolol, hydralazine, nifedipine, prazosin, clonidine. I.V. nifedipine, hydralazine, labetalol	Methyldopa, labetalol, nifedipine

Supplementary file 3. Continued

	WHO (2011)	ACOG (2013)	Queensland Brisbane (2016)	NVOG (2011)
Magnesium sulfate				
Indication	Eclampsia; severe PE	Eclampsia; severe PE	Eclampsia; HELLP; severe PE; neuroprotection	Eclampsia; severe PE, consider in mild pre-eclampsia
Loading dose	Not specified	4-6 (time ?)	4 g IV in 20 min	4-6 g in 10-30 min
Maintanance	Not specified	1-2 g per hour	1 g per hour	1 g in 60 min
2nd seizure	Not specified	No specific recommendations	2 g in 5 min (may repeat after 2 min) Other possibilities: diazepam 5-10mg IV (2-5mg/min), midazolam 5-10 mg IV in 2-5min	2 g in 5 min (max. twice) Other possibilities: lorazepam 4mg i.v. slowly, sedate and intubate
Stop treatment	Not specified	At least 24 hours after last convulsion	At least 24 hours after birth or last seizure	At least 24 hours after initiation
Other				
Corticosteroids	Not specified	GA <34 weeks	GA <34 weeks	GA <34, birth expected in 2-10 days; Betamethason 12mg i.m. 2x (24hr apart)
Vital signs	Not specified	Every 8 hours	At least every 4 hours	Not specified
Fluids	Not specified	Not specified	No large volumes of fluids. Restrict to 1.5L/24 hrs after birth. Strict fluid balance	Not specified
Delivery timing in severe PE	Unviable: induction. Term: delivery asap Before term: expectant unless uncontrolled hypertension or foetal distress	Depends on severity; GA and NICU-facility. Deliver shoud be shortly after stabilisation.	Stabilise (control hypertension, correct coagulopathy, initiate $MgSO_4$, control fluids) and deliver	Not specified
Post partum medication	Not specified. Severe post partum hypertension; in all women treated antenatally	Not specified. Initiate when BP systolic ≥ 150 OR diastolic ≥ 100 mm Hg.	Avoid abrupt withdrawal of antihypertensives. Cease methyldopa (depression). Consider nifedipine.	Not specified
Other recommendations	Not specified	No NSAIDS, promote breastfeeding. Consider postnatal counseling.	Consider VTE profylaxis (during admission); postnatal counseling. Follow-up 6 weeks	Not specified

Legend: BP = blood pressure, GA = gestational age, HT = hypertension, IV = intravenous, $MgSO_4$ = magnesium sulfate, NNT = number needed to treat, VTE = venous thrombo-embolism, NSAID = non-steroidal anti-inflammatory drugs.

Supplementary file 4. Comparison of international PPH guidelines

	WHO (2011)	ACOG (2013)	RCOG (2014)	NVOG (2011)
Definition	PPH: >500mL Severe PPH >1 L	Vaginal > 500mL Caesarean >1 L	Minor: >500mL Moderate: 1-2 L Major: >2 L	Vaginal > 500mL Caesarean >1 L
Incidence	2%	4-6%	3.7/1000 (> 5 PC)	3.8% (2003) 6.2% (2009)
Risk factors	Minimally described	Elaborately described	Elaborately described with odds ratio	Elaborately described
Prevention	AMTSL (CCT after 30 min)	Not discussed	AMTSL Placenta location	AMTSL
Oxytocin	10 IU i.m. / i.v. in all births	Not specified	Oxytocin 5 or 10 IU i.m. / 5 IE i.v. (CS) Ergometrin 0.5 mg i.m. Combined if Hb low	Oxytocin 5 or 10 IU i.m. / 5 IE i.v. (CS) followed by 10 IU i.v. in 4 hours
Resuscitation				
Access	Not specified	Ample intravenous access	Intravenous access 2x	Intravenous access 2x
Fluids	Crystalloids	Crystalloids	Crystalloids, warm/ rapid Max. 2 L (+ 1.5L colloids)	Crystalloids, warm/ rapid (1 : 1 blood loss)
Oxygen	Not specified	10-15 L per minute	10-15 L / min over NRM	Not specified
Blood products	Not specified	Blood as needed and blood bank notification	As soon as possible 6 PC : 4 FFP	4 PC : 4 FFP
Uterine massage	Recommended, contin-uously. Bimanual, aorta compression advised	Not specified	Not specified	Recommended, continuously
Coagulation screening	Blood loss up to 1500mL or >2 uterotonics	Not specified	>1L blood loss	>1L blood loss or >2L cristalloids
Medical treatment				
Oxytocin infusion	Recommended	10-40 IU i.v. or 10 IU i.m.	5 IU i.v. may repeat or 40 IU in 500mL à 4 hrs	10 IU i.v. followed by 10 IU i.v. à 4 hrs
Misoprostol	If oxytocin not available: 600ug oral or 800ug sublingual	800-1000ug rectal	1000 ug rectal	Not recommended
Ergots	If oxytocin not available Not in retained placenta	Methyl-ergonovine 0.2 mg i.m. every 2-4 hr	Ergometrine 0.5mg i.m. or i.v.	Metergin 0.2mg i.m or i.v.
Others	Not specified	Carboprost 0.25mg i.m. Dinoprostone 20mg PV. Factor VIIa 50-100ug/kg every 2 hours	Carboprost 0.25mg i.m. (max 8 doses)	Sulproston 500 ug / 30 mins (followd by 60-120 ug per hour). Fibrinogen 2g (in >2L blood loss)

Supplementary file 4. Continued

	WHO (2011)	ACOG (2013)	RCOG (2014)	NVOG (2011)
Tranexamic Acid	Recommended in case of persistent bleeding	Not specified	Not recommended	Recommended, 1-2 g
Antibiotic profylaxis in MPR	Ampicillin or cefazolin	Not specified	Not specified	Cefazolin/metronidazol or amoxicillin/clav. acid
Surgical treatment				
Uterine packing	Not recommended	4-inch gauze 5000U thrombin in 5mL saline	Not recommended	Not recommended
Balloon tamponade	Refractory bleeding/ Uterotonics unavailable	Foley (60-80mL) Bakri (300-500mL)	Leave for 4-6 hrs	In refractory bleeding Bakri (300-500mL)
Brace suture	Not specified	B-Lynch, square	B-Lynch, square	B-Lynch, square
Vessel ligation	Uterine and iliac artery	Uterine and iliac artery	Uterine and iliac artery	Not specified
Embolization	If bleeding stable	Not specified	Yes, consider	Yes, consider
Hysterectomy	In refractory bleeding despite vessel ligation	Not specified	Rather sooner than later	In case of placenta accreta, uterine rupture or Jehova's witnesses

Legend: AMTSL = active management of the third stage of labour. CCT = controlled cord traction. FFP = fresh frozen plasma. Hb = hemoglobin. MPR = manual placenta removal. NRM = non-rebreathing mask. PC = packed cells.

11

From passive surveillance to response: Suriname's efforts to implement Maternal Death Surveillance and Response (MDSR)

Lachmi R. Kodan
Kim J.C. Verschueren
Geertje E. Boerstra
Inder Gajadien
Robert S. Mohamed
Lily D. Olmtak
Satish R. Mohan
Kitty W.M. Bloemenkamp

Submitted

BACKGROUND

The reduction of maternal deaths was the focus of Millennium Development Goal 5 in 2000 and remained a priority in the Sustainable Development Goals established in 2015.[1-3] It is essential to identify underlying causes and contributing factors to gain more insight into the gaps in care next to solely counting maternal deaths to prevent avoidable deaths.[4] A maternal death review is a medical audit with an in-depth qualitative investigation of the causes and circumstances of death.[5] By performing audits, an attempt is made to understand the "how and why" of the death, analyze substandard care, and formulate "lessons learned" to initiate steps for improvement. Combining audits with national guideline development, training, and monitoring of implementation could improve guidelines adherence.[6,7] The different types of medical audits are verbal autopsy (at community level), clinical audit (at facility level, by involved healthcare workers), and confidential enquiry (at national level, by an independent committee).[5]

A Maternal Death Surveillance and Response (MDSR) cycle is a continuous action cycle that provides information on maternal mortality surveillance and audit and on the actions needed to improve care and avert avoidable maternal deaths.[5,8] The WHO introduced the MDSR approach in 2012 to establish accurate data collection and translate “lessons learned” to action plans and national policies, followed by monitoring to capture the effects.[9] In Latin America and the Caribbean (LAC), MDSR was implemented in 2015 in six countries: Brazil, El Salvador, Columbia, Jamaica, Mexico, and Peru, which serve as an example for other countries.[10]

Although the maternal mortality ratio (MMR) declined with time from 226 per 100,000 live births in 1991-1993 to 154 per 100.000 live births in 2010, Suriname was designated by the Pan American Health Organization (PAHO) as one of the ten priority countries in LAC for reduction of maternal mortality in 2010.[11-13] Several intentions existed to improve surveillance and classification in Suriname for years, but integrated maternal deaths reviews were not performed until the installation of a national maternal mortality review (MaMS, Dutch acronym) Committee in

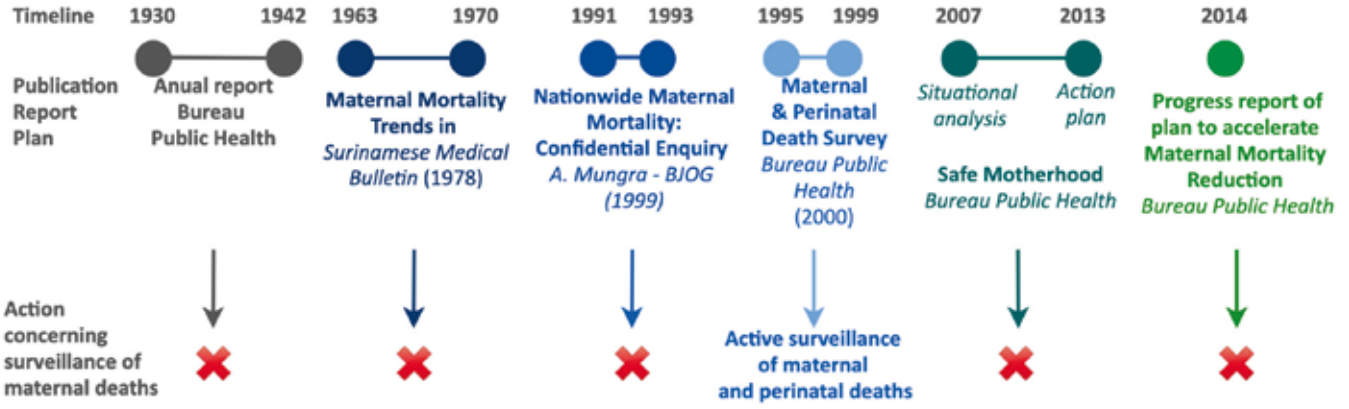
2015. This article aims to describe the MDSR implementation in Suriname and its facilitators and barriers. We share the "lessons learned", as experienced by the health care providers and public health experts involved in MDSR implementation. This MDSR process is described in three time slots: 1) pre-2015, MDSR and safe motherhood initiatives before the installation of Committee MaMS; 2) 2015 – 2019, during the MDSR implementation process; 3) 2020 and beyond, the way forward to fulfil the MDSR cycle.

Maternal death surveillance and safe motherhood initiatives before 2015 in Suriname

Suriname is a middle-income country in South America with 583.200 inhabitants.[14] There is an average of 10.000 deliveries in a year, of which 86% in the five major hospitals, 6% in primary care, 4% at home and 4% at an unknown location.[15] The Ministry of Health (MOH) coordinates the health care systems in Suriname. The Bureau of Public Health (BOG, Dutch acronym) is responsible for public health programs and manages the surveillance and analysis of health data. Although every hospital is collecting data on maternal health key indicators, no comprehensive national health information system exists.[16]

The registration of deaths in Suriname goes back to the 19th century. At the time the death of inhabitants was registered only if they were not enslaved.[17] An official civil registration system is in place in Suriname since 1917 and vital events, including births and deaths of all inhabitants, are registered.[18] The Central Bureau of Civil Affairs (CBB, Dutch acronym) is responsible for civil registration. Notification of death is obliged by law and must occur within 24 hours in the capital and within seven days in the districts.[19] Death notification is through a death certificate consisting of an 'A-form' with personal information, and a 'C-form' with medical information about the cause and circumstances of the death filled in by the medical doctor. The Bureau of Public Health (BOG) registers the C-form.[20] However, in practice, the C-form is often completed a long time after the burial.[12] In 2000 BOG received 85% of the of C-forms, which is higher than the 58% in 1995.[21]

Figure 1. Overview of local plans of action on maternal mortality in Suriname until 2015



The first confidential enquiry into maternal mortality in Suriname was conducted in 1991-1993 and reported that 53% of the maternal deaths were not certified - in contrast with the 15% non-certification of the general deaths.[22] The problems with C-forms leads to underreporting or late reporting of maternal deaths.

Figure 1 presents a timeline of the initiatives carried out to improve maternal health care in Suriname. Specific reports on maternal deaths were published by vital registry (BOG) in the annual reports of 1930-1942 for the first time. Subsequently, in 1978, the MMR of 1963-1970 was reported in a publication in the Surinamese Medical bulletin.[23] These reports did not provide information on the identification procedure of maternal deaths.[23] Maternal death reviews in Suriname were performed for the first time in 1991-1993 as part of a confidential enquiry conducted by Mungra et al.[13] This study highlighted substantial underreporting (63%, n=41/63) and entailed several recommendations:[22,23]

1) use various methods and sources to improve maternal death surveillance, such as Reproductive Age Mortality Surveys (RAMoS) and active case detection instead of only the C-forms (i.e., capture and recapture), and
2) perform maternal death audits to identify substandard care factors and provide recommendations.[13]

Following these recommendations and a maternal death underreporting of 31% in a 1995-1999 BOG survey, BOG initiated active maternal death surveillance in 2000 through a monthly enquiry for deaths in all hospital obstetric units.[21] The attending physician was responsible for the cause of death attribution and no multidisciplinary review or classification of these deaths was performed. As a consequence of the lack of classification, every death in pregnancy, including coincidental and accidental, was counted as a maternal death by vital registration.[12] In addition, this surveillance method did not capture maternal deaths in non-obstetric wards.

To reduce the maternal and perinatal mortality, the MOH performed a situation analysis in 2007: safe motherhood needs assessment.[25] This analysis concluded several gaps in the surveillance system and recommended to:

1) create more awareness about the definition of maternal deaths, so that accidental and incidental deaths are excluded when determining MMR;
2) add information to the C-form about (recent) pregnancy/delivery when a woman of childbearing age dies;
3) create a central notification point for possible maternal deaths;
4) make confidential enquiry mandatory and introduce maternal and perinatal death audit for a continued process of identification, analysis, and action to improve maternal care and prevent avoidable deaths.

Following the situation analysis in 2007, the National Safe Motherhood and Newborn Health Action Plan commenced in 2013 and was evaluated in 2017.[26,27] In 2014, Suriname's progress in the regional "Plan to Accelerate Maternal Mortality Reduction and Serious Maternal Morbidity" was published.[28,29] The abovementioned reports demonstrated the same gaps assessed in 2007 and the 1991-1993 confidential enquiry.[25,30] There was little awareness of safe motherhood and regional plans among health care providers and other stakeholders and they were not involved in the implementation of these plans.[27,28] Besides, due to a lack of capacity, communication and scarce coordination mechanism for the monitoring of actions, implementation was most likely not as successful as intended. [27,28] Surveillance barely improved since the previous scaling up of surveillance (active case detection in hospitals) in 2000. Maternal death audits were not yet part of the existing surveillance system mid-2015.[12,21]

MDSR implementation status of Suriname between 2015 and 2019

In 2015, a Reproductive Age Mortality Survey (RAMoS) was performed by health care providers to retrospectively identify and audit all maternal deaths between 2010 and 2014.[12] Various methods were used to identify pregnancy-related deaths, as described in previous publications.[12,13,24] Different medical experts determined the death causes and analyzed substandard care. Recommendations were to:

1) Improve maternal death surveillance,
2) Install a maternal mortality review committee to audit every pregnancy-related death,

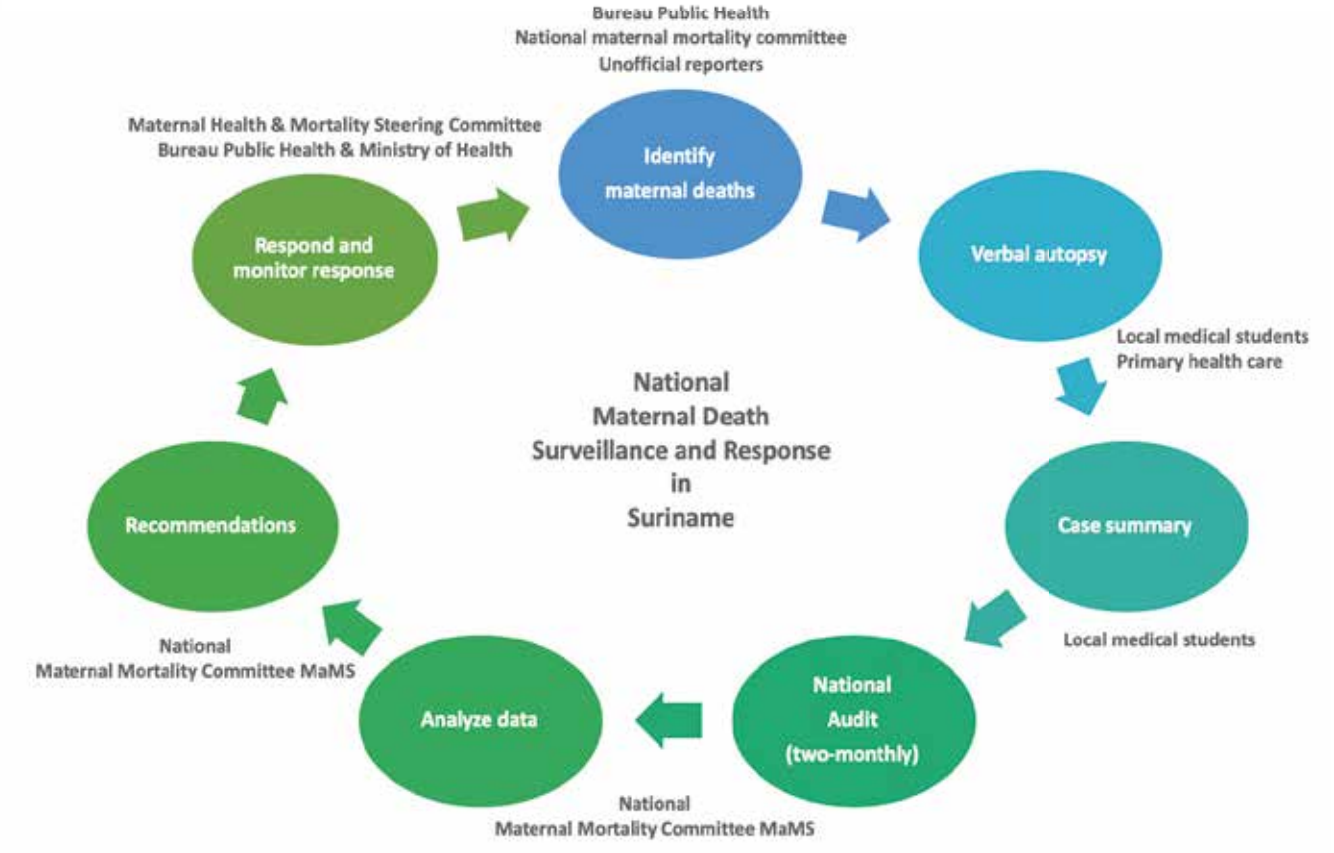
3) Implement national guidelines, early warning scores, and
4) Improve postnatal care strategies.

Response to a recommendation - Installation of a national maternal mortality review committee

To ascertain that recommendations would be pursued, the study investigators of the 2010-2014 RAMoS sought collaboration with the MOH, BOG, PAHO, midwifery, and gynecology/obstetric organizations. Consequently, a maternal mortality review committee (MaMS, Dutch acronym) was established in November 2015.[31] Committee MaMs members gather (bi)monthly and audit every pregnancy-related death in the nation. The committee consists of four gynecologists/obstetricians, one midwife, one internal medicine specialist, one BOG representative, two medical students, and several external consultants.[31] Most members are consultants from four of the five major hospitals in Suriname where most of the births take place; primary health care is not represented. Figure 2 depicts the activities currently conducted by the committee MaMS in the MDSR cycle:

1) Active case detection by various sources: (in)formal notification, notification by BOG (C-forms or active surveillance).
2) Sharing of cases (exchange of data) with BOG and vice versa; however, this is not performed regularly yet.
3) Composition of a case summary.
4) Collecting additional case information if necessary, e.g., laboratory results, interview with the health care provider.
5) Verbal autopsy with family members if this may contribute to gain more insight into the circumstances of the death.
6) Maternal death review/audit, classification using the International Classification of Diseases for Maternal Mortality (ICD-MM), and substandard care analysis according to the three-delay model.[32]
7) Dissemination of recommendations with relevant institutions and the MOH and BOG, however, this is not yet consistently done.

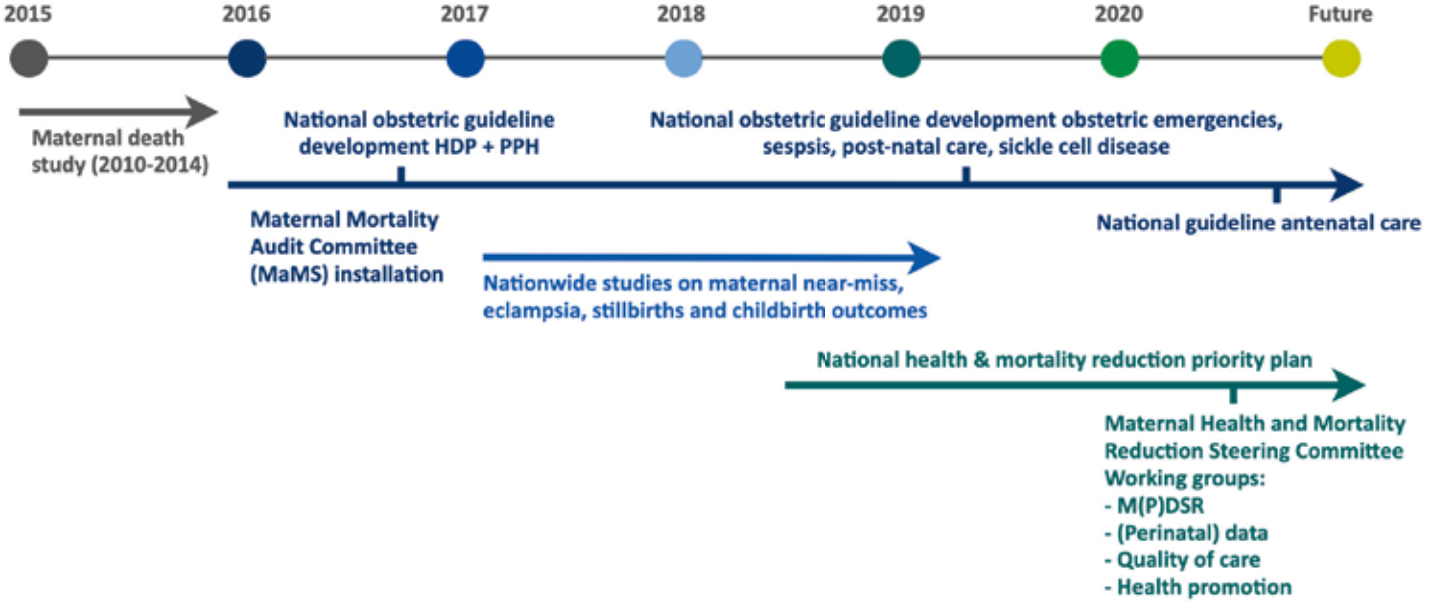
Figure 2. MDSR in Suriname in 2020, adapted from the WHO [10]



Some hospitals perform a facility-based review of maternal deaths and report to the committee MaMS. All audits are conducted, guaranteeing the "no blame, no shame" culture.[5,33] Committee MaMS ensures that no litigation of healthcare workers is initiated. Unfortunately, maternal deaths are still not structurally identified and depend on informal notification of health care workers, family, or news sites. Death certificates do not have a pregnancy box, and notification is not obliged.[12] Active surveillance of all deceased women of reproductive age are not yet completely incorporated in BOG's surveillance. Medical students are responsible for a part of the surveillance, data acquisition, case presentation at the audit, and summarize the analysis and recommendations. Figure 3 summarizes the facilitators and barriers experienced by committee MaMS in the completion of the MDSR cycle. Sustainable MDSR is still not accomplished since routine surveillance methods are not further improved, facility-based reviews are incidentally performed, no established institution exists responsible for the general coordination and the members of the committee MaMS work voluntarily.

Figure 3. Suriname's facilitators and barriers in installation of MDR committee

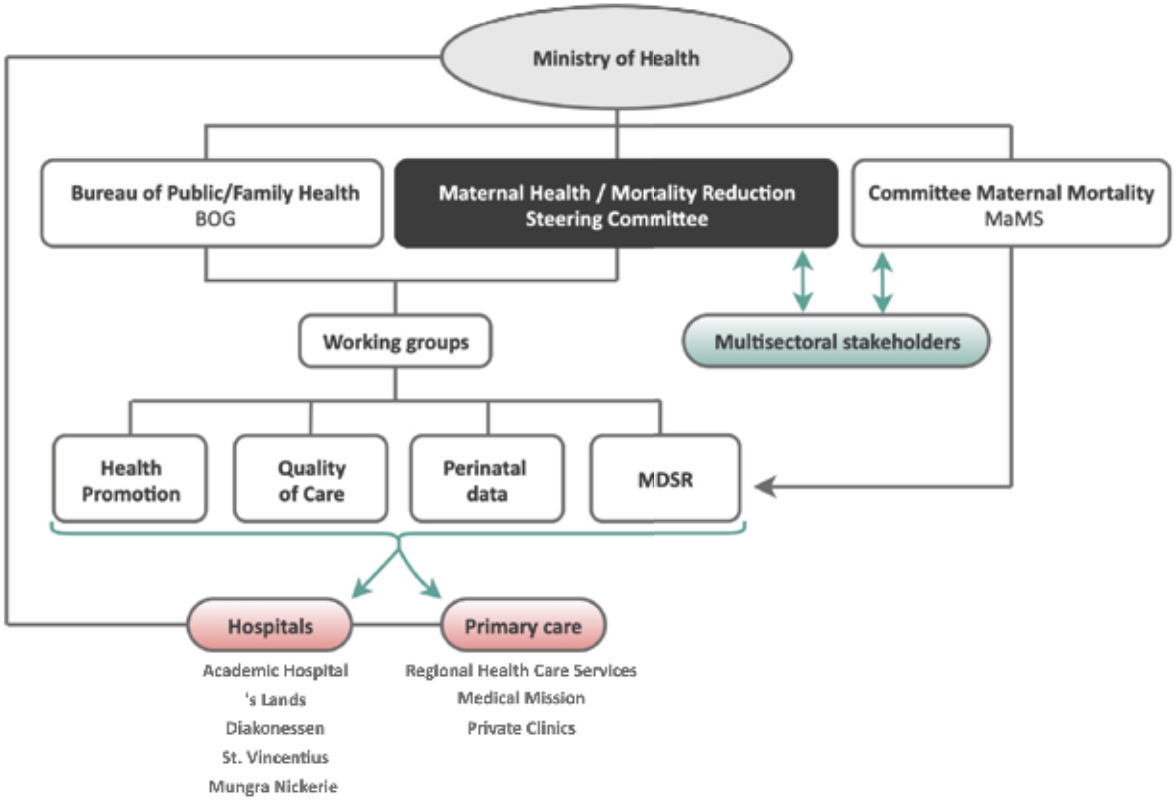
Figure 4. Timeline of maternal health initiatives in Suriname, 2015 to present



Legend

HDP: hypertensive disorders of pregnancy, MaMS: Maternal Mortality Suriname, M(P)DSR: maternal (& perinatal) death surveillance and response, PPH: post-partum haemorrhage

Figure 5. Flowchart of organization of maternal health in Suriname, adapted from the National Maternal Health and Mortality Reduction Priority Plan[3]



Response to another recommendation – guideline development

One of the recommendations on quality of care improvement of the 2010-2014 RAMoS was responded on by the committee MAMS in 2016 (Figure 4). This response included the "bottom-up" guideline development of the most important causes of maternal deaths, namely postpartum hemorrhage (PPH), hypertensive disorders of pregnancy (HDP) and obstetric emergency training.[34] Non-Pneumatic Anti Shock garments (used in hypovolemic shock in case of severe hemorrhage) were provided by PAHO, followed by training in 2018 and 2019 to reduce and treat PPH.[11] Subsequently, the evaluation of the previous guidelines and the development of guidelines on postnatal and antenatal care, sepsis, sickle cell anemia, emergency obstetrics, and early warning scores followed in April 2019. Facility-based obstetric emergency training was guided by BOG, PAHO and the recently installed maternal health quality of care committee, to enhance guideline implementation and adherence as advised in earlier studies.[6,7] In addition to the quality of care improvement projects, committee MaMS was involved in conducting nationwide studies on maternal morbidity and near-miss (2017-2019), childbirth outcomes, and stillbirths.[16,35]

Next steps toward fulfilling the MDSR cycle in Suriname

Similar to Suriname, other countries in the region have not made great progress in the reduction of maternal deaths.[3,36] Subsequently, the PAHO and its Latin American Centre of Perinatology women and reproductive health (CLAP) called for awareness-raising and accountability.[36]

MOH/BOG and PAHO presented an advocacy paper in April 2020 to call for a multisectoral effort to reduce maternal deaths.[37] They also created an organogram to reinforce the coordination of the maternal health program in Suriname. This organogram includes a national steering committee for maternal health and mortality reduction, overseeing the following working groups (Figure 5):

1. MDSR working group: responsible for improving *surveillance* and maternal death audit, dissemination of *recommendations* and delineation of roles for *response* by specifying specific tasks and responsibilities.

2. Quality of Care working group: responsible for the development and monitoring of national standards of care, update and validate national guidelines facility-based and support national training.
3. Perinatal (data) working group: responsible for introducing, collecting, synchronizing, and analyzing data on perinatal health in Suriname.
4. Health Promotion working group: responsible for the development of a health promotion plan, execute recommendations following maternal death reviews, maternal health education, family planning, and contraception in the communities.

Table 1. Summary of the implementation status of Maternal Death Surveillance and Response (MDSR) in 2020

Already established	To be established
Installation of national Maternal health/mortality reduction steering committee	Official installation of the committee MAMS and the four working groups for maternal health, reinforce the health promotion and perinatal data working group[1]
Coordination framework and terms of references	MDSR focal points supervising facility-based audits
Institutional MDSR focal points designated and trained in surveillance and active case detection	MDSR focal points reinforce performing verbal autopsies
Quality of care working group operational	Specialized assessors for facility audit preparation (nurses, doctors) and external audits (BOG)
	Timely dissemination of recommendations
	Monitoring and evaluation

Legend

[1] Perinatal data working group was installed, but only sporadically active

Table 2. Summary of specific recommendations needed to strengthen Maternal Death Surveillance and Response (MDSR) in Suriname

Legislation
Ensure no disciplinary / litigation measures
Notification of maternal death within 24 hours[1]
Include pregnancy checkbox in death certificate[2]
Timely completion of death certificate
Oblige autopsy for maternal deaths of unknown cause
Finances and human resources
Empower BOG by capacity strengthening
Support committee MaMS (administrative personnel, logistics)
Capacity building institutional MDSR focal points
Include MDSR in preservice training curricula
Involve healthcare workers and create awareness (bottom-up approach)
Involve and educate the community
Funding
Enabling policies
Ensure structural facility-based review
Install special secretariat for MDSR at BOG/MOH
Enable communication and dissemination of findings and recommendations

Legend

[1] Institutions and funeral agencies were recently requested to report maternal deaths within 24 hours;

[2] As a temporary solution, a pregnancy checkbox slip is attached to the "C-form".

This steering committee was installed by the MOH in February 2020, and guides, advises, and closely monitors planned interventions of the working groups and reinforces accountability and multisectoral coordination. MOH has identified multisectoral focal points in non-health ministries and institutions and currently prepares the national Maternal and Neonatal Health Strategy (2021-2025) and Operational Plan (2021-2023).

Strategies to institutionalize MDSR in Suriname

To guarantee sustainable surveillance and improve *identification and notification* of maternal deaths MDSR focal points (midwives/doctors) in each institution (the five hospitals, Medical Mission, and Regional Health Services) are designated. The MDSR focal point in a hospital is responsible for active case detection by monthly

medical file investigation of deceased women of reproductive age. The primary care MDSR focal point assesses community deaths. The MOH issued instructions on the procedure of early reporting and active case detection to health facilities and burial agencies. In addition, the PAHO/CLAP organized training in active case detection, verbal autopsy and review to improve MDSR. Following the identification of a possible maternal death, BOG must be notified via a hotline number, and the case must be entered in an anonymized password protected online database. Also, zero maternal deaths must be reported. The focal point is responsible for the coordination of the facility-based review and reports to BOG and committee MAMS. An external case assessment by specialized trained nurses or medical doctors of BOG will be performed with the assistance of committee MAMS. The monthly audits to determine underlying causes and classification on the national level by committee MaMS should continue. Committee MAMS formulates the recommendations and disseminates them to the relevant institutions and the MOH/BOG. The latter is responsible for an adequate response on the recommendations, evaluation and monitoring, in order to judge the impact on maternal death reduction. In table 1, an overview is given of the implementation status of abovementioned strategies in 2020.

Recommendations to strengthen MDSR in Suriname

In table 2 we summarize the recommendations following the "lessons learned" since the implementation of MDSR in Suriname in 2015. Critical steps in fulfilling the complete MDSR cycle in Suriname (action and response) are the delineation of roles and responsibilities for action, establishment of accountability mechanisms for results, and influencing those in a position to act. The fulfillment of this cycle is challenged by a lack of financial and human resources, leadership, legislation, and inadequate government enabling policies.

MDSR in the future - adding perinatal deaths to the cycle

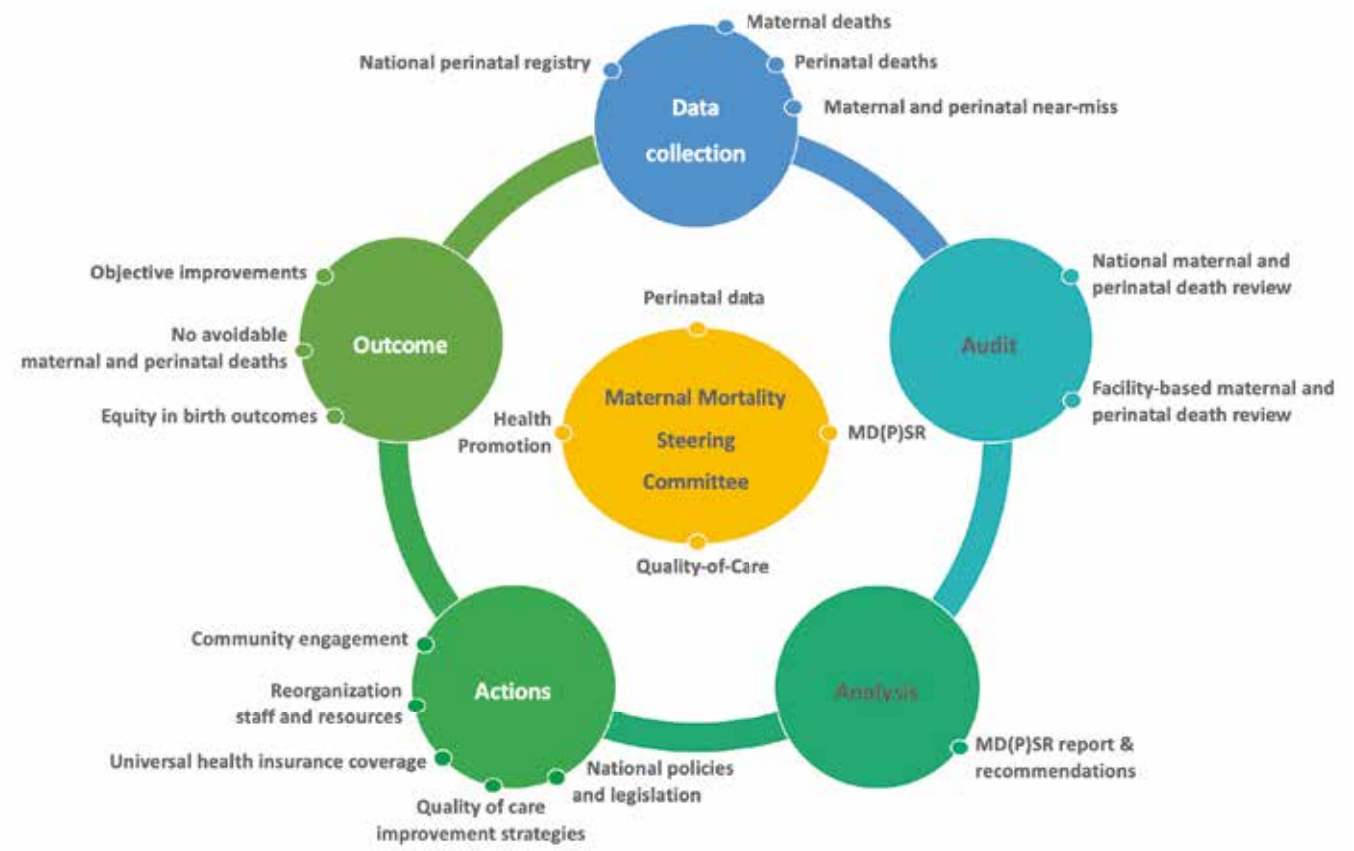
The following steps after the institutionalization of MDSR implementation will be the inclusion of perinatal deaths to the cycle, the Maternal and Perinatal Death

Surveillance and Response (MPDSR) (Figure 6). Maternal conditions often influence perinatal outcomes.[38,39] Additionally, gathering perinatal data and perform perinatal mortality audits in the future, extend the MDSR cycle, linking maternal and perinatal care. Besides focusing on maternal and perinatal deaths, maternal morbidity and near-miss data gathering and audit will be another essential step.

CONCLUSIONS

For decades, several attempts by the MOH alone were insufficient to institutionalize maternal death audits. Structural national maternal death review in Suriname was introduced after a timely and complicated process. Stakeholders' involvement, ownership and leadership were essential to step up in the MDSR cycle from insufficient surveillance to structural audits in 2015. These first steps created a base where the institutions in charge can build on to ensure sustainability. Therefore, a strongly committed government, enabling clear policies and laws to improve MDSR is crucial. In summary, the key elements for successful MDSR implementation are Commitment, "no blame, no shame" Culture, Collaboration, Coordination, and Communication (5 Cs).

Figure 6. The ideal paradigm of the maternal and perinatal death surveillance and response (MDPSR) cycle for Suriname



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General discussion

12

It's more important to know what sort of person has a disease than to know what sort of disease a person has

~ Hippocrates

DISCUSSION

This thesis aimed to improve the quality of obstetric health care in Suriname and reduce severe maternal and perinatal outcomes. The Plan-Do-Study-Act (PDSA) cycle was applied to the studies on maternal mortality, maternal near-miss and stillbirths within the Suriname Obstetric Surveillance System (SurOSS). These studies provided lessons learned to improve the quality of obstetric care in Suriname (figure 1).

Figure 1. The PDSA-cycle applied in Suriname, adapted from the ItOSS[1]

In conclusion, a reduction of severe maternal outcomes (maternal mortality and near-miss) and stillbirths in Suriname can be achieved by (1) improving the surveillance of maternal deaths and childbirth outcomes, (2) improving the facility-based quality of care, and (3) eliminating disparities in obstetric care. The global maternal health community can contribute to this goal in countries like Suriname by (1) reporting barriers and enablers of the implementation of specific interventions, (2) addressing the challenges experienced with the classification of maternal deaths, maternal near-misses and stillbirths, and (3) expanding the indicators to evaluate the quality of obstetric care.

Surveillance system - maternal mortality

Suriname's maternal mortality ratio (MMR) declined by 42% since 1990 to an MMR of 130/100.000 live births in 2015.[2] To achieve the Sustainable Development Goals (SDGs), Suriname will need to progress to an MMR of 44/100.000 live births by 2030.[3-5] A crucial step in achieving this goal includes using adequate surveillance to capture all maternal deaths. Maternal Death Surveillance and Response (MDSR, PDSA-cycle) aims to translate lessons learned to action plans and policies to monitor the effects, which is currently being institutionalised in Suriname. Several countries in Latin America and the Caribbean (LAC) have already implemented MDSR, each country with its own challenges.[6] The biggest bottleneck in completing the PDSA-cycle is the 'Act' aspect. Even countries with well-established maternal and perinatal death review committees struggle with the 'action' part of the continuous improvement cycle.[7-9] Long-term commitment of researchers, in close collaboration with health care providers, policymakers and the community, can contribute significantly to the 'Act' aspect. The national guideline development (chapter 10)[8] and the implementation of MDSR (chapter 11)[9] are examples in which global health researchers successfully reduce the theory-practice gap and assist health care providers with the implementation of specific recommendations. Many recommendations, however, are beyond the scope of health care providers and researchers and require strong governmental commitment, leadership and financial support. Making a maternal death a notifiable event is, for example, not possible solely with the commitment of researchers and health care providers. Additionally, the implementation of a nationwide digital perinatal registry is not possible without financial resources. A legislation framework, financial resources, leadership and capacity strengthening, are required to overcome the barriers Suriname currently experiences in MDSR implementation (chapter 11).[9]

Surveillance system - maternal near-miss and perinatal deaths

Permanent integration of maternal near-miss (MNM) and perinatal deaths into MDSR is not feasible due to a lack of human and financial resources. Sustainability

is more likely with a national digital perinatal data registry in place, as the Brazilian Network has demonstrated.[10] However, three challenges remain.

The main challenge with MNM-surveillance is the time-consuming and resource-demanding aspect. The organ-dysfunction criteria require daily review of vitals, laboratory results and interventions and the digital imputation of this data. Feasibility can probably be increased by the adoption of well-defined disease-based criteria. For example, the criteria developed by the International Network of Obstetric Surveillance System (INOSS) are more clinically relevant and allow cross-country comparison of disease prevalence and risk factors.[11,12] The main challenges with perinatal mortality in Suriname, similar to many other LMIC, include that (1) no stillbirth reduction plan is in place, (2) stillbirths are not formally registered by vital statistics (though they are reported in the childbirth books), and (3) early neonatal deaths are likely to be underreported when they occur after hospital discharge (though they are reported by vital statistics).[13-20] Potential solutions are clear and include the development of a national perinatal mortality reduction plan and closer collaboration with the national vital registration system.

Lastly, the elements mentioned earlier necessary to improve MDSR in Suriname, financial resources, leadership and capacity-strengthening, are also required for sustainable maternal near-miss and perinatal death studies and surveillance.

Perinatal data registry

Implementation of a perinatal data registry is essential, as it operates as a surveillance system for maternal mortality, near-miss and perinatal mortality. Additionally, it serves as the reference group (denominator) when studying incidences and risk indicators for severe maternal and perinatal outcomes. The greatest challenge of perinatal registries in high- and middle-income countries is to guarantee uniform data imputation and straightforward data extraction.[21-23] Additionally, the implementation is complicated, expensive and requires strong local commitment.[13] Although Suriname has no existing digital registry, the standardization of the childbirth books in 2018 by Committee MaMS form a platform for the digital Perinatal Information System (SIP, Sistema Informático

Perinatal – implemented in 34 LAC), which will be implemented in the near future. Involving the end-users in early stages (bottom-up) and discussing the facilitators and barriers other countries have experiences with SIP-implementation is crucial.[8,23,24]

Classification - maternal and perinatal deaths

Classification of diseases in maternal and perinatal health is necessary and useful to analyse trends and make cross-country comparisons. The World Health Organization (WHO) International Classification of Diseases for Maternal Mortality (ICD-MM)[25] and Perinatal Mortality (ICD-PM)[26] are applicable tools for middle-income countries such as Suriname.[27-29] Despite WHO's efforts, structural and local challenges associated with the classification persist (chapter 4 and 6).[20,27]

One challenge which compromises global comparability, is where to attribute the cause of maternal or perinatal death in the chain of events. ICD-MM heterogeneity has been described between two high-income countries.[30] A woman with severe hypertension, placental abruption and hypovolemic shock leading to her death, was classified as 'hypertensive disorders' (the Netherlands) and 'obstetric haemorrhage' (United Kingdom).[30] ICD-PM heterogeneity is seen even within one country: a stillbirth caused by a placental abruption was classified differently in two studies in South Africa.[31,32] Another challenge is the large proportion of 'unknown' or 'unspecified' causes of maternal and perinatal deaths (respectively 47% and 39% in Suriname)[20,33], which hinders health care providers, researchers and policymakers in establishing interventions to reduce the number of maternal and perinatal deaths.[15,20,32-36] The lack of autopsies performed in Suriname (3-5% in maternal deaths, 0% in stillbirths)[5,20], due to the costs and cultural or religious beliefs, plays the most significant role in the high proportion of 'unknown' causes. Reducing deaths of 'unknown' causes can be achieved making autopsy mandatory by law, by decreasing autopsy costs, by introducing the more affordable and culturally acceptable minimal invasive tissue sampling (MITS) or other investigations (radiology), and by developing post-mortem guidelines.

Classification - maternal near-miss

WHOs aim of establishing globally comparable MNM criteria is subverted by the different adaptation by different countries following underreporting of the WHO-MNM criteria in high-income (HIC), low- and middle-income (LMIC) settings.[37-40] Regardless how, amendments of the current WHO-MNM criteria are necessary to reduce underreporting, but enhance global uniformity and applicability.[38,39,41] We advocate for the use of well-defined disease-based and contextually-tailored criteria (chapter 5).[41] The prevalence of women with severe pre-eclampsia and eclampsia is more clinically relevant than the prevalence of women with severe thrombocytopenia, which is merely one example of why disease-based criteria are found to be more intuitive and relevant by many health care providers, policymakers and researchers.[38,39,42] Establishing clear definitions and indicators of quality of care is crucial to compare disease prevalence, risk factors and quality of care within and between countries, as seen in eclampsia studies between high-income countries.[11,12,43,44] Simultaneously, however, few women in low-resource settings will, for example, meet the INOSS' criteria for severe obstetric haemorrhage (two litres and/or four blood transfusions) due to poor blood loss measurement and less availability of blood products.[11,45,46] Therefore, maintaining the use of one global uniform MNM tool remains implausible, as the problems and solutions for low-income countries are incomparable to those in high-income countries. Contextually-tailoring MNM criteria per obstetric transition stage may be the most constructive solution to allow MNM comparison within and between countries in the same stage (e.g. stages I-II focus on direct causes, availability of resources and access to care, while stages IV-V focus on rare diseases, non-communicable diseases and over-medicalization).[47,48]

Beyond the numbers – quality of care

While counting (near) deaths and classifying causes according to a framework is necessary to facilitate global comparison and prioritize interventions, it does not explain *why* women and babies (like Ms X and Baby Y, in the beginning of this thesis) died and *how* this can have been averted.

Contrary to what health care providers, researchers and policymakers in Suriname presumed, poor performance on maternal and perinatal health indicators was not the consequence of low coverage, patient or transport delay, but the consequence of suboptimal quality of care in facilities (i.e. delay in diagnosis and treatment and inadequate monitoring) (chapter 2 and 7-9).[5,49-51] Similar to Suriname, increasingly many LMIC are reaching obstetric transition stage III, where women reach health care facilities and increased coverage needs to be accompanied by improved quality throughout the continuum of care to achieve the SDGs. The importance of measuring the quality of care is increasingly recognised by the international community, and several global initiatives are developing quality statements, indicators and process outcomes.[11,29,43,52,53] Measuring care in a uniform and systematic manner is crucial for comparison. However, researchers and health care providers have to remain aware of the pitfall of reporting only numbers without thinking 'out-of-the-box'. For example, the global WHO process measure 'proportion of women with eclampsia who received magnesium sulfate ($MgSO_4$)' did not reveal that the $MgSO_4$ dosage regimen was inadequate in the majority of women in Suriname (chapter 7).[52] A comprehensive global maternal morbidity study confirms that, solely, the availability of an intervention, such as $MgSO_4$, does not lead to a reduction of maternal mortality.[10] Another example is that outcome measure 'proportion of women with post-partum haemorrhage who died' does not take the accuracy of blood measurement into account, resulting in a widely different PPH prevalence and case fatality rate within countries (chapter 8)[50] and between countries.[8,50,52,54] An audit of the complete cases therefore remains crucial.

Beyond the numbers – health inequity and ethnic disparities

Latin America and the Caribbean is a region marked by social inequality, affecting the most marginalised populations.[55] Health inequity particularly affects Indigenous and African-descendent women; a continuing effect of colonialism.[55-57] Measuring and monitoring health equity on a national level, as done in Brazil[58], Chile[59], Colombia[60], Mexico[61] and Uruguay[62], is a priority for Suriname to achieve the SDGs. Even though creating awareness of ethnic disparities is only the

beginning of the process of change and insufficient by itself, it is necessary before further actions (fundamental social and structural changes) can translate these findings into better health outcomes for all. In Suriname, similar to other LAC, severe maternal and perinatal outcomes disproportionately affect African-descendent (Maroon) women, and adolescent pregnancies are particularly high among Indigenous women (chapter 3)[24], both marginalised peoples.[55] Simultaneously, inequalities in caesarean section rates within and between countries are substantial, reflecting 'too little, too late and too much, too soon'.[63] Similar to most LAC, caesarean sections in Suriname are highest among women with the lowest obstetric risks, i.e. Asian-descendent women (generally from wealthier socioeconomic strata).[24,64] In conclusion, disparities in maternal and perinatal outcomes in Suriname and beyond reflect structural drivers of socioeconomic inequity and inequitable application of timely evidence-based care. Health equity research, targeted interventions, and universal access to and provision of high-quality, respectful maternity care is essential in the achievement of the SDGs.

The way forward - Globally

There is no quick fix to reduce maternal and perinatal mortality. If a substantial reduction of maternal and perinatal mortality is to be achieved, universal coverage needs to be matched with high quality respectful women-centred care. WHO maternal and perinatal quality statements, process and outcome measures are very useful and important and now need to be implemented at a national level in LMIC.[52] Simultaneously, a core outcome dataset for severe maternal and perinatal diseases, including the option to disaggregate data to identify inequity, can significantly contribute to improved global and local data monitoring.[11,43,53] Re-defining WHO maternal near-miss criteria (well-defined, disease-based, contextually-tailored) can reduce underreporting, while enhancing uniformity and applicability and facilitate sustainable surveillance and audit of maternal near-miss into national MDSR.[38-41,65] Lastly, the global research agenda needs to focus on generating (implementation) evidence from LMIC to enhance contextualised high-quality

care.[66] 'Bottom-up' development and implementation of interventions (chapter 10-11)[8,9], instead of a direct translation of evidence from high-income countries, is key in improving care.

The way forward - Locally

Improving institutionalisation of MDSR in Suriname requires strong political commitment, strengthening of death identification and notification systems, an adequate legal framework, financial support, and rapid dissemination of recommendations, while maintaining the current 'no shame, no blame' culture and the firm local ownership Committee MaMS has established.[9] Nationwide implementation of facility-based maternal death audits (internal), next to national guidelines, will most likely be beneficial to improvements in local practice and the general organization and provision of care in the facility.[8,9] These internal audits may reveal lessons to be learned complimentary to national (external) audits. Implementation of a national perinatal data registry is a priority to efficiently and effectively monitor trends in maternal and perinatal outcomes and health inequities in Suriname. While awaiting the introduction of a digital perinatal registry, analysis of data can and should be done through the digitalised manual childbirth books (uniform since 2018) to monitor trends.[24] The silence around perinatal deaths needs to be broken, also in Suriname. Next steps include embedding a perinatal death reduction target in the national health plan, including early neonatal deaths to stillbirth studies and investing in surveillance, audit and research of perinatal mortality. The high proportion of maternal deaths and stillbirths in Suriname with 'unspecified' underlying causes needs to be tackled by developing post-mortem investigation guidelines and normalizing and institutionalising autopsy and/or MITS in mothers and babies who die of unknown causes.[24,33] Finally, continuous surveillance of MNM and perinatal mortality may not yet be feasible in Suriname due to the human and financial resources required. However, periodic studies are realizable with strong leadership and commitment and should be conducted every five years to monitor trends and evaluate interventions.

Progress towards the SDGs, despite the severe economic recession in Suriname, is highly dependent on strong governmental commitment and effective prioritisation of interventions. A multisectoral approach is necessary with a focus on eliminating social drivers of inequity. Essential interventions, beyond maternal and perinatal care, include increasing women's roles in society and ensuring their rights to a dignified life (e.g. equal access to education, equal employment opportunities, equal health care access and quality, free contraception and safe abortion for all). An essential health system intervention to improve quality of care, beyond the recommendations of this thesis, includes strengthening the position of midwives in Suriname, who are the driving forces of care during pregnancy, childbirth and in the postnatal period in the country.

Key findings

1. Maternal mortality reduction in Suriname can be accelerated by implementing Maternal Death surveillance and Response, improving the quality of care in facilities through local audits, national guidelines and trainings, and by ensuring universal access to care.
2. Women of African-descent and older age are at highest risk of maternal death, near-miss and stillbirth in Suriname.
3. ICD-MM classification varies between high- and middle-income countries, with only moderate consensus achieved between committees.
4. The high number of maternal deaths and stillbirths due to 'unspecified' causes is alarming and restrains our understanding of why they occur.
5. WHO criteria underreport maternal near-miss, while lower-threshold (Sub-Saharan Africa and Namibian) criteria risk overreporting and compromise global comparability.
6. Substandard quality of care in health care facilities (third delay) contributes most significantly to maternal deaths in Suriname and also explains the high prevalence of eclampsia and recurrent seizures.
7. Contextually-appropriate 'bottom-up' strategies enhance local ownership, acceptability and feasibility and are required for sustainable implementation.

Research questions, answers and recommendations

Part I: Surveillance	
What is the national maternal mortality ratio and the degree of underreporting in Suriname?	The MMR was 130 per 100.000 live births in 2010-2014, and 120 per 100.000 live births in 2015-2019. There was 24% underreporting.
What is the cause of maternal mortality in Suriname?	Sepsis, hypertension and haemorrhage are the most important causes of maternal deaths and a large proportion of deaths is of unknown cause. Most maternal deaths in Suriname occur due to substandard quality of care in facilities (third delay).
Do childbirth health care disparities exist in Suriname and if so, which women are most at risk?	Women of Maroon descent, and/or aged 35 years or older, and/or are grand multiparous, are at higher risk of severe pregnancy-related complications leading to death, stillbirth, preterm delivery or a baby with a low Apgar score. Women of Hindustani descent have less pregnancy complications, yet receive more caesarean sections.
What are the recommendations to improve surveillance and reduce underreporting of maternal mortality in Suriname?	- Install a maternal mortality committee - Implement Maternal Death Surveillance and Response (MDSR) - Make a maternal death a notifiable event - Include a pregnancy check box on death certificates - Institutionalise autopsies and other post-mortem investigations in women of reproductive age who die of unknown causes - Perform facility-based reproductive age mortality surveys
What are the recommendations to improve national perinatal data acquisition in Suriname?	- Develop a workgroup responsible for national childbirth data collection and analysis - Short term: create a uniform national childbirth book for all hospitals and primary health care centres - Long term: implement a digital perinatal registry, such as SIP, while safe-guarding straightforward data imputation and extraction
What are the most important recommendations to reduce maternal mortality in Suriname?	- Improve facility-based quality of care - Ensure universal access to high-quality care - Improve data surveillance, implement MDSR and develop and implement national obstetric guidelines (set standards)

Part II: Classification	
What is the difference in underlying causes of maternal deaths when comparing classification by local experts and international experts?	The cause of maternal death was classified differently by the attending physician and national audit committee MaMS in 47% of cases. Experts from the Netherlands, Jamaica and Suriname achieved only moderate consensus on the causes of death and disagreed in 15% whether the pregnancy-related death was a 'maternal death'.
What is the maternal near-miss ratio and what are the most important challenges of WHO-MNM application?	The MNM-ratio is 8 per 1000 live births (2017), based on the WHO organ-based criteria. Two important challenges of WHO-MNM criteria are that (1) severe diseases are not captured with the tool and many countries have made local amendments of the criteria, compromising comparability; and (2) data collection is resource-intensive, especially when using organ-based criteria.
What is the stillbirth rate and what are the underlying causes of stillbirths?	The stillbirth rate is 15 per 1000 live births (2016-2017), of which the majority (85%) occur during the antepartum period. The most important underlying causes are 'hypoxia' (46%) and 'unspecified' (41%), and maternal hypertensive disorders contribute to many of the stillbirths (43%) in Suriname.
How can the applicability and feasibility of the global classification tools (ICD-MM, WHO-MNM and ICD-PM) be improved?	- ICD-MM: (1) clarify on where in the chain-of-events to attribute the cause of death, (2) provide instructions for classification in specific circumstances (e.g. lack of evidence of pregnancy, death of resident in another country, suicide in early pregnancy) - WHO-MNM: (1) amend criteria by considering well-defined disease-based criteria instead of organ-based criteria and (2) contextually-tailored criteria per obstetric transition stage. - ICD-PM: (1) create classification opportunity even when timing of stillbirth (antepartum or intrapartum) is unknown, (2) develop a post-mortem work-up scheme to reduce the high proportion of stillbirths of unknown cause, and (3) amend criteria in such a way that contributing factors are not mutually exclusive

Part III: Beyond the Numbers	
Why do women die or nearly die due to severe obstetric complications maternal sepsis, eclampsia and major obstetric haemorrhage in Suriname?	Most direct obstetric maternal deaths in Suriname are the result of third delay (substandard quality of care). - Women who died of sepsis were not given antibiotics in the first hour of presentation (golden hour) in any case; - Women with eclampsia were given therapeutic magnesium sulfate according to protocol in only 43%; - Women with major obstetric haemorrhage received prophylactic oxytocin in 61% and therapeutic tranexamic acid in 5%. Patient delay due to a delay in seeking care (first delay) or reaching care (second delay) played a less significant role in Suriname.
How can future (near) deaths due to maternal sepsis, eclampsia and major obstetric haemorrhage be prevented in Suriname?	A reduction of these direct obstetric deaths and near-misses (and the resulting severe perinatal outcomes) can be achieved in Suriname by: - Developing and implementing local national obstetric guidelines - Introducing early warning scores to recognize severely ill women - Providing (simulation-based) trainings at all levels of care - Monitoring severe maternal outcomes by collecting data and reviewing the cases (audits) at facility-level

Part IV: Response	
What is the most important enabler of obstetric guideline development?	The 'bottom-up' strategy, i.e. involving end users in early stages
What is necessary to implement Maternal Death Surveillance and Response (MDSR) in Suriname?	- Legislation framework - Financial resources - Leadership - Capacity building

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Summary
Samenvatting

13

Pe e kumbatitei beri

[Where your umbilical cord is buried]

SUMMARY

This thesis present studies on maternal mortality, maternal near-miss and stillbirths in Suriname with the aim to reduce maternal and perinatal mortality. The studies, conducted in a nationwide setting between 2015 and 2019, give insights into the incidence, case fatality rate, risk factors and substandard care of maternal mortality, maternal near-miss and stillbirths in Suriname.

PART I of the thesis describes the importance of maternal death and perinatal data surveillance and how surveillance contributes to developing adequate strategies and recommendations to reduce severe maternal and perinatal outcomes.
Chapter 2 describes the reproductive age mortality survey, conducted from 2010 to 2014, to identify and review all maternal deaths in Suriname. With a total of 65 maternal deaths, the maternal mortality ratio (MMR) was 130/100.000 live births. The most important underlying causes were direct obstetric causes and more than half of the deaths were deemed preventable. The most critical factors were delay in diagnosis and treatment. Recommendations to reduce maternal mortality included to improve the quality of care, install a maternal death audit committee and improve data surveillance for maternal mortality, near-miss and stillbirths.
Chapter 3 gives an overview of maternal and perinatal outcomes of close to 20.000 women who gave birth in the five hospitals (86% of total) in 2016 and 2017, and describes the ethnic disparities in health outcomes in multi-ethnic Suriname. While maroon women were at highest risk of a stillbirth, preterm birth, a baby with a low birth weight and low Apgar score, Hindustani women had the highest caesarean section rate (32%), almost twice that of Maroon women (17%). Teenage pregnancy was significantly higher in Maroon (18%) and Indigenous (21%) girls than in Hindustani (9%) and Chinese (3%) girls. These ethnic disparities call for targeted action by health professionals, researchers and policymakers.

PART II increases the understanding of *how* women and baby die or nearly die by applying the World Health Organization classification tools for maternal mortality, near-miss and perinatal mortality. Furthermore, part II evaluates the applicability

and feasibility of the tools and made recommendations to enhance uniformity and facilitates comparison within and between countries.

In **Chapter 4** the International Classification of Diseases (ICD) - Maternal Mortality (MM) was applied to all pregnancy-related deaths in Suriname from 2010 to 2014 (n=89). Classification between the attending physician and audit committee was compared and showed no coherence in underlying causes in 47% of all cases. Furthermore, classification was compared with audit committees from high-income country (the Netherlands) and another middle-income country (Jamaica). In 12% of cases no consensus was achieved on whether the death was maternal or coincidental/accidental. Deaths were more frequently 'unspecified' according to the Netherlands (17%) than to Jamaica (6%) or Suriname (4%). We describe the specific encountered challenges and suggested revisions to improve the ICD-MM.

Chapter 5 presents a one-year nationwide prospective study on maternal near-miss (MNM) in Suriname where three classification tools were applied: the WHO-MNM, suggested Namibian-criteria and Sub Sahara African (SSA)-MNM. The WHO MNM-ratio was 8/1000 live births (n=71), mortality-index 12%. While the WHO-tool may underreport diseases with high case fatality rates (e.g. eclampsia and uterine rupture), the other two adapted tools use lower threshold criteria and may overreport MNM. MNM was associated with advanced maternal age, maroon ethnicity, no antenatal care and adverse perinatal outcomes. The use of well-defined disease-based criteria, with tailored thresholds per obstetric transition phase, may better endeavour feasibility, uniformity and enhance global comparison and reduce underreporting in low-, middle- and high-income settings.

In **Chapter 6** the ICD - Perinatal Mortality (ICD-PM) is applied to stillbirths in Surinamese hospitals in 2017. The stillbirth rate was 14/1000 births (n=131). One-third of foetal death occurred during hospital admission and majority occurred antepartum (85%). The leading causes were 'hypoxia' (46%) and 'unspecified' (39%) and hypertension was present in half of all stillbirths. The ICD-PM could not provide Suriname with the necessary recommendations to reduce stillbirths. The greatest challenge was that there were many stillbirths with

unknown causes (of hypoxia), which calls for perinatal death audits, post-mortem investigations and improved diagnostic guidelines for stillbirths.

PART III goes beyond the numbers. While ratio's and classifications provide us numbers (such as Part I and II of this thesis), they often fail to explain *why* events, such as maternal death, near-miss or stillbirth, occur and what we can do to prevent these events from happening. The next chapters go beyond the numbers, aimed at improving the quality of care and eliminating avoidable deaths.

Chapter 7 presents a two-year nationwide prospective surveillance study (2017-2019) on eclampsia and reports a prevalence of 37/10.000 live births (n=72). The majority of the women had their first seizure in the hospital (65%) and more than half of the women had more than one seizure (60%). Adolescents with eclampsia had a significantly lower blood pressure than adults. Therapeutic magnesium sulfate ($MgSO_4$) was given to 99% of women, although audit revealed that in majority of cases (57%) it was not administered adequately (too low dosage, short duration or stopped for caesarean section). The median interval between fit and delivery was more than 24 hours, and more than half of the women (54%) had a high blood pressures during caesarean section. These findings imply that more emphasis is necessary on how $MgSO_4$ is administered, the ideal timing of childbirth and the definition of stabilization. The most important recommendation is to improve implementation of the eclampsia guideline. Additionally, studies are necessary to establish whether lowering the threshold for hypertension diagnosis in teenagers can contribute to reducing the burden of eclampsia in countries with high eclampsia and adolescent pregnancy rates (i.e. Latin America and Caribbean).

In **Chapter 8** the magnitude, risk factors and management of postpartum haemorrhage (PPH) in Suriname in 2017 is explored. The prevalence of PPH was 9% (n=808), which is similar to the global prevalence, however with variation from 4 to 12% between hospitals. Blood loss amount correlated poorly with severity (ICU admission/amount of transfusions), which implies that the measurement of blood loss is inconsistent. Women with severe PPH received oxytocin prevention in 62% and tranexamic acid therapy was given in only 5% of severe PPH. By addressing

these gaps (inaccurate blood loss measurement and substandard quality of care), severe outcomes due to PPH will likely be reduced.

Chapter 9 describes sepsis-related maternal deaths in Suriname from 2010-2014 (n=29). The most frequent underlying cause was pneumonia (n=14, 48%). None of the women received antibiotic treatment within the first (golden) hour of diagnosis. Other factors leading to the death were inadequate monitoring (59%) and delay of diagnosis (63%). Sepsis-related maternal mortality can be reduced by timely diagnosis and immediate antibiotic therapy (within the golden hour). The diagnosis 'maternal sepsis', however, needs to be further clarified to enhance timely identification.

Part IV of this thesis is part of the 'response' following the previous chapters. The descriptive process of facilitators and barriers of obstetric guidelines development and maternal death committee implementation can contribute to more efficient and effective interventions in Suriname and in other countries.

Chapter 10 emphasizes the importance of using a 'bottom-up' approach to develop guidelines. The involvement of health care providers in the earliest stages enhanced ownership and commitment in Suriname. **Chapter 11** summarizes our five-year contribution to the Maternal Death Surveillance and Response (MDSR) in Suriname. The practical issues, facilitators and barriers of maternal mortality committee installation are laid out, and recommendations are made for further improvement of the MDSR cycle.

SAMENVATTING

Dit proefschrift bestaat uit onderzoek verricht naar maternale sterfte, ernstige maternale morbiditeit (near-miss) en foetale sterfte in Suriname, met als doel dit te verminderen. Het landelijk onderzoek, verricht tussen 2015 en 2019, heeft inzicht gegeven over de prevalentie, risicofactoren en oorzaken van maternale sterfte, near-miss en foetale sterfte in Suriname.

DEEL I van dit proefschrift beschrijft het belang van data verzameling omtrent maternale en foetale sterfte en hoe dit bijdraagt aan het ontwikkelen van de juiste strategieën en aanbevelingen om maternale en foetale sterfte te verminderen.
Hoofdstuk 2 beschrijft het landelijk maternale sterfte onderzoek in Suriname (2010-2014). Er waren in totaal 65 maternale sterftes en de maternale sterfte ratio (MMR) bedroeg 130/100.000 levendgeborenen. Directe obstetrische oorzaken waren hierbij het belangrijkst en meer dan de helft van de sterftes was te voorkomen. De belangrijkste factoren waren vertraging in het stellen van de juiste diagnose en starten van een behandeling. De aanbevelingen om maternale sterfte in Suriname te verminderen waren: de kwaliteit van zorg verbeteren, een audit commissie instellen en data surveillance voor maternale sterfte, near-miss en foetale sterfte verbeteren.
Hoofdstuk 3 geeft een overzicht van maternale en foetale uitkomsten van de bijna 20.000 vrouwen die in één van de vijf ziekenhuizen (86% van totaal) bevielen tussen 2016 en 2017, en beschrijft de etnische verschillen in geboorte uitkomsten in multi-etnisch Suriname. Terwijl Marronvrouwen het hoogste risico hadden op foetale sterfte, kregen Hindoestaanse vrouwen bijna twee keer zo vaak een keizersnede (32% vs. 17%)), bijna twee keer vaker dan Marronvrouwen (17%). Bevallingen onder tieners kwamen het meest voor bij Marronse (19%) en Inheemse (21%) vrouwen, en het minst bij Hindoestaanse (9%) en Chinese (3%) vrouwen. Deze etnische verschillen vragen om aandacht en een meer op maat gerichte aanpak van zorg door zorgverleners, onderzoekers en beleidsmakers.

DEEL II vergroot het begrip van *hoe* vrouwen en baby's (bijna) overlijden aan de hand van de Wereldgezondheidsorganisatie (WHO) classificatiesystemen voor oorzaken van maternale sterfte, near-miss en foetale sterfte. De toepasbaarheid wordt geëvalueerd en er worden aanbevelingen gedaan om de uniformiteit te bevorderen en vergelijking binnen en tussen landen te vergemakkelijken.

In **Hoofdstuk 4** wordt de Internationale Classificatie van Ziekten - Maternale Mortaliteit (ICD-MM) toegepast op de zwangerschap gerelateerde sterfte in Suriname (2010-2014, n=89). Verschil in classificatie tussen de behandelend arts en auditcommissie liet tegenstrijdige doodsoorzaken zien in de helft van de gevallen. Verder wordt de classificatie van maternale sterfte door Suriname vergeleken met een hooginkomensland (Nederland) en een ander middeninkomens land (Jamaica). Hieruit blijkt dat er in 12% onenigheid was of de sterfte überhaupt een 'maternale sterfte' betrof. Maternale sterfte werden vaker als 'niet gespecificeerd' door Nederland (17%) geduid, dan door Jamaica (6%) en Suriname (4%). We beschrijven de problemen waar de drie landen tegenaan liepen bij gebruik van de ICD-MM om bij te dragen aan mogelijke revisies in de toekomst.

Hoofdstuk 5 beschrijft een landelijke prospectieve studie in Suriname naar ernstige maternale morbiditeit, ofwel near-miss (MNM), waarbij drie classificatiesystem werden gebruikt: de WHO-MNM, Namibië-MNM en Sub Sahara Afrika (SSA)-MNM. De WHO MNM-ratio bedroeg 8/1000 levendgeborenen (n=71) met sterfte-index van 12%. Terwijl de WHO-MNM-criteria, op basis van orgaandysfunctie, onder-rapporteert, wordt door de aangepaste (Namibië en SSA) criteria met lagere inclusiedrempel juist over-gerapporteerd. MNM was geassocieerd met leeftijd $\geq$ 35 jaar, Marronse etniciteit, ontbreken van antenatale zorg en slechte perinatale uitkomsten. Het gebruik van ziekte gebaseerde criteria, eventueel met verschillende drempels per obstetrische transitiefase, kan onder- en over-rapportage voorkomen en de uniformiteit, haalbaarheid en het gebruik van de WHO-MNM bevorderen.

In **Hoofdstuk 6** wordt de Internationale Classificatie van Ziekten - Perinatale Mortaliteit (ICD-PM) toegepast bij foetale sterfte in Surinaamse ziekenhuizen. De foetale sterfteratio bedroeg 14/1000 geboortes (n=131). Een derde hiervan vond

plaats tijdens een ziekenhuisopname en de meerderheid trad antepartum op (85%). De belangrijkste oorzaken waren hypoxie (46%) of 'niet gespecificeerd' (39%) en de helft van de moeders met foetale sterfte had hypertensie in de zwangerschap. Doordat de meeste foetale sterfte geen duidelijke doodsoorzaak hadden, konden er minder lessen uit geleerd worden. Implementatie van perinatale sterfte-audits, obductie en diagnostische richtlijnen zijn noodzakelijk om onderbouwde strategieën te ontwikkelen voor de reductie van foetale sterfte.

In DEEL III wordt er verder gekeken dan de cijfers. Hoewel ratio's en classificatie van oorzaken van maternale sterfte, near-miss en foetale sterfte ons cijfers opleveren (zoals deel I en II van dit proefschrift), verklaren ze vaak niet *waarom* het is gebeurd en wat we eraan kunnen doen om het te voorkomen. De volgende hoofdstukken gaan om deze reden in op de kwaliteit van zorg met het doel te achterhalen *waarom* zwangere of bevallen vrouwen wel, of net niet overlijden. Daarnaast worden er gerichte aanbevelingen gegeven.

Hoofdstuk 7 betreft een landelijke prospectieve studie (2017-19) naar eclampsie. De prevalentie bedroeg 37/10.000 levendgeborenen (n=72). De meerderheid van vrouwen had hun eerst insult in het ziekenhuis (65%) en meer dan de helft (60%) kreeg meer dan één insult. Tieners met eclampsie hadden een significant lagere bloeddruk tijdens het insult dan volwassenen. Magnesiumsulfaat werd aan bijna alle vrouwen gegeven, echter werd via audit achterhaald dat het meestal niet adequaat was toegediend (te lage dosis, te korte duur en/of gestopt voor de sectio caesarea). Het gemiddelde interval tussen eclampsie en bevallen was meer dan 24 uur en meer dan de helft van de vrouwen had een te hoge bloeddruk tijdens de sectio. De belangrijkste aanbeveling is om de eclampsie richtlijnen beter te implementeren. Vervolgonderzoek zou zich moeten richten op een lagere drempel voor de diagnose hypertensie in tienerzwangerschappen, om op deze manier de eclampsie prevalentie onder tieners te verlagen (met name in Latijns-Amerika).

In **Hoofdstuk 8** worden de omvang, risicofactoren en de behandeling van hemorragie post partum (HPP) in Suriname onderzocht (2017). De prevalentie bedroeg 9% (n=808), wat vergelijkbaar is met andere landen, echter met grote variatie tussen ziekenhuizen (4-12%). De hoeveelheid bloedverlies kwam niet goed

overeen met de ernst (bloedtransfusies, IC-opname), wat duidt op onbetrouwbare metingen. Vrouwen met een ernstige HPP bleken maar in 82% van de gevallen oxytocine preventie te hebben ontvangen en tranexaminezuur was aan slechts 5% van de vrouwen met een ernstige HPP gegeven. Door deze hiaten in zorg in kaart te hebben gebracht, kunnen gerichte interventies plaatsvinden om de kwaliteit van zorg te verbeteren.

Hoofdstuk 9 beschrijft de sepsis gerelateerde maternale sterfte in Suriname (2010-2014, n=29). De meest frequente onderliggende oorzaak was een pneumonie (n=14, 48%). Geen van de vrouwen ontving binnen het eerste (gouden) uur na diagnose antibiotica. Andere belangrijke elementen waren slechte monitoring (59%) en vertraging in het stellen van de diagnose (63%). Sepsis gerelateerde maternale sterfte kan verminderd worden door snelle diagnose en directe (antibiotische) behandeling. Verduidelijking van de diagnose 'maternale sepsis' is echter een vereiste om de identificatie te vergemakkelijken.

Deel IV van dit proefschrift vormt de 'respons' op de voorgaande hoofdstukken en beschrijft het proces van het ontwikkelen van obstetrische richtlijnen en de implementatie van de auditcommissie maternale sterfte in Suriname.

Hoofdstuk 10 beschrijft hoe de 'bottom-up' benadering tijdens het ontwikkelen van richtlijnen door betrokkenheid van zorgverleners in de vroegste stadia het eigenaarschap en de betrokkenheid verstrekt.

Hoofdstuk 11 vat onze vijfjarige bijdrage aan de Maternal Death Surveillance and Response (MDSR) in Suriname samen. De uitdagingen van de implementatie van de commissie maternale sterfte worden uiteengezet en er worden aanbevelingen gedaan voor verbetering van de Materale Sterfte Surveillance en Response (MDSR) in Suriname.

Appendix

ABOUT THE AUTHOR

Kim Verschueren was born on September 15th, 1993 on St. Maarten, Dutch Caribbean. Rob Verschueren en José Sommers are her parents and Joris (1995) is her brother. Kim graduated from secondary education (VWO), Milton Peters College, St. Maarten in 2011, afterwhich she studied Medicine at Utrecht University, the Netherlands, from 2011 to 2017. Following her gynaecology rotation in Suriname in 2015, Kim initiated the investigation into maternal deaths in collaboration with Lachmi Kodan, which transformed into their PhD trajectories. Kim later combined her PhD with clinical work as a medical doctor (ANIOS gynaecologie) in Suriname (St. Vincentius, 2017-2018) and the Netherlands (Haaglanden Medical Centre, 2018-2019). In 2020, she worked in Covid-19 / internal medicine department in St. Maarten Medical Center and in Moria refugee camp (Lesvos, Greece). In October 2020, she started her six-year Obstetrics & Gynaecology residency program in HMC, cluster Leiden, the Netherlands. Next to her residency programme, she remains involved with maternal and perinatal health and research projects in low- and middle-income countries.

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12. Kodan LR, **Verschueren KJC**, Paidin RR, et al. Trends in maternal mortality in Suriname: comparing three confidential enquiries in three decades. 2020; *submitted.*

THE SAFE MOTHERHOOD SERIES

The Dutch Working Party 'International Safe Motherhood and Reproductive Health' aims to contribute to improvement of the reproductive health status of women around the globe, in particular by collaborating with local health workers (http://www.safemotherhood.nl). The Working Party is part of both the Dutch Society of Obstetrics and Gynaecology (NVOG) and the Dutch Society for International Health and Tropical Medicine (NVTG). The activities that are undertaken under the umbrella of the Working Party can be grouped into four pillars: education, patient care, research and advocacy.

Research activities are undertaken by (medical) students, Medical Doctors International Health and Tropical Medicine and many others. Some research activities develop into PhD-trajectories. PhD- candidates all over the world, Dutch and non-Dutch, work on finding locally acceptable and achievable ways to improve the quality of maternal health services, supervised by different members of the Working Party. Professor Jos van Roosmalen initiated the Safe Motherhood Series, which started in 1995.

THE SAFE MOTHERHOOD SERIES

- The role of oral (methyl)ergometrin in the prevention of postpartum haemorrhage. (**Akosua de Groot**), Radboud UMC, Nijmegen, the Netherlands, 1995
- Perinatal assessment in rural Tanzania. (**Gijs Walraven**), Radboud UMC, Nijmegen, the Netherlands, 1995
- Confidential enquiries into Maternal Deaths in the Netherlands, 1983- 1992. (**Nico Schuitemaker**), UMC Leiden, the Netherlands, 1998
- Confidential enquiries into Maternal Deaths in Surinam. (**Ashok Mungra**), UMC Leiden, the Netherlands, 1999
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- Maternal mortality in Suriname: Implementation of Maternal Death Surveillance and Response to reduce preventable maternal deaths (**Lachmi Kodan**), UMC Utrecht, the Netherlands, 2020

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Most maternal deaths and stillbirths are preventable with quality health care during pregnancy and childbirth. Improving maternal health care is therefore a key priority and a human right. This book presents evidence-based research in Suriname on the incidence, causes, ethnic disparities and other risk factors of maternal deaths, maternal near-miss and stillbirths. Recommendations were carried out by the research team by implementing different interventions on a national scale (i.e. establish a perinatal data registry, install a maternal death review committee and develop obstetric guidelines). Other recommendations are geared towards the WHO and include to address the challenges of the classification tools (ICD-MM, MNM, ICD-PM) and expand indicators to assess the quality of obstetric care.