Maternal morbidity and mortality in the Netherlands and their association with obstetric interventions

Kallianidis, A.F.

PART 3

Discussion and summary

General discussion

MAIN RESULTS

In this thesis, I present the latest trends in maternal mortality in the Netherlands, the association of caesarean section with maternal morbidity and mortality and an analysis of postpartum laparotomy and peripartum hysterectomy as a specific indicator of severe morbidity at national, continental and global levels.

With the results from thirteen years of confidential enquiry into maternal deaths in the Netherlands, performed by the Dutch Audit Committee on Maternal Morbidity and Mortality (*Auditcommissie Maternale Sterfte en Morbiditeit, AMSM*), this thesis gives an update on the maternal mortality ratio (MMR), causes of death and lessons learned from maternal death audit. In 2006-2018, the MMR in the Netherlands dropped to half that of 1993-2005, and we have now entered a 'new era' for the further reduction of maternal mortality in the Netherlands, where for the first time pre-eclampsia is not the leading cause of death anymore, having been overtaken by cardiac disease. The inner circle of mortality has become smaller than ever before, however the outer circles of morbidity remain substantial in size and importance. (Figure 1)

Caesarean section rates are rising worldwide.[1] Given its surgical character, complications are inherent, leading to the procedure contributing to or even initiating the chain of events leading to morbidity or death in some women. When complications of childbirth arise, ultimately surgical intervention may be necessary to prevent further deterioration and avoid mortality. Therefore, though caesarean section, if performed for a clear evidence-based indication and under safe circumstances can save lives of women and neonates, possible maternal complications -however rare- should not be neglected or underestimated. Continuing along the line of surgical interventions during childbirth, we demonstrate that laparotomy postpartum is performed more frequently among women who underwent caesarean section compared to vaginal birth, with postpartum hysterectomy being performed as the main intervention during such surgery.

Thanks to the International Network of Obstetric Survey Systems (INOSS) the prevalence, indications and outcomes of peripartum hysterectomy could be compared between nine European countries on a nation-wide scale. In this multi-country study, it becomes clear that countries with higher rates of caesarean section and rates of women with previous caesarean section, have higher national prevalence figures of peripartum hysterectomy. Additionally, management of severe postpartum haemorrhage, in terms of surgical interventions and transfusion rates, differs greatly, with some countries performing hysterectomy relatively early in the course of morbid events, while others attempt multiple alternative uterus-sparing options before eventually removing the uterus. This might, to some extent, be explanatory for the observed differences in prevalence. Finally, peripartum hysterectomy is associated with substantial rates of maternal morbidity, not

only in high-income countries, but also in low- and middle-income countries as demonstrated in our worldwide meta-analysis.

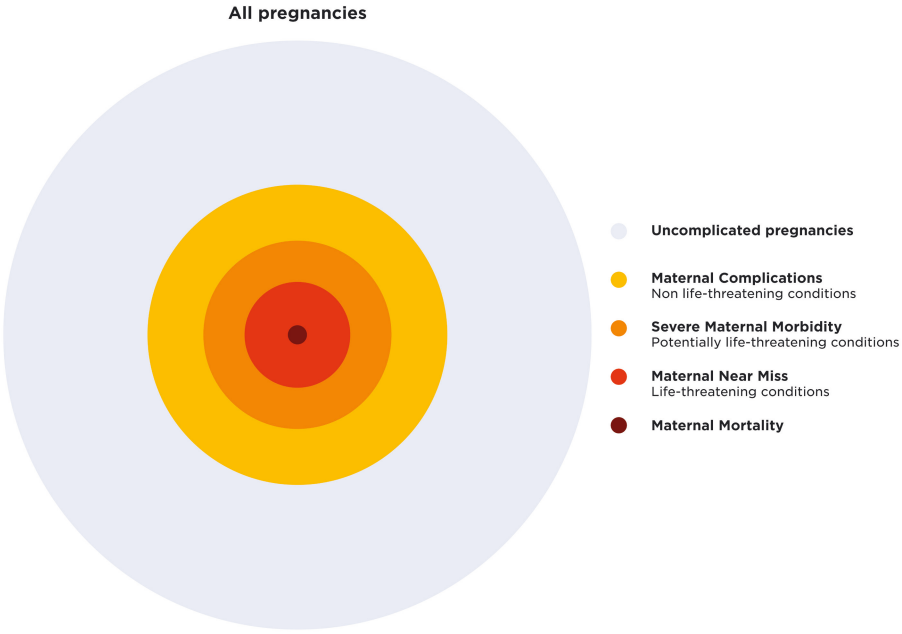

Figure 1. The circle of disease. From uncomplicated pregnancy to maternal mortality. Adapted from the Pyramid of Disease.

MATERNAL MORTALITY– A STEEP DECLINE

With global trends of maternal mortality dropping, the Netherlands now also follows this trend with the MMR dropping to 6.2 per 100,000 livebirths, the lowest ever described in our country.[2] This means that a decreasing trend has been achieved after the previous increase of the MMR in the Netherlands, when the MMR rose from 9.7 in 1982–1992 to 12.1 per 100,000 livebirths in 1993–2005.[3] This finding is comparable to the trend of other high-income countries, where mortality rates seemed to stabilise or even rise in the nineties, followed by a steeper decline afterwards.[4] The decrease of maternal mortality however, is under pressure and close monitoring remains crucial, also in high-income countries. In the US, a high-income county with generally high standards of care, a considerable increase in maternal mortality was observed, between 2000 – 2014 with an increase of by 26.6%, from 18.8 to 23.8 .[5] Contributors to this increase are sociodemographic risk factors, such as advanced maternal age or pre-existing non-communicable conditions such as diabetes, obesity and hypertension. There is also considerable inequity, with

women of black (non-Hispanic) ethnicity having a much higher chance to die. This increasing trend in MMR is not only a matter of concern in the US. From a global perspective, the recent COVID-19 pandemic did not only have a major impact on the well-being of the general population, but notably also on maternal health. While the first publications suggested no increased risk of adverse maternal outcomes among pregnant women, a recent systematic review and meta-analysis showed that there is an increased risk on ICU admission especially for women with pre-existing morbidity, advanced maternal age and obesity.[6,7] This was also confirmed in a Dutch cohort of pregnant women with COVID-19, revealing that infected pregnant women were at increased risk of hospital admission, ICU admission and birth by caesarean section.[8] Also, on a bigger scale, concerning the total pregnant population, concerns have been raised about the indirect impact on maternal and child health services, such as the effect that lockdowns had on e.g. accessibility of healthcare disruption of health systems and decreased access to food. Prediction models foresee a relative increase of 8.3 – 38.6% in maternal deaths per month in low- and middle-income countries.[7] More recent publications, from the first year after the pandemic, from Brazil and Mexico, confirmed these concerns, showing substantial increase in the national maternal mortality rates.[9,10]

Our findings are also in line with data from the EuroPeristat report in 2015, where the MMR was shown to be below 10 per 100,000 livebirths in most European countries.[11] Comparisons, however, should take place with caution since the vast majority of countries provide data from routine statistics and only very few are able to provide data from *enhanced systems* (i.e. record linkage usually combined with confidential enquiry). Maternal mortality reporting with information from only routine statistics leads to considerable underestimation.[12, 13] As such, it may seem like the Netherlands or the UK have high MMRs compared to countries like Belgium, Germany, Greece and Spain which report exceptionally low MMRs (2.9 – 4.6). These differences may well be explained by differences in reporting and incomplete case ascertainment. Our findings underline once more that comparisons are only fair when these take into account the different strategies used to identify maternal deaths.

Best possible comparisons of the Dutch numbers are with Italy, France and the UK, countries within the same European region, of comparable high-income status, and with maternal morality committees conducting confidential enquiries into maternal deaths. Both Italy (2007-2013) and France (2010 – 2012) reported higher rates of maternal deaths, the MMR being 9.2 and 10.3 per 100,000 livebirths respectively with haemorrhage being the leading cause of death in both countries.[13,14] In the MMBRACE report from the UK for 2015-2017, the national MMR was 9.2, with indirect causes of death exceeding direct ones, and leading cause of death being cardiac disease.[15] As such, in the Netherlands, the distribution of direct and indirect is comparable to that of Italy and France, with the leading cause of death, cardiac disease, the same as that of the UK.

Neurologic causes are now the third most common along with suicides when including late deaths. This implies that maternal mortality ceases to be a purely 'obstetric' problem. In the general population, there is an increased number of women with pre-existing health conditions who, thanks to improved medical care before conception reach fertile age and are now able to conceive and have 'high-risk' pregnancies. The physiological changes in pregnancy can aggravate pre-existing diseases (such as cardiological and neurological diseases) and make these women vulnerable for complications and adverse outcomes. Effort should be made to achieve early identification and counselling of these women. Pre-conception counselling and family planning must be a conjoined effort from general practitioners, other treating physicians and obstetricians. Women may not discuss family planning during routine follow up of chronic diseases, awareness should be created amongst all specialists (such as cardiologists, neurologists, internal medicine specialists, oncologists and psychiatrists) to bring up the topic. It should be routine practice to advise women proactively on these matters during their reproductive years. Pre-conception counselling is becoming a growing matter of interest, with non-obstetric specialists calling for timely counselling for women with cardiac disease, rheumatic disease and organ transplantation like kidney and pancreas.[16-18] Additional insight into the causes of maternal mortality, and how pre-existing morbidities are influenced by pregnancy and vice versa, will hopefully lead to concrete advice for daily practice and improve future maternal outcome.

PURSUIT OF COMPLETENESS

For epidemiological studies of infrequent events, accuracy of prevalence relies on the quality of identification and collection processes. In the pursuit of completeness, complete case ascertainment will lead to more robust conclusions and validity. In the Netherlands, annual reports on causes of death are published by Statistics Netherlands relying on vital statistics, with information extracted from death certificates. Causes of death are coded according to ICD codes, and those related to maternal and pregnancy related death (ICD10 O00 – O99) represent the estimated number of maternal mortality.[19] Parallel monitoring of maternal deaths is performed by the AMSM which is based on reporting of maternal deaths by clinicians. And while we find it hard to imagine that obstetricians in the Netherlands will omit to report the death of a woman under obstetric care, it is questionable whether the same applies for specialists outside the obstetric field. During early pregnancy or late postpartum, when no obstetric caregiver is involved, a death might not be attributed or related to pregnancy and thus not reported as such in the death report forms or to the AMSM.

These omissions may be compounded by the fact that maternal mortality has become such an infrequent event, not only for obstetricians but even more for other

specialists and general practitioners. In the previous maternal death reports in the Netherlands, cross-checking with Statistics Netherlands resulted in identification of additional cases, not reported to the AMSM, underreporting being 11%.[3] And while information about these deaths was limited to age and cause of death, rendering external auditing impossible, addition of these cases makes the actual number of maternal deaths more accurate, enabling more robust MMR calculations and comparisons with other countries.

Even while the MMR is decreasing, caution should be taken first of all to remain vigilant and improve case ascertainment while keeping high quality of data available for enquiry. In other countries, for example Italy and France, case identification is performed after cross linkage of hospital discharge or birth and death registries.[13, 20] Linkage of electronic databases provides a way to identify underreporting, which is likely when relying only on reporting by clinicians without double-checking, such as is currently the situation in the Netherlands. However, despite this limitation, the Dutch system, with anonymous medical records being fully available rendering confidential enquiry a possibility in almost all reported deaths, still enables a unique insight into the care received during the chain of events leading to death. As such, there seems to be a complementary balance between complete exhaustivity on the one hand, where the actual number of maternal deaths is identified but information is sometimes incomplete and does not allow for full enquiry, and the quality of data on the other hand, accepting some degree of underreporting. The numbers themselves do not suffice in understanding the true reasons that led to the deaths of these women. It is the stories behind them that eventually, when understood in-depth, lead to lessons learned and improvements in care and avoid future maternal deaths by informing changes in clinical practice.

OVERCOMING CLASSIFICATION DIFFERENCES

Traditionally, causes of death are classified into direct, indirect and non-pregnancy related.[21] The difference between direct and indirect may seem intuitive at first sight, but differences between countries suggest otherwise. By definition, indirect deaths are those from pre-existing disease aggravated during or due to pregnancy. However, pre-exiting diseases might not be diagnosed beforehand or be present in a subclinical stage. Clear example are psychiatric disorders, with pre-existing disease often remaining undiagnosed if women never sought psychiatric evaluation before pregnancy. This resulted in different categorisation of suicide-related deaths between countries. Maternal suicides were previously categorised as indirect deaths. Later, in order to conform to the definition of indirect deaths (aggravation of pre-existing disease) these were categorised as direct or indirect depending on the presence of pre-existing psychiatric conditions.[22] However, after the recommendation of the new ICD-MM, these are now categorised as direct

maternal deaths. Comparable difficulties are faced when deaths due to malignant conditions are categorised. During pregnancy, diagnostics and treatment are sometimes -often unjustified- adjusted to protect the foetus, leading to potential delays in diagnosis and therapy. Also, growth and malignant potential might be influenced by the hormonal status of pregnancy.

These dilemmas arise also in the attribution of the cause of death. This was previously demonstrated by comparison of differences in designating the cause of deaths between the UK and the Netherlands.[23, 24] In the Netherlands, cause of death is attributed to the initial event initiating morbidity, while in the UK it is attributed to the most important morbid event.

All of the above lead to differences in categorisation of deaths between countries, not only with regard to direct and indirect but also in terms of the designated cause of death. This hampers comparisons between countries and settings. In light of declining numbers of maternal mortality it is time to shift the focus from the division into arbitrary categories, and work towards uniformity. The goal of maternal morbidity research ultimately is to reduce preventable deaths. We therefore agree with the previously suggested concept of addressing and comparing all pregnancy-related maternal deaths, using cause of death as the main category identifier. For this to succeed, uniformity of attribution of causes of death should be reached. In the absence of guidelines from the WHO, we propose an international comparison of classification strategies, between countries with an enhanced maternal mortality system and use of confidential enquiry, within a collaborative platform such as INOSS.

The latest trend in the Netherlands shows a reduction by fifty percent of the MMR. Efforts of past studies on morbidity and mortality seem to have contributed to shrinking the inner circle of morbidity: mortality.(Figure 1) In the conceptual framework of maternal morbidity, the proportions of these two inner most circles (severe morbidity and mortality) are correlated with each other. The progress from non-life-threatening complications to, eventually, maternal death is a continuum of the same pathophysiological morbidity pathway. The size of the circles is influenced directly by external factors such as demographic changes (older women, increase in migration), rising prevalence of risk factors (e.g. obesity), and changes in obstetric practice (such as increasing caesarean section rates). The results of the LEMMoN study, demonstrated substantial rates of severe maternal morbidity and a concordant increase in mortality in the nineties and early 2000 was also documented by Schutte et al. .[3, 25] It was time to curb the increase. It is likely that these results created increased awareness for maternal conditions among obstetricians and patients. The NethOSS study on eclampsia revealed, for the first time, that the circle of life-threatening conditions had shrunk, with a decrease in eclampsia rates. With our results now also demonstrating a decrease in mortality, the lowest ever reported during 30 years of maternal morbidity and mortality registration. However, the progress should not always be taken for granted. Particularly in this time of

COVID-19, past gains are not to be taken for granted. Such unanticipated factors, can have serious rebound effects, and contribute to increases in maternal morbidity and mortality. Therefore, ongoing monitoring of the outcomes of maternity care is necessary. Only by timely recognition of increasing morbidity rates can new interventions lead to stable or smaller inner circles.

CAESAREAN SECTION – SHIFTING THE FOCUS FROM RATES TO OUTCOME

Caesarean section can be a lifesaving procedure when performed on strict medical indications such as correctly identified foetal distress, confirmed failure to progress or placenta praevia amongst others. It is the second most common performed surgery in the EU-27, performed more than 1.16 million times in 2018 and comprises almost 1/3 of all surgeries in very low-expenditure WHO member states.[26, 27] However, this procedure is also associated with short- and long-term complications and, given its frequency, these complications deserve being scrutinized. The global caesarean section rate has risen, from 12.1% in 2000 to 21.1% in 2015.[1] This, contrary to previous advice by the WHO that rates above 9-16% do not lead to improved maternal or neonatal outcome.[28] Increase in caesarean section rates will concurrently lead to increases in complications rates. While in the poorest countries, at the population level, underuse and poor accessibility have to be overcome for maternal outcomes to further improve, at facility level in low-income and across the board in middle- and high-income settings increasing attention is rightly attributed to curb the unjustified increase of caesarean section rates. Proposed strategies aim to introduce clinical interventions such as external cephalic version (and in some settings re-introducing vaginal breech birth), promoting trial of labour after caesarean and midwife-led care, as well as approaches to educate women on unfunded beliefs with regard to mode of birth and promoting the dialogue between obstetricians, midwives and women on fear of childbirth.[29] In order to come to a change in actual clinical practice, clinicians and women and their communities must be made aware of the impact of surgery on maternal and neonatal outcome.

The most serious complication of caesarean section is maternal death, although this is infrequent in high-income settings. With absolute numbers of maternal mortality in high-income settings being low, the association with or contribution of caesarean section to mortality is difficult to estimate. Estimations are hampered by small numbers, differences in categorisation of elective and emergency caesarean, confounders like pre-existing morbidity or the indications that lead to caesarean section which can, in turn, be the cause of death. The results of our study demonstrate a threefold higher risk of death after caesarean section compared to vaginal birth, in line with previous literature from the US, Brazil, France.[30-32] With use

of detailed information from medical charts, we were able to distinguish cases in which the surgery was not related to the death, was the direct cause of death or was associated with the death somewhere in the chain of morbid events. By subtracting the first group from our analyses, we are able to calculate the contribution of caesarean section to maternal mortality. While previous studies aimed for a comparison of women with an uncomplicated medical history, undergoing either vaginal birth or caesarean section in a case-control study design, we were interested in maternal outcome of all women undergoing caesarean section from a nationwide perspective. In two other studies from Ireland and Turkey, a decreasing or stable MMR was observed during a period of increasing caesarean section rates.[33, 34] The Irish study was based on one single hospital and two maternal deaths, making it too thin to generalise conclusions to the country or other facilities. The nationwide study from Turkey demonstrated that in an 11-year period with CS-rates rising above 50%, maternal mortality decreased simultaneously. However, better maternal outcomes were likely attributable to improved health care facilities rather than to the increased caesarean section rate. Our study goes beyond calculating the association of caesarean section with rates of mortality, but gives an estimation of the contribution of surgery to maternal mortality.

As caesarean section influences the size of the inner circle, mortality, it also influences the outer circles of maternal life-threatening events. In a previous nationwide study in the Netherlands, caesarean section (planned or emergency) was associated with five times higher risk of Severe Acute Maternal Morbidity (SAMM) and this was also the case for women with a previous caesarean section.[25] Caesarean section in a previous pregnancy increased the risk of SAMM threefold. (35) In the 2007 NICE guideline on caesarean section, reference is made to the potential complications of caesarean section. Referring to nine prospective studies that compared planned vaginal birth to planned caesarean section with the risk of postpartum hysterectomy, caesarean section was found to be six to ten times higher compared to vaginal birth. The studies included healthy women, with no previous caesarean section and uncomplicated pregnancies, and did not include women from low-income settings. Level of evidence of these studies was assessed to be low.

These results are supported by the three studies on laparotomy and hysterectomy in this thesis. Incidence of laparotomy postpartum after caesarean section is fifteen times higher compared to vaginal birth and even twenty-fold after emergency caesarean. This risk increase does not cease to exist at the end of the puerperium, which was demonstrated for long-term complications in a Danish population-based study where risk of re-laparotomy after hysterectomy was shown to be increased later in life among women with a history of caesarean section compared to women who only had vaginal birth(s).[36] Additionally, we demonstrate that hysterectomy is more prevalent in countries with higher caesarean section rates, and national rates of women with previous caesarean section. This is in line with

the fact that haemorrhage is one of the major short-term complications during and after caesarean section as well, the risk of abnormally invasive placentation being linearly associated with the number of previous caesarean sections, posing women at higher risk of bleeding complications and hysterectomy.

Although these complications may seem infrequent, it is only a matter of time before clinicians or women are confronted with them. In order to further unravel the extent to which caesarean sections contribute to maternal mortality, more robust studies can be performed by combining data from multiple countries, which should preferably have nationwide coverage. The INOSS has to date provided new insights into gaps of knowledge and has turned out to be a valuable platform to proceed with such research. This platform will help collect robust number of deaths for analysis and also, when studies are performed prospectively and in collaboration, may help eliminate problems arising from retrospectively pooled data, such as different study periods or categorisations.

For the Netherlands, where the latest rate of caesarean sections (17% in 2020 [37]) are generally relatively low compared to most other European countries, our results can contribute to: 1) improved counselling of women on mode of birth, 2) enhanced motivation to curb the increase in caesarean rates, 3) supporting future monitoring of maternal morbidity and its association with caesarean section.

PERIPARTUM HYSTERECTOMY, A SUFFICIENT INDICATOR FOR MAJOR OBSTETRIC HAEMORRHAGE?

Major obstetric haemorrhage is the leading cause of maternal mortality worldwide, accounting for almost one out of three deaths globally.[38] In high-income countries, haemorrhage has been pushed back to third place accounting for 16.3% of all deaths, as was shown in a systematic analysis by the WHO. At the same time, in some high-income countries, like Italy and France, haemorrhage has remained the commonest cause of death.[13, 14] The incidence of postpartum haemorrhage has been shown to increase in many high-income countries, including the Netherlands where it rose from 4.1% in 2000 to 6.4% in 2013.[39] As such, although haemorrhage-related mortality rates are dropping in high-incomes settings, the incidence of postpartum haemorrhage appears to be increasing paradoxically. The burden of disease thus lies in bigger outer circles of morbidity (Figure 1) which, due to earlier recognition and improved management may be prevented from progressing to the inner circle of mortality. In the Netherlands, this rise was also observed in the increase of "mild" postpartum haemorrhage (1000 – 1500ml), and the concomitant decrease in transfusion rates.[40]

During the first stages of bleeding, administration of colloids or crystalloid fluids, uterotonics and also the recent insight of adding tranexamic acid, is somewhat consistently reflected in international haemorrhage protocols. However,

the management of persistent bleeding is still a matter of ongoing debate. A population-based study, between six INOSS members (France, UK, Italy, Australia, the Netherlands and Denmark), on women with massive transfusion post-partum (eight or more units of red blood cells), identified great variation in the incidence of massive transfusion, as well as large differences in transfusion management and obstetric management.[41] Striking was that 74% of women in Italy underwent hysterectomy, compared to approximately half of all women in the UK, France and Australia, versus just under 30% in the Netherlands and Denmark. The same trends are demonstrated in our studies, where prevalence of women who underwent hysterectomy varied considerably between nine countries participating in the INOSS, and also the same variation in surgical and obstetric management was observed. Both studies, with a different manner of identifying women with severe postpartum haemorrhage (massive transfusion vs. hysterectomy) arrive at the same conclusions and demonstrate similar differences in management, strengthening the validity of the conclusions. Studies comparing different interventions have, until now, not provided conclusive evidence on the optimal management sequence, leaving a large gap of knowledge.[42] Additional research is therefore necessary to unravel and compare the effectiveness of surgical management of postpartum haemorrhage such as arterial embolisation and intrauterine balloon tamponade.

Severe obstetric haemorrhage is an important indicator of severe maternal morbidity. Unlike maternal mortality, which is a binary outcome, tools to measure maternal mortality have always been prone to discussions on matters of definition. The near-miss approach as defined by the WHO is based on organ-dysfunction criteria. As such, the approach enables identification of women with complications of severe postpartum haemorrhage when bleeding leads to organ disfunction such as shock, oliguria, failure to form clots or massive transfusion (≥5 units).[43] Peripartum hysterectomy performed for indication of infection or haemorrhage is one of the suggested clinical criteria. By identifying women with 'near miss', comparison of quality of health systems and facilities may perhaps be improved. The approach may also enable comparisons of prevalence and maternal outcomes of women with postpartum haemorrhage. Laparotomy postpartum with or without hysterectomy, transfusion with blood products or interventional radiology may all serve as indicators of severe postpartum haemorrhage. Prevalence of peripartum hysterectomy in low- and middle-income settings was found to be higher than in high-income countries, reflecting the different timing at which the procedure is performed, namely earlier in the course of bleeding in absence of conservative alternatives. In high-income countries, uterus-sparing interventions such as blood products, intrauterine balloon tamponade, interventional radiology are increasingly available.

As such, in the train of events during massive haemorrhage, not all women will reach the clinical and laboratory criteria to be identified as a "near-miss", which should not be taken to imply that these women did not have a severe clinical course

after childbirth or potentially-life threatening events. For example, women who underwent timely laparotomy for bleeding complications without hysterectomy, or averted hysterectomy by radiological interventions should be regarded as having sustained severe maternal morbidity. This suggests that the WHO tool may be more valuable for maternal morbidity identification in low- and middle-income settings.[44] Multiple other sets of indicators have been proposed, including recently by the American College of Obstetrics and Gynaecology and the EuroPeristat group, for maternal morbidity indicators in high-income settings. [45, 46] The abundance of sets of indicators however make comparability across settings even more difficult. As proposed by prof Marian Knight from the University of Oxford, the next step could be a core indicator set, with core criteria applicable for all income settings with the ability to personalise for individual regions and countries.[47] An outcome set for conditions of severe maternal morbidity had already been proposed though a Delphi process by the INOSS.[48]

Hysterectomy itself is an outcome of interest, but will not suffice as the optimal evaluation of all critical haemorrhage cases. In order to address all women with severe postpartum haemorrhage, we propose including all advanced clinical interventions used such as laparotomy for bleeding complications (with or without performing hysterectomy), radiological intervention or receiving ≥4 units of red cells. These data are relatively easy to collect retrospectively from clinical registries as well as prospectively in a manner comparable to what is already used by many of the INOSS countries. Such a definition does not vary greatly form the core outcome set proposed by the INOSS, except for the addition of radiological interventions, which are increasingly used in many European counties.[48]

RECOMMENDATIONS

1. Raise awareness for reporting maternal deaths among all medical specialists and general practitioners, by involving them into the study of maternal mortality, presenting them outcomes and performing specific enquiries into cardiological, neurological or psychiatric related causes of mortality.
2. The Netherlands appears to be lagging behind in identification of late maternal deaths. Cross-checking with information from Statistics Netherlands should be re-introduced in order to minimise underreporting. Ideally, this is followed by access to medical records from the hospitals of midwifery practices enabling confidential enquiry.
3. Address all important underlying pregnancy-related causes of death and important non-pregnancy related conditions, with clear identification of lessons learned rather than focusing on arbitrary categorisation into direct and indirect.
4. Overcome differences in attribution of cause of death, by collaboration of different maternal mortality committees or through international obstetric collaborations such as the INOSS.
5. Broaden indicators for severe obstetric haemorrhage by incorporating additional clinical interventions other than peripartum hysterectomy only, such as mass transfusion, laparotomy and interventional radiology.
6. Harmonise definitions and outcome sets of obstetric haemorrhage within the INOSS collaboration. Thereby, future studies could create additional insight into the optimal management of major obstetric haemorrhage.
7. Data on obstetric haemorrhage and hysterectomy in the Netherlands are now outdated by almost a decade or longer. New prospective NethOSS studies on major obstetric haemorrhage including pregnancy-related hysterectomy should be set up in combination with the INOSS.

REFERENCES

1. Boerma T, Ronsmans C, Melesse DY, Barros AJD, Barros FC, Juan L, et al. Global epidemiology of use of and disparities in caesarean sections. Lancet. 2018;392(10155):1341-8.
2. Souza JP, Tunçalp Ö, Vogel JP, Bohren M, Widmer M, Oladapo OT, et al. Obstetric transition: the pathway towards ending preventable maternal deaths. Bjog. 2014;121 Suppl 1:1-4.
3. Schutte JM, Steegers EA, Schuitemaker NW, Santema JG, de Boer K, Pel M, et al. Rise in maternal mortality in the Netherlands. BJOG. 2010;117(4):399-406.
4. Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS, Shackelford KA, Steiner C, Heuton KR, et al. Global, regional, and national levels and causes of maternal mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9947):980-1004.
5. MacDorman MF, Declercq E, Cabral H, Morton C. Recent Increases in the U.S. Maternal Mortality Rate: Disentangling Trends From Measurement Issues. Obstet Gynecol. 2016;128(3):447-55.
6. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. Bmj. 2020;370:m3320.
7. Roberton T, Carter ED, Chou VB, Stegmuller AR, Jackson BD, Tam Y, et al. Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study. Lancet Glob Health. 2020;8(7):e901-e8.
8. Overtoom E RA, Zwart J, Vovelvang T, Schaap T, van den Akker T, Bloemenkamp K. SARS-CoV-2 infection in pregnancy during the first wave of COVID-19 in the Netherlands: a prospective nationwide population-based cohort study. BJOG Submitted October 2020. 2020.
9. Gurzenda S, Castro MC. COVID-19 poses alarming pregnancy and postpartum mortality risk in Brazil. EClinicalMedicine. 2021;36:100917.
10. Mendez-Dominguez N, Santos-Zaldivar K, Gomez-Carro S, Datta-Banik S, Carrillo G. Maternal mortality during the COVID-19 pandemic in Mexico: a preliminary analysis during the first year. BMC Public Health. 2021;21(1):1297
11. Europeristat. THE EUROPEAN PERINATAL HEALTH REPORT 2015 https://www.europeristat.com/index.php/reports/european-perinatal-health-report-2015.html2018 [
12. Saucedo M, Bouvier-Colle MH, Chantry AA, Lamarche-Vadel A, Rey G, Deneux-Tharaux C. Pitfalls of national routine death statistics for maternal mortality study. Paediatr Perinat Epidemiol. 2014;28(6):479-88.
13. Donati S, Maraschini A, Lega I, D'Aloja P, Buoncristiano M, Manno V. Maternal mortality in Italy: Results and perspectives of record-linkage analysis. Acta Obstet Gynecol Scand. 2018;97(11):1317-24.
14. Deneux-Tharaux C, Saucedo M. [Epidemiology of maternal mortality in France, 2010-2012]. Gynecol Obstet Fertil Senol. 2017;45(12S):S8-S21.
15. Maternal NaICORP. Saving Lives, Improving Mothers' Care Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2015-17. 2019.
16. Caretto A, Caldara R, Castiglioni MT, Scavini M, Secchi A. Pregnancy after pancreas-kidney transplantation. J Nephrol. 2020;33(5):1009-18.

17. Tromop-van Dalen C, Fairley SL, Aitken A, Grace Li WY. Contraception and Pre-Conception Counselling in Cardiac Patients: We Can Do Better. Experience From a Tertiary Centre in New Zealand. Heart Lung Circ. 2020.
18. Tsuda S, Sameshima A, Sekine M, Kawaguchi H, Fujita D, Makino S, et al. Pre-conception status, obstetric outcome and use of medications during pregnancy of systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and inflammatory bowel disease (IBD) in Japan: Multi-center retrospective descriptive study. Mod Rheumatol. 2020;30(5):852-61.
19. Netherlands S. Statline, Doodsoorzakenstatistiek.
20. Saucedo M, Deneux-Tharaux C, Bouvier-Colle MH, French National Experts Committee on Maternal M. Ten years of confidential inquiries into maternal deaths in France, 1998-2007. Obstet Gynecol. 2013;122(4):752-60.
21. WHO. ICD-10 to deaths during pregnancy, childbirth and the puerperium: ICD-MM.
22. Lommerse K, Knight M, Nair M, Deneux-Tharaux C, van den Akker T. The impact of reclassifying suicides in pregnancy and in the postnatal period on maternal mortality ratios. Bjog. 2019;126(9):1088-92.
23. van den Akker T, Bloemenkamp KWM, van Roosmalen J, Knight M. Classification of maternal deaths: where does the chain of events start? Lancet. 2017;390(10098):922-3.
24. van den Akker T, Nair M, Goedhart M, Schutte J, Schaap T, Knight M. Maternal mortality: direct or indirect has become irrelevant. Lancet Glob Health. 2017;5(12):e1181-e2.
25. Zwart JJ, Richters JM, Ory F, de Vries JI, Bloemenkamp KW, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide population-based study of 371,000 pregnancies. Bjog. 2008;115(7):842-50.
26. Weiser TG, Haynes AB, Molina G, Lipsitz SR, Esquivel MM, Uribe-Leitz T, et al. Size and distribution of the global volume of surgery in 2012. Bull World Health Organ. 2016;94(3):201-9f.
27. Eurostat. Surgical operations and procedures statistics 2020 [Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php/Surgical_operations_and_procedures_statistics#Number_of_surgical_operations_and_procedures.
28. Betran AP, Torloni MR, Zhang J, Ye J, Mikolajczyk R, Deneux-Tharaux C, et al. What is the optimal rate of caesarean section at population level? A systematic review of ecologic studies. Reprod Health. 2015;12:57.
29. Betrán AP, Temmerman M, Kingdon C, Mohiddin A, Opiyo N, Torloni MR, et al. Interventions to reduce unnecessary caesarean sections in healthy women and babies. Lancet. 2018;392(10155):1358-68.
30. Balayla J, Lasry A, Badeghiesh A, Volodarsky-Perel A, Gil Y. Mode of delivery is an independent risk factor for maternal mortality: a case-control study. J Matern Fetal Neonatal Med. 2020:1-7.
31. Deneux-Tharaux C, Carmona E, Bouvier-Colle MH, Breart G. Postpartum maternal mortality and cesarean delivery. Obstet Gynecol. 2006;108(3 Pt 1):541-8.
32. Esteves-Pereira AP, Deneux-Tharaux C, Nakamura-Pereira M, Saucedo M, Bouvier-Colle MH, Leal Mdo C. Caesarean Delivery and Postpartum Maternal Mortality: A Population-Based Case Control Study in Brazil. PLoS One. 2016;11(4):e0153396.
33. O'Dwyer V, Hogan JL, Farah N, Kennelly MM, Fitzpatrick C, Turner MJ. Maternal mortality and the rising cesarean rate. Int J Gynaecol Obstet. 2012;116(2):162-4.
34. Uzuncakmak C, Ozcam H. Association between Maternal Mortality and Cesarean Section: Turkey Experience. PLoS One. 2016;11(11):e0166622.
35. van Dillen J, Zwart JJ, Schutte J, Bloemenkamp KW, van Roosmalen J. Severe acute maternal morbidity and mode of delivery in the Netherlands. Acta Obstet Gynecol Scand. 2010;89(11):1460-5.

36. Lindquist SAI, Shah N, Overgaard C, Torp-Pedersen C, Glavind K, Larsen T, et al. Association of Previous Cesarean Delivery With Surgical Complications After a Hysterectomy Later in Life. JAMA Surg. 2017;152(12):1148-55.
37. Perined. Stichting Perined, Utrecht, The Netherlands [Available from: https://www.perined.nl/.
38. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014;2(6):e323-33.
39. van Stralen G, von Schmidt Auf Altenstadt JF, Bloemenkamp KW, van Roosmalen J, Hukkelhoven CW. Increasing incidence of postpartum haemorrhage: the Dutch piece of the puzzle. Acta Obstet Gynecol Scand. 2016;95(10):1104-10.
40. Ramler P. Thesis: "Postpartum haemmorhage: from inside to action."; Leiden University. 2022
41. McCall SJ, Henriquez D, McKinnon H, van den Akker T, van der Bom J, Bonnet MP, et al. A total blood volume or more transfused during pregnancy or after childbirth: individual patient data from six international population-based observational studies. Manuscript submitted for publication. 2020.
42. Kellie FJ, Wandabwa JN, Mousa HA, Weeks AD. Mechanical and surgical interventions for treating primary postpartum haemorrhage. Cochrane Database Syst Rev. 2020;7:CD013663.
43. Say L, Souza JP, Pattinson RC, Mortality WHOwgoM, Morbidity c. Maternal near miss--towards a standard tool for monitoring quality of maternal health care. Best Pract Res Clin Obstet Gynaecol. 2009;23(3):287-96.
44. Witteveen T, Bezstarosti H, de Koning I, Nelissen E, Bloemenkamp KW, van Roosmalen J; Validating the WHO maternal near miss tool: comparing high- and low-resource settings. BMC Pregnancy and Childbirth 2017;17(1):194.
45. Chantry AA, Berrut S, Donati S, Gissler M, Goldacre R, Knight M, et al. Monitoring severe acute maternal morbidity across Europe: A feasibility study. Paediatr Perinat Epidemiol. 2020;34(4):416-26.
46. Himes KP, Bodnar LM. Validation of criteria to identify severe maternal morbidity. Paediatr Perinat Epidemiol. 2020;34(4):408-15.
47. Knight M. Defining severe maternal morbidity-When is it time to stop? Paediatr Perinat Epidemiol. 2020;34(4):384-5.
48. Schaap T, Bloemenkamp K, Deneux-Tharaux C, Knight M, Langhoff-Roos J, Sullivan E, et al. Defining definitions: a Delphi study to develop a core outcome set for conditions of severe maternal morbidity. BJOG. 2019;126(3):394-401.