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

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PART 1

Maternal mortality

Confidential enquiry into maternal deaths in the Netherlands, 2006-2018

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ABSTRACT

Introduction: To calculate the maternal mortality ratio (MMR) for 2006-2018 in the Netherlands and compare with 1993-2005. Describe women's characteristics, causes of death and improvable factors.

Methods: We performed a nationwide, cohort study of all maternal deaths between January 1st, 2006, and December, 31st, 2018 reported to the Audit Committee Maternal Mortality and Morbidity. Main outcome measures were the national MMR and causes of death.

Results: Overall MMR was 6.1 per 100,000 livebirths, a decrease from 12.1 in 1993-2005 (Risk Ratio (RR) 0.5). Women with non-Western ethnic background had an increased MMR compared to Dutch women (MMR 6.5 vs 5.0, RR 1.3). The MMR was increased among women with a background from Surinam/Dutch Antilles (MMR 14.7, RR 2.9). Half of all women had an uncomplicated medical history (79/161, 49.1%). Of 171 pregnancy-related deaths within one year postpartum, 102 (60%) had a direct and 69 (40%) an indirect cause of death. Leading causes within 42 days postpartum were cardiac disease (n=21, 14.9%), hypertensive disorders (n=20, 14.2%) and thrombosis (n=19, 13.5%). Up to one year postpartum, commonest cause of death was cardiac disease (n=32, 18.7%). Improvable care factors were identified in 76 (47.5%) of all deaths.

Conclusions: Maternal mortality halved in 2006-2018 compared to 1993-2005. Cardiac disease became the main cause. In almost half of all deaths improvable factors were identified and women with a background from Surinam/Dutch Antilles had a threefold increased risk of death compared to Dutch women without migration background.

INTRODUCTION

In 2017, 295,000 women worldwide died during pregnancy or postpartum, over 90% in low- and middle-income countries.[1] However, also in high-income countries, reporting and reviewing maternal deaths remains important: from every death, lessons can be drawn to improve obstetric care and prevent future deaths. The national maternal mortality ratio (MMR) is an important healthcare indicator. To further unravel reasons why women die, several countries have established systems of confidential enquiry into maternal deaths.[2, 3]

While the global rate of maternal mortality dropped by 43% between 1990 and 2015, in some high-income countries, like the United States, the MMR rose.[4, 5] In the Netherlands, the MMR increased from 9.7 in 1982-1992 to 12.1 per 100,000 livebirths in 1993-2005.[6-8] This was attributed to demographic changes, upcoming risk factors like obesity and chronic hypertension, and reduced underreporting.[6] In light of these trends, an updated national maternal mortality report was deemed necessary.

In 1993-2005, the commonest cause of death was (pre-)eclampsia, accountable for almost one in three deaths. In 2013, the Netherlands Obstetric Surveillance System (NethOSS) was introduced for nationwide registration of severe maternal morbidity (and later also mortality). Results showed a 70%-reduction in eclampsia rates comparing timeframes 2004-2006 and 2013-2016.[9] This was attributed to increased awareness of the hypertension-related risk, combined with improved management (earlier treatment with magnesium sulphate and antihypertensives, early term induction) and obstetric emergency training.[10, 11] It is not yet known whether this decline in eclampsia incidence is also reflected in the number of hypertension-related deaths.

Primary aim was to calculate the MMR for 2006-2018, and compare it to 1993-2005. Secondary aims were to describe women's and obstetric characteristics, causes of deaths and improvable factors.

METHODS

This was a nationwide cohort study of maternal deaths between January 1st, 2006 and December 31st, 2018.[12]

Maternal mortality is the death of a woman during pregnancy, childbirth, or within 42 days postpartum or after termination of pregnancy. Death after 42 days up to one year postpartum is defined as late maternal mortality.[13] In the Netherlands, maternal deaths until one year postpartum are reported to the Audit Committee Maternal Mortality and Morbidity (*Auditcommissie Maternale Sterfte en Morbiditeit, AMSM*) as stated in a national guideline by the Netherlands Society of Obstetrics and Gynecology.[14] The AMSM consists of eight consultant obstetrician-

gynecologists, one obstetric anesthesiologist and two registrars in obstetrics and gynecology, employed at academic and non-academic teaching hospitals.

Deaths are reported to the AMSM by medical specialists, midwives or general practitioners using a case report form, requesting basic pregnancy and birth data.[14] Starting from 2016, electronic reporting of deaths was also available through NethOSS. A monthly email is sent out to assigned clinicians in every hospital with a maternity ward requesting to report cases meeting inclusion criteria or declare 'nothing to report'.[9] Thereafter, the AMSM requests all medical records necessary for external audit.

To ensure completeness of reporting, a cross-check with Statistics Netherlands, the national authority collecting vital statistics, was performed annually until December, 31st, 2011. After 2011 Statistics Netherlands did not allow further cross-checking, since anonymity of data was considered to be potentially compromised due to small numbers. Statistics Netherlands relies on information from death certificates, including only cause of death and women's age.[15] Postpartum deaths identified from cross-checking were included as non-late deaths to avoid underestimation.

Main outcome was the MMR for 2006-2018, compared with that of 1993-2005. A sensitivity analysis was conducted for the absence of cross-checking after 2011, comparing the MMR with and without additional deaths from Statistics Netherlands. Maternal and obstetric characteristics are presented alongside those of the general pregnant population that were extracted from the Netherlands Perinatal Registry.[16] For parity, age groups and ethnic background groups an MMR was calculated, with the number of livebirths obtained from Statistics Netherlands.[17]

We analyzed underlying causes of death, as described by the confidential enquiry. A cause-specific MMR was calculated and compared with 1993-2005. Underlying cause is defined as the disease or condition that initiated the morbid chain of events.[1] Causes are classified as 'direct', 'indirect', or 'non-pregnancy-related' according to the WHO classification. [1] Non-pregnancy-related deaths, e.g. traffic accidents, non-pregnancy-related malignancies and violence, were excluded from further analyses. Late maternal deaths were excluded from calculations of the MMR, but included in other analyses. According to the tenth revision of the International Classification of Diseases to deaths during pregnancy, childbirth, and the puerperium (ICD-MM), with regard to the classification of suicide as a direct cause of death, all suicide deaths were re-classified into that category.[18] Deaths due to malignancy were categorised as non-pregnancy related unless disease course, treatment or diagnosis were affected or delayed by the pregnancy.

Causes of death were categorised according to the classification applied by 'Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries in the UK' (MBRRACE-UK), which is based on the ICD-MM, but has more extensive subclassifications. In the previous national maternal mortality report, a classification that differed from international standards had been applied.[6] To compare our

results with those from 1993-2005, whilst still seeking international uniformity, the previous time period was reclassified according to the MBRRACE-UK categories. (Supplementary material 1)

In all deaths available for enquiry, quality of care was assessed with regard to possible improvable factors. These refer to events that may have contributed to the death, but do not necessarily imply that it could have been avoided. Care received was compared with the standard of care, laid out in national guidelines or -in case these were absent- determined by best available evidence. To overcome possible information bias, considerable effort was put into collecting all information necessary for enquiry, from all levels of care, both information documented in the medical records and additional information collected over the phone through contacting involved care givers. Improvable factors could be patient-, primary obstetric care- (general practitioner or midwife) or hospital care-related (obstetricians and other medical specialists).[6] Additionally, lessons learned were proposed by the AMSM, translating improvable factors into generalised clinical recommendations, aiming to promote care improvements at all levels. Lessons were categorised in a manner similar to that of the national perinatal mortality audit, with regard to guidelines, communication and training of health professionals.[19]

We compared improvable factors for women with different ethnic backgrounds. Ethnic background was based on medical records, without further information available as to whether women were native or foreign-born. Categorization into Western and non-Western, was based on definitions of Statistics Netherlands. Western women were those originating from Europe (excluding Turkey), North-America, Oceania, Indonesia and Japan, and non-Western women those from Africa, Latin-America, Turkey and the remainder of Asia.[20] Dutch women were natives without a migration background. Dutch women and Western women were grouped together for comparison with non-Western women, due to the very small proportion of non-Dutch women with a Western ethnic background. This is in line with studies from the US, where the risk of maternal death was comparable for US-native white and foreign-born white women, but much lower than that of black women, born in the US or elsewhere.[21]

The MMR is defined as the number of maternal deaths during pregnancy or within 42 days postpartum per 100,000 livebirths.[1] Livebirths were collected from Statistics Netherlands.[17] Obesity was defined as a body mass index (BMI) of ≥30 kg/m^2 at booking, or when obesity was explicitly mentioned in medical records. Caesarean sections are classified into 'planned' in case vaginal birth was never intended, even if the woman presented in labor, and 'unplanned' when decision for caesarean section was made during labor. In the Netherlands, "low risk" women receive maternity care and give birth in midwife-led primary care, or are referred to hospital obstetrician-led care if assessed as being "high-risk" at booking or if complications arise according to national guidelines.[22]

Risk ratios (RR) were calculated to compare the MMR between groups. Statistical analyses were performed using IBM SPSS for Mac (SPSS Inc., Chicago, IL, USA).

Ethical approval

In the Netherlands, ethical approval is not required for confidential enquiry, which is considered an essential element to improve birth care. Data collected in the database are strictly de-identified and none of our published outcomes can be traced back to individual patients or health workers. Therefore, approval of the Ethics Committee was previously waived.

RESULTS

A total of 206 maternal deaths were reported to the AMSM during the thirteen-year period. After cross-checking with Statistics Netherlands for 2006-2011, 11 additional mortalities were identified. In 46 women, death was classified as non-pregnancy-related. They were excluded from further analysis (Supplementary material 2). In 30/171 (17.5%), death occurred after 42 days postpartum. In 94.5% of all deaths (205/217), medical records were available for enquiry. Statistics Netherlands documented 83 deaths in 2006-2018, compared to 206 reported to the AMSM, amounting to 60% underreporting in routine vital statistics.

The MMR for 2006-2018 was 6.1 per 100,000 livebirths (141/2,304,271), lower than 12.1 for 1993-2005 (RR 0.5). Excluding deaths identified after cross-checking with Statistics Netherlands did not substantially alter the reduction (MMR 5.7 vs 10.4 per 100,000 livebirths, RR 0.5). Considerable decreases were seen in both direct and indirect deaths (Table 1). When excluding numbers from Statistics Netherlands these decreases remained similar: 3.6 vs 7.2 per 100,000 livebirths for direct deaths (RR 0.5) and 2.1 vs 3.2 per 100,000 livebirths for indirect deaths (RR 0.7).

Of the 130 maternal deaths within 42 days postpartum (excluding numbers from Statistics Netherlands), 62 (47.7%) were in nulliparous women. Nulliparous women and women of higher parity had a higher risk of death compared to women with a second ongoing pregnancy, who had the lowest MMR: RR 1.5 and 2.2 respectively (Table 2). Mean age was 31.9 years (range 17 - 53). Compared to Dutch women, women with a non-Western ethnic background had an increased MMR (6.5 vs 5.0 per 100,000; RR 1.3). Compared to Dutch and Western women, women with a non-Western ethnic background more often had pre-existing medical conditions (23/41 vs 33/119, RR 2.0), obesity (13/41 vs 19/119, RR 2.0) and teenage pregnancies (4/41 vs 0/119, RR 25.7) (Supplementary material 3). Women with a background from Surinam and the Dutch Antilles (n=13) had a considerably increased MMR (14.7 per 100,000).

Table 1. Maternal mortality ratio and underlying causes of death in the Netherlands, 2006-2018 vs 1993-2005. Classified according to MBRRACE-UK classification.

	1993-2005			2006-2018			
	Livebirths: 2,557,208			Livebirths: 2,304,271			
	≤ 1 year (n)	**≤ 42 days (n)**	**MMR**	**≤ 1 year (n)**	**≤42 days (n)**	**MMR**	**RR**
All maternal deaths	333	309	12.1	171	141	6.1	0.5
Direct deaths	236	224	8.8	102	90	3.9	0.4
Indirect deaths	97	85	3.3	69	51	2.2	0.7
Underlying cause of death	**n (%) [a]**	**n (%)**	**MMR**	**n (%) [a]**	**n (%)**	**MMR**	**RR**
Cardiac disease	45 (13.5)	40 (12.9)	1.6	32 (18.7)	21 (14.9)	0.9	0.6
Hypertensive disorders of pregnancy	99 (29.7)	95 (30.7)	3.5	21 (12.3)	20 (14.2)	0.9	0.2
Thrombosis	44 (13.2)	42 (13.6)	1.6	19 (11.1)	19 (13.5)	0.8	0.5
Neurological - indirect	17 (5.1)	17 (5.5)	0.7	19 (11.1)	15 (10.6)	0.7	1.0
Unascertained - direct	22 (6.6)	21 (6.8)	0.9	14 (8.2)	14 (9.9)	0.6	0.7
Haemorrhage	25 (7.5)	25 (8.1)	1.0	13 (7.6)	13 (9.2)	0.6	0.6
Suicide	7 (2.1)	4 (1.3)	0.3	19 (11.1)	8 (5.7)	0.3	2.2
Amniotic fluid embolism	11 (3.3)	11 (3.6)	0.4	8 (4.7)	8 (5.7)	0.3	0.8
Sepsis – non obstetric	10 (3.0)	10 (3.2)	0.4	9 (5.3)	8 (5.7)	0.3	1.0
Pregnancy-related infection	20 (6.0)	19 (6.1)	0.7	6 (3.5)	6 (4.3)	0.3	0.4
Other indirect	15 (4.5)	13 (4.2)	0.5	6[b] (3.5)	5[b] (3.5)	0.2	0.4
Early pregnancy death	7 (2.1)	7 (2.3)	0.3	2 (1.2)	2 (1.4)	0.1	0.3
Indirect malignancy	3 (0.9)	1 (0.3)	0.0	3[c] (1.8)	2[c] (1.4)	0.1	2.2
Anaesthesia	2 (0.6)	2 (0.6)	0.1	0	0	0	
Other direct	6 (1.8)	2 (0.6)	0.3	0	0	0	

a Late deaths, up to 1 year postpartum, included
b Other indirect within 42 days: systemic lupus erythematosus (1), antiphospholipid syndrome (1), upper gastrointestinal bleeding (1), relapsing polychondritis (1), pheochromocytoma (1). After 42 days: aplastic anaemia (1)
c Indirect malignancy within 42 days: brain tumour (1), cervix carcinoma (1). After 42 days: melanoma (1)
RR= Risk Ratio, MMR= Maternal Mortality Ratio (≤42 days postpartum).

Table 2. Maternal mortality ratio for parity, age and ethnic background. Numbers from Statistics Netherlands excluded for age and ethnic background.

	N	Livebirths	MMR	RR
Parity				
0	62	1,052,002	5.9	1.5
1	34	844,224	4.0	Ref
2	23	293,585	7.8	1.9
3+	10	114,460	8.7	2.2
Missing	1			
Age [a] (years)				
15-19	3	19,562	15.3	3.9
20-24	13	190,412	6.8	1.8
25-29	25	642,711	3.9	Ref
30-34	50	886,680	5.6	1.4
35-39	36	469,620	7.7	
40-44	9	90,656	9.9	2.6
≥45	1	4,630	21.6	5.6
Missing	4			
Ethnic background				
Dutch native	83	1,644,594	5.0	Ref
Western [b]	9	231,180	3.9	0.8
Non-western [c]	38	588,888	6.5	1.3
Surinam/Dutch Antilles	13	88,581	14.7	2.9
African	11	156,741	7.0	1.4
Turkey	5	79,453	6.3	1.3
Morocco	4	99,750	4.0	0.8
Asian	3	133,116	2.3	0.6

a Numbers from Statistics Netherlands included
b Western: European (5), Indonesian (3), Japanese (1)
c Non-western: additionally Syrian (1), South American (1)
MMR= Maternal Mortality Ratio, RR = Risk Ratio

Of 160 women who died up to one year postpartum, 60 (37.5%) were booked as "high-risk" and received antenatal care in secondary or tertiary obstetrician-led care. Eighty-seven (54.4%) were initially booked at primary care, nine (5.6%) received no antenatal care at all. Sixty-five women (40.6%) were referred from primary care to secondary or tertiary care during pregnancy (n=52, 80%), childbirth (n=5, 7.7%) or postpartum (n=5, 7.7%). A total of 119 women (74.4%) died postpartum, of whom 13 had given birth at home (10.9%). Caesarean section was performed in 60 (50.4%) women: 40 were unplanned (66.7%) and 14 (2.3%) were perimortem caesarean sections during resuscitation. Autopsy was performed in 68 women (42.5%) (Table 3).

Table 3. Pregnancy, birth and obstetric care characteristics of all deaths up to one year postpartum.

	Maternal deaths n (%)	General population [a] (%)
Initial antenatal care	**N=160**	84.6
Primary maternity care	87 (54.4)	15.4
Obstetrician	60 (37.5)	
Not (yet) under obstetric care	9 (5.6)	
Unknown	4 (2.5)	
Referral by primary care giver	**N=65**	61.8
During pregnancy	52 (80.0)	35.9
During birth	5 (7.7)	2.2
Postpartum	5 (7.7)	
Unknown	3 (4.6)	
Time of death	**N=160**	
During pregnancy	38 (23.8)	
Postpartum	119 (74.4)	
Within 1 day	27 (22.7 [b])	
Between 1-7 days	28 (23.5 [b])	
Between 8-42 days	33 (27.7 [b])	
Late death (>42 days)	30 (25.2 [b])	
Unknown	1 (0.8 [b])	
1st trimester pathology [c]	3 (1.9)	
Place of death	**N=160**	
At home	37 (23.1)	
In hospital	119 (74.4)	
Start lethal event out of hospital	43 (36.1 [b])	
Unknown	4 (2.5)	
Twin pregnancy	3 (1.9)	1.6
Birth	**N=119**	15.9
At home	13 (10.9)	82.7
In hospital	97 (81.5)	
During transport	1 (0.8)	
Unknown	8 (6.7)	
Mode of birth	**N=119**	80.6
Vaginal	51 (42.9)	6.9
Instrumental	8 (6.7)	14.9
Caesarean section	60 (50.4)	
- Planned	6 (10.0 [b])	
- Unplanned	40 (66.7 [b])	
- Perimortem	14 (2.3 [b])	
Autopsy performed	**N=160**	
Yes	68 (42.5)	
Unknown	3 (1.9)	

Table 3. Continued.

	Maternal deaths n (%)	General population [a] (%)
Intrauterine foetal death	**N=160**	
< 24 weeks	27 (16.9)	
≥ 24 weeks	6 (3.8)	
Perinatal death [d]	24 (14.9)	0.4 [e]
Smoking	**N=160**	24.9
Yes	38 (23.8)	
Unknown	36 (22.5)	12.0
Obesity	37 (23.1)	

[a] *National reference values from Perinatal Registry the Netherlands (Perined), 2006-2018*
[b] *Percentages of their subheading*
[c] *Women who died shortly after miscarriage (2) or abortion (1)*
[d] *Perinatal death defined as stillbirth with birthweight ≥ 1000g or ≥28 weeks of gestation, or neonatal death in the first 7 days postpartum.*
[e] *Only numbers until 2016 available.*

Medical history was uncomplicated in 79/160 (49.4%) women before conception. Thirteen (8.1%) women had a previous thromboembolic event, 20 (12.5%) were known to have a cardiovascular condition and 12 (7.5%) a mental health condition (Supplementary material 4).

Following confidential enquiry of all 171 deaths within one year postpartum, 102 (59.6%) were categorised as direct and 69 (40.4%) as indirect. For 141 maternal deaths within 42 days postpartum, leading causes were cardiac disease (n=21, 14.9%), hypertensive disorders of pregnancy (n=20, 14.2%) and thrombosis (n=19, 13.5%). Up to one year postpartum, cardiac disease (n=32, 18.7%) and hypertensive disorders (n=21, 12.3%) remained the commonest causes (Table 1). For late deaths, cardiac disease and suicide were commonest (n=11, 13.3%) (Supplementary material 5).

Assessment of quality of care for cases available for enquiry up to one year postpartum (n=160) identified improvable factors in 76 women (47.5%) (Table 4). The majority of these pertained to secondary or tertiary care (n=46, 28.8%), mostly due to inadequate management (n=27, 16.9%) and delay in diagnosis (n=18, 11.3%), followed by delay in diagnosis in primary care (n=14, 8.8%). Lessons learned during audit are presented in Box 1.

Table 4. Improvable factors in care, compared between women with different ethnic background. Late deaths included.

	Dutch and Western women (N= 119)	Non-Western women (N= 41)	Total (N=160)
Improvable factors in care	55 (46.2)	21 (51.2)	76 (47.5)
Patient			
Delay consulting doctor	7 (5.9)	2 (4.9)	9 (5.6)
Refusing medical advice	9 (7.6)	2 (4.9)	11 (6.9)
Communication difficulties	1 (0.8)	5 (12.2)	6 (3.8)
Primary obstetric care*			
Delay in diagnosis	12 (10.1)	2 (4.9)	14 (8.8)
Delay in referral to hospital	2 (1.7)	2 (4.9)	4 (2.5)
Inadequate referral to perinatal centre	0	1 (2.4)	1 (0.6)
Secondary or tertiary care **			
Inadequate antenatal visits	0	1 (2.4)	1 (0.6)
Delay in diagnosis	15 (12.6)	3 (7.3)	18 (11.3)
Inadequate management	19 (16.0)	8 (19.5)	27 (16.9)

**Primary midwifery care and/or general practitioner, ** Obstetricians and/or other medical specialists.*

Box 1. Lessons learned as deducted from the improvable factors formulated by the AMSM during audit of maternal deaths in the Netherlands, 2006-2018.

Guidelines and obstetric care

- Generate awareness among pregnant women for alarm symptoms in pregnancy especially for hypertensive disorder and cardiac symptoms. Every woman should be encouraged to seek medical advice in case of new symptoms without experiencing any barriers in terms of communication or other. Maternity care givers should invest time and effort in overcoming language barriers with women of non-native ethnic background.

- Manage hypertensive diseases timely and appropriately with administration of magnesium sulphate and antihypertensive medication. Plan adequate or more frequent antenatal visits for woman at risk of hypertensive disorders or monitor more intensively at home or in hospital.

- Implement screening methods at booking, to identify women at risk of developing perinatal depression, such as the Edinburgh Postnatal Depression Scale. For women with estimated high risk of mental problems, organise a multidisciplinary care pathway in pregnancy and postpartum.

- Implement obstetric early warning scores for monitoring and early detection of critically ill or deteriorating women, especially post-operatively.

- Stabilise critically ill women, before proceeding to birth or transportation to another facility/department. Maximise the use of multidisciplinary expertise when caring for critically ill pregnant women.

- Consider timely postpartum hysterectomy in the management of major haemorrhage, especially in women refusing blood transfusion. Delay due to applying serial conservative options might lead to adverse outcome.

Communication

- Women with severe pre-existing medical conditions require a timely multidisciplinary approach and preferably even pre-conceptional counselling.

- Improve communication, collaboration and comprehension between obstetricians and anesthesiologists by joint team training sessions in obstetric emergencies.

Training

- Be aware of non-specific complaints in the postpartum period. Shortness of breath should not be attributed to hyperventilation without further analysis, but prompt medical evaluation including vital parameters, especially oxygen saturation.

DISCUSSION

Maternal mortality decreased by 50% in the Netherlands in 2006-2018 compared to 1993-2005. This trend was contrary to the previous increase in maternal deaths, though changes in case ascertainment method might have contributed to the observed differences. Improvable factors in care were identified in nearly half of all deaths. Women with a background from Surinam and the Dutch Antilles had an almost threefold higher MMR, remarkably higher than other women with a non-Western background. Commonest causes of death were cardiac disease, hypertensive disorders and thromboembolism.

Compared with other high-income countries, the Netherlands has one of the lowest MMRs, although differences in case ascertainment must be considered. In the UK, the MMR was 9.8 in 2015-2017, which has remained stable in the last decade. In contrast with the Netherlands, indirect causes of death have been more prevalent than direct causes ever since 2003. [23] In France, the MMR was 10.3 in 2010-2012, the commonest cause being obstetric haemorrhage with double the haemorrhage-related MMR compared to the Netherlands (1.6 vs 0.6 per 100,000 livebirths).[24] In Italy, the MMR was 9.2 per 100,000 livebirths in 2006-2012 with obstetric haemorrhage being the leading cause (1.9 per 100,000 livebirths).[25, 26] Differences in rates of deaths caused by obstetric haemorrhage and hypertensive disorders might partly be explained by classification differences, which were previously demonstrated between the UK and the Netherlands.[27] However, such differences are unlikely to substantially impact on these comparisons.

Leading cause of death has become cardiac disease, in line with the UK and the US.[4, 23] However, in the UK rates of mortality due to cardiac disease, are more than twice as high as in the Netherlands (MMR 2.1 vs 0.9 per 100,000 livebirths), accounting for 23.0% of deaths. In the US, cardiovascular diseases account for 15.5% of maternal deaths. Possible explanations for the growing contribution of cardiac disease are changes in risk profiles with more pregnant women being older, obese and having pre-existing cardiac conditions. Some women with congenital heart defects now reach fertile age due to improved care, and have increased risk of adverse outcome.[28, 29]

We recommend that women with pre-existing conditions including cardiac disease access pre-conception counselling and multidisciplinary care by a dedicated team of obstetricians and other specialists. In-depth analysis of cardiac deaths may help identify additional lessons. Our findings stress the importance of efforts to stop smoking and reduce obesity.

In 1993-2005, hypertensive disorders accounted for one third of maternal deaths, compared to 14% in 2006-2018 and a dramatic decrease in MMR from 3.5 to 0.9. [6, 7] This is in line with the demonstrated decline in incidence of eclampsia, related to more timely management of hypertensive disorders following an updated national guideline.[9, 11] Nevertheless, the proportion of hypertensive disorders-related

deaths remains considerable, with improvable factors still present with regard to frequency of antenatal monitoring and timely treatment of severe hypertensive disorders.

Suicide was one of the commonest causes of death up to one year postpartum, more than twice as many as reported in 1993-2005. This rise is in line with other high-income countries. In Austria and Italy, suicides represented 11% and 12% of maternal deaths up to one year postpartum respectively.[30, 31] The increased suicide rate in the Netherlands may also be partly explained by better reporting of suicides and late maternal mortality. According to Statistics Netherlands, a similar trend was observed in the general Dutch population with suicide rates dropping from 1991 to 2007, but then showing a steady increase until 2017.[32] We endorse recommendations of implementing methods to identify women at risk of depression during pregnancy or postpartum, promote joint efforts between obstetric care and mental health professionals for pregnancy-related mental health matters and increase awareness among women and their families to timely recognise symptoms and seek care. Also, the number of suicide-related maternal deaths, most of which occur after 42 days postpartum, underlines the importance of addressing late deaths.

The number of autopsies performed hardly changed compared to 1993-2005 (40%) and in 8% of all deaths cause of death remained unascertained. We believe that in a large proportion of these deaths, a cause could have been identified had autopsy been performed. Therefore, we underline the importance of autopsy, especially in women without apparent pre-existing or obstetric disease, also in case of death at home. In these cases, we recommend consultation of a forensic pathologist.

Although outcomes of women with a non-Western ethnic background appear to have improved, women from Surinam and the Dutch Antilles continue to lag behind. In this group of second or third generation migrants, risk factors for adverse outcome appear to be more common, with almost double the rate of obesity during pregnancy, around 40%.[33] Previously this group was also found to have higher rates of severe acute maternal morbidity.[34] They require particular vigilance from health professionals.[35]

Major strength of this study is its nationwide character, with collection of data over thirteen years. Based on the systematic confidential enquiry performed in all reported deaths, we were able to distil lessons for care based on access to actual medical records. We adjusted categorization of deaths to that used by the MMBRACE-UK, which is based on the ICD-MM, to conform with international literature, enabling future comparisons.[23]

Although it appears that deaths during pregnancy and up to 42 days postpartum are reported to the AMSM with great compliance, the relatively low number of late maternal deaths compared to other enhanced maternal mortality systems suggests possible underreporting. Compared to the previous Dutch maternal mortality report where 23/333 (12%) of pregnancy-related deaths were

late, the reporting of late deaths seems to have increased to 30/171 (17.5%), which is still low compared to for instance Italy (>40%).[25] Besides cross-checking with Statistics Netherlands, there is no way to identify unreported maternal deaths. Therefore, re-establishing such cross-checking, or including a pregnancy-checkbox in the death certificates has been prioritised by the AMSM.[6]

CONCLUSION

The MMR in the Netherlands is among the lowest in the world and the decline of maternal mortality implies improvements in quality of obstetric care, particularly with regard to management of hypertensive disorders. The decrease, however, should not be taken for granted, as risk factors for developing pregnancy-related complications increase nationally and globally. Effort should be made to optimise care for women at higher risk of mortality such as women from Surinam and the Dutch Antilles and women with pre-existing conditions. Maternal mortality should not be seen as a mere obstetric problem given the latest trends in causes of mortality with increases in cardiac and mental health related deaths.

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SUPPORTING INFORMATION

Supplementary material S1. Reclassification of deaths from the categories used by Schutte et al to the categories used by MBRRACE-UK

Schutte et. A.	MBRRACE-UK
Direct causes of death	
Hypertensive disorders of pregnancy Acute fatty liver of pregnancy	Hypertensive disorders of pregnancy
Complications of abortion Ectopic pregnancy	Early pregnancy death
Obstetric haemorrhage Genital tract trauma Complications of caesarean section	Haemorrhage
Miscellaneous-direct	Other direct
Indirect causes of death	
Cerebrovascular accidents (not related to hypertensive disorders) 'Other neurological disorders' from the miscellaneous category	Indirect neurological
'HIV' Form the miscellaneous category Infectious diseases	Sepsis – non obstetric
'Miscellaneous' - Steinert disease, - Systemic lupus erythematosus, - Liver cirrhosis, - Renal disorders Diseases of blood forming organs Endocrine diseases Pulmonary disorders	Other indirect

Supplementary material S2. Causes of non-pregnancy related deaths in the Netherlands, 2006-2018.

Cause of death	N
Malignancies	28
Neurological	6
Breast	4
Gastrointestinal	4
Melanoma	4
Gynaecological	2
Haematological	2
Liver	2
Vestibular	1
Lung	1
Liposarcoma	1
Adrenal	1
Violence	4
Accidents	4
Unknown	3
Neurological	2
Infectious[a]	2
Other	3
Total	46

a Including cardiac ischemia, (1) Thromboembolic event, 330 days postpartum (1), Wegener vasculitis.

Supplementary material S3 . Risk factors compared between different ethnic background groups. Including late deaths. Values denoted as n (%). RR = Risk Ratio, CS = Caesarean Section, BMI = Body Mass Index

	Dutch and Western women (N = 119)	**Non-Western women (N = 41)**	**RR**
Pre-existing medical conditions	33 (27.7)	23 (56.1)	2.0
Previous CS	8 (6.7)	5 (13.2)	1.8
BMI ≥ 30	19 (16.0)	13 (34.2)	2.0
Parity			
0	50 (42.0)	12 (31.6)	0.7
1+	40 (33.6)	26 (63.4)	1.9
Age			
15-19	0	4 (10.5)	25.7
20-29	26 (21.8)	9 (22.0)	1.0
30-39	59 (49.6)	22 (53.7)	1.1
>40	6 (5.0)	3 (7.3)	1.5

Supplementary material S4. Pre-existing medical conditions of women who died up to one year postpartum.

Pre-existing medical conditions (N = 160)	
Uncomplicated medical history	79 (49.4)
Thrombosis	13 (8.1)
Cardiovascular	20 (12.5)
Hypertension	9 (5.6)
Valvular disease	4 (2.5)
Cardiomyopathy	2 (1.3)
ASD/VSD	2 (1.3)
Other [a]	3 (1.9)
Mental	12 (7.5)
Depression	6 (3.8)
Neurological	14 (8.8)
Epilepsy	10 (6.3)
CVA	4 (2.5)
Pulmonary	9 (5.6)
COPD	5 (3.1)
Asthma	4 (2.5)
Haematological	
Inherited blood disorders	4 (2.5)
Malignancies	4 (2.5)
Haematological	2 (1.3)
Cervical	1 (0.6)
Astrocytoma	1 (0.6)
Other	
Hepatitis B/C	5 (3.1)
SLE	3 (1.9)
Renal disorders	3 (1.9)
Bariatric surgery	2 (1.3)
Diabetes Mellitus	1 (0.6)

Multiple conditions per woman possible, thus sum is more than 161. Values denoted as n (%).
[a] Other cardiovascular diseases: ischaemic event (1), heart failure (1), aortic bifurcation graft (1)
ASD = atrial septal defect, VSD = ventricular septal defect, CVA = cerebrovascular accident, COPD = Chronic obstructive pulmonary disease

Supplementary material S5. Late maternal deaths and underlying causes of death in the Netherlands, 2006-2018. Classified according to MBRRACE-UK classification.

	>42 days (n)
Late maternal deaths	30
Direct deaths	12
Indirect deaths	18
Underlying cause of death	**n (%)**
Cardiac disease	11 (36.6)
Hypertensive disorders of pregnancy	1 (3.3)
Thrombosis	0 (0)
Neurological - indirect	4 (13.3)
Unascertained - direct	0 (0)
Haemorrhage	0 (0)
Suicide	11 (36.6)
Amniotic fluid embolism	0 (0)
Sepsis – non obstetric	1 (3.3)
Pregnancy-related infection	0 (0)
Other indirect	1 (3.3)
Early pregnancy death	0 (0))
Indirect malignancy	1 (3.3)
Anaesthesia	0 (0)
Other direct	0 (0)

MMR= Maternal Mortality Ratio (≤42 days postpartum).