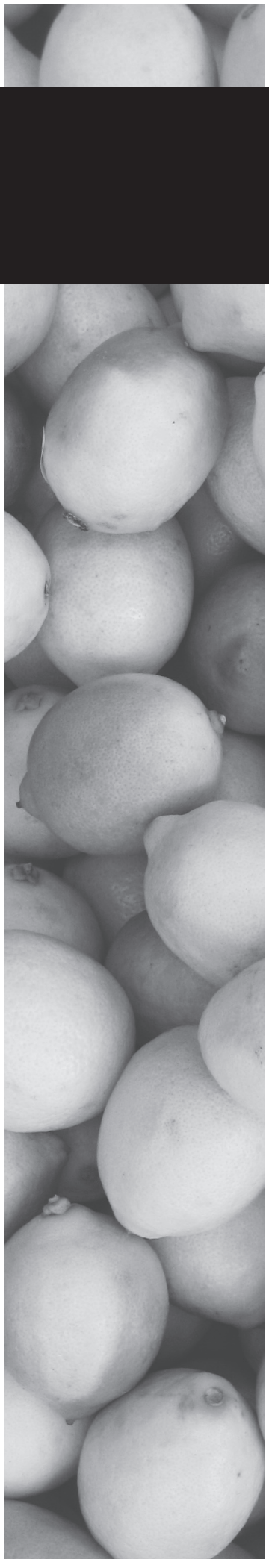
CHAPTER 9



Maternal mortality and severe maternal morbidity in Jehovah's witnesses in the Netherlands

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Abstract

Objective: To determine the risk of maternal mortality and serious maternal morbidity because of major obstetric haemorrhage in Jehovah's witnesses in the Netherlands.

Design: A retrospective study of case notes.

Setting: All tertiary care centres, general teaching hospitals and other general hospitals in the Netherlands.

Sample: All cases of maternal mortality in the Netherlands between 1983 and 2006 and all cases of serious maternal morbidity in the Netherlands between 2004 and 2006.

Methods: Study of case notes using two different nationwide enquiries over two different time periods.

Main outcome measures: Maternal mortality ratio (MMR) and risk of serious maternal mortality.

Results: The MMR for Jehovah's witnesses was 68 per 100,000 live births. We found a risk of 14 per 1000 for Jehovah's witnesses to experience serious maternal morbidity because of obstetric haemorrhage while the risk for the total pregnant population was 4.5 per 1000.

Conclusions: Women who are Jehovah's witnesses are at a six times increased risk for maternal death, at a 130 times increased risk for maternal death because of major obstetric haemorrhage and at a 3.1 times increased risk for serious maternal morbidity because of obstetric haemorrhage, compared to the general Dutch population.

Introduction

Jehovah's witnesses form a religious society with more than six million members worldwide, 29,500 of which live in the Netherlands. Based on biblical textures, Jehovah's witnesses refuse transfusion of blood or one of its primary components (red and white blood cells, platelets and plasma), even when red blood cell transfusion would be life saving.[1;2]

Major obstetric haemorrhage is the most frequent cause of serious maternal morbidity and is one of the most important causes of maternal mortality.[3;4] Refusal of blood in this medical emergency exposes women who are Jehovah's witnesses to an increased risk of maternal death.[5] We have undertaken a retrospective study of case notes to determine the maternal morbidity and mortality because of major obstetric haemorrhage in Jehovah's witnesses in the Netherlands.

Methods

A retrospective study of case notes of Jehovah's witnesses experiencing serious maternal morbidity and mortality was performed, using two different nationwide enquiries over two different time periods.

All deaths related to pregnancy in the Netherlands are reported to the Maternal Mortality Committee of the Dutch Society of Obstetrics and Gynaecology. Cases reported between 1983 and 2006 were included in a nationwide Confidential Enquiry into Maternal Deaths in the Netherlands. Maternal death was defined according to the World Health Organization's (WHO) International Classification of Diseases, tenth revision (ICD-10).[2;3]

Details about the patients (including religious affiliation) and the course of events that preceded the death of the women were present for all the cases that were included in this confidential inquiry and we selected all Jehovah's witnesses. If available, the original medical files were studied. Cases of serious maternal morbidity were selected from a nationwide enquiry into ethnic determinants of severe maternal morbidity (LEMMoN). All 98 maternity units in the Netherlands participated in this nationwide study. Cases of severe maternal morbidity were included during a 2-year period from 1 August 2004 until 1 August 2006 and classified in one or more of the following five categories: (1) Intensive Care Unit admission, (2) uterine rupture, (3) eclampsia or HELLP syndrome with liver haematoma or rupture, (4) obstetric haemorrhage requiring transfusion of 4 units of red blood cells or more and (5) other serious complications, not meeting the criteria of the other categories.[4] Detailed information and copies of relevant parts of the files were present for all cases that were included in the study. We selected and studied all cases of Jehovah's witnesses reported to this enquiry.

The incidence of maternal mortality and serious maternal morbidity in Jehovah's witnesses was compared with the total incidence of maternal mortality as reported to the Maternal Mortality Committee and with the total incidence of maternal morbidity as reported to the LEMMoN study. The total number of deliveries among Jehovah's witnesses was calculated using the annual national birth rate and the

total number of Jehovah's witnesses in the Netherlands in the years 1983 through 2006. These data are carefully registered by Statistics Netherlands (CBS) and the Watchtower Society respectively.[1;6]

Results

Mortality

In the period of 1 January 1983 to 1 January 2007, 538 cases of maternal mortality were reported to the Maternal Mortality Committee and included in the Confidential Enquiries into Maternal Deaths in the Netherlands. The number of direct maternal deaths (late maternal deaths included) was 385 and 30 of these direct maternal deaths were caused by obstetric haemorrhage.

Six cases of mortality in Jehovah's witnesses were identified. All were direct maternal deaths caused by major obstetric haemorrhage and the refusal of red blood cell transfusion was an important factor in the course of events leading to the death of these six women. Hypovolaemic shock causing cardiac failure or post-anoxic encephalopathy was the mode of death. The underlying causes of haemorrhage were: complication of caesarean section (n = 1),[7] uterine atony after manual removal and after spontaneous delivery of the placenta (n = 2). One woman was readmitted after 3 weeks because of severe haemorrhage because of retained placental fragments. Two women had HELLP syndrome. One of them developed disseminated intravascular coagulation (DIC) and postpartum haemorrhage. The other woman with HELLP syndrome also had sickle cell anaemia. She underwent a caesarean section. The procedure was uncomplicated and with limited blood loss, but she died on the ICU because of post-anoxic encephalopathy and cardiac failure (Table 1).

Hysterectomy was not performed in any of these women. The two women suffering from uterine atony were treated with uterine tamponade using an intrauterine balloon and in one of them, arterial embolisation was performed because of persistent bleeding (Table 1).

Between 1983 and 2006, the number of cases of direct and indirect maternal mortality in the Netherlands varied yearly between 10 and 31 cases. The total maternal mortality ratio (MMR) during the study period was 11.7 per 100,000 live births.[4,5] The MMR for direct maternal deaths was 8.4 and the MMR for maternal deaths caused by major obstetric haemorrhage was 0.67. When the six cases of maternal death in Jehovah's witnesses are subtracted, the MMR's are 11.4, 8.2 and 0.52 respectively.

The six selected cases were all direct maternal deaths because of obstetric haemorrhage. They represented 1.1% of total maternal deaths, 1.6% of total direct maternal deaths and 20% of direct maternal deaths caused by obstetric haemorrhage reported to the Maternal Mortality Committee between 1983 and 2006. The total number of deliveries in Jehovah's witnesses during these years was calculated to approximate 8850. This yields a MMR of 68 per 100,000 live births, which is six times higher than the MMR for the general Dutch population and 130 times higher than the MMR for maternal deaths because of major obstetric haemorrhage.

Table 1. Maternal mortality in Jehovah's witnesses.

Nr	Year , age and obstetric history	Course of events	Total blood loss and lowest Hb
1	1986 41y, G3P2	Delivery at term. VE because of prolonged second stage. Major haemorrhage. Readmission after 3 weeks because of persistent bleeding due to placental rest. Manual removal of placental rest. The next day hypovolemic shock due to haemorrhage caused myocardial infarction and death. Autopsy confirmed death due to haemorrhage. **Substandard care**: Not enough data available to identify substandard care	unknown
2	1986 21y, unknown parity OH: unknown	Admitted at 31 weeks because of eclampsia. Fetal death, spontaneous vaginal delivery. Haemorrhage, HELLP and DIC. Death 9 days post partum. **Substandard care:** Not enough data available to identify substandard care	unknown
3	1988 40y, G3P2	Emergency caesarean section at 40,6 weeks because of prolonged second stage and suspected CPD. Difficult extraction. Haemorrhage due to laceration of uterine incision and rupture of uterine vessels. Autopsy confirmed death due to hypovolemic shock. **Substandard care:** Complication of CS not identified as substandard care	4500 ml 1.8 g/dl
4	1995 22y, G4P0 OH: recurrent SA (3x)	Induction of labour at 40,6 weeks with syntocinon because of ruptured membranes for 24 hours. Epidural. Oxytocin because of prolonged first stage. VE because of fetal distress. Placenta spontaneous after oxytocin iv. Haemorrhage due to uterine atony and secondary coagulopathy. **Management:** oxytocin, methylergometrin, tamponade of uterus, sulproston iv and in utero. ICU admission. Volume replacement therapy. Death 3.5 hours post partum due to hypovolemic shock. **Substandard care:** No hysterectomy performed	Unknown 4.0 g/dl
5	1996 30y, G2P1 OH: PROM at 20 weeks, CS at 28 weeks.	Sickle cell anaemia. Admitted twice for sickle cell crisis. Threatening preterm labour at 29 weeks. Nifedipine as tocolytic. HELLP syndrome. At 30 weeks thrombocytopenia (49 x 10^9/L). CS because of maternal condition. ICU admission, death due to cardiac failure and postanoxic encephalopathy . **Substandard care:** CS performed on unstable patient	Unknown 5.9 g/dl (before CS)
6	2006 25y, G3P1 OH: CS, placenta praevia	Delivery at 40,4 weeks. VE because of prolonged second stage. Retained placenta with limited haemorrhage (300 ml). MRP. Haemorrhage due to uterine atony. **Management:** Oxytocin, misoprostol, sulproston, cyklokapron. Tamponade with uterine balloon. Embolisation of internal iliac arteries because of persistent bleeding. Recombinant factor VIII. Death on ICU due to cardiac failure. **Substandard care:** No hysterectomy performed	> 4000 ml 1.3 g/dl

VE = vacuum extraction, DIC = disseminated intravasal coagulation, CPD = cephalo-pelvic disproportion, SA = spontaneous abortion, PROM = premature rupture of membranes, CS = caesarean section, EPO = erythropoietin, IUFD = intrauterine fetal death, MRP = manual removal of the placenta,

Serious maternal morbidity

A total of 2552 cases were included in the nationwide enquiry into ethnic determinants of severe maternal morbidity. Among these, there were 1606 cases of major obstetric haemorrhage. From this study, we identified ten cases of serious maternal morbidity in Jehovah's witnesses (0.39% of included cases). The serious maternal morbidity in all ten cases were because of major obstetric haemorrhage (0.62% of cases of major obstetric haemorrhage) and refusal of red blood cell transfusion was an important causative or contributory factor in all of these.

The ten selected cases delivered in tertiary care centres (n = 4), general teaching hospitals (n = 3) and other general hospitals (n = 3). Home delivery under supervision of a midwife was planned in one woman (patient no. 15). She was transferred to hospital because of a prolonged first stage of labour and fever.

In seven women, haemorrhage occurred after vaginal delivery, one of which was a vacuum extraction and in the other three after caesarean section. The underlying causes of haemorrhage were: retained placenta (n = 2), uterine atony (n = 3), laceration of cervix and vagina (n = 2) and retained placental fragment with laceration of cervix (n = 1). The woman who underwent a vacuum extraction developed sepsis with coagulopathy and experienced haemorrhage without signs of uterine atony or laceration. One woman was readmitted 3 weeks after initial discharge from hospital because of severe haemorrhage of unidentified cause (Table 2).

Active management of the third stage of labour with oxytocin was carried out in all cases. Haemorrhage was treated with volume replacement, one or more uterotonic agents (oxytocin, sulproston, methylergometrin, misoprostol) and ferrous sulphate. In five women (patients no. 7, 8, 9, 10 and 16), this treatment was sufficient. Five patients (patients no. 11, 12, 13, 14 and 15) had haemoglobin concentrations of 3.7 g/dl or less. All five were admitted to the intensive care unit and received erythropoietin. One was treated with arterial embolisation and in two women, hysterectomy was performed. Two women (patients no. 11 and 13) were transferred to the Academic Medical Centre in Amsterdam because of the availability of hyperbaric oxygen therapy in this hospital, but in both cases, the treatment eventually was not necessary. One woman (patient no. 16) initially refused blood, but she decided to accept transfusion 1 day postpartum (Table 2).

In the years 2004 through 2006, the number of deliveries in the Netherlands was 358,874, corresponding with a birth rate of 11.9 per 1000 inhabitants.[4,6] A total of 1606 cases of serious morbidity caused by major obstetric haemorrhage were included in the LEMMoN study, yielding a risk of 4.5 per 1000 births.

During these years, a stable number of 29,500 active members were registered at the society of Jehovah's witnesses in the Netherlands.[1] Using national fertility statistics, it is estimated that, in the study period, there were 700 deliveries in women who are Jehovah's witnesses. This yields a 14 per 1000 risk for Jehovah's witnesses, 3.1 times higher than the risk for the total pregnant population.

Table 2. Severe maternal morbidity in Jehovah's witnesses.

Nr	Age, parity and obstetric history	Course of events	Total blood loss and lowest Hb
7	39y, G10P6 OH: IA, SA (2x) , preterm labour (4x)	Cerclage and progesterone because of recurrent SA and preterm labour. Spontaneous vaginal delivery at 41,4 weeks. Haemorrhage due to retained placental fragment and cervical laceration. **Management:** Oxytocin, sulproston. MRP. Suturing of cervix. Ferrous sulphate. **Substandard care:** Not identified	3800 ml 6.6 g/dl
8	40y, G18P7 OH : IUFD, recurrent SA (10 x), placental abruption, VE	Preterm labour at 35,5 weeks. Elective CS because difficult VE in obstetric history. Peroperative haemorrhage due to uterine atony. **Management:** Oxytocin, methylergometrin, sulproston, ferrous sulphate. **Substandard care:** Not identified	1500 ml 6.9 g/dl
9	27y, G2P1 OH: obstetric haemorrhage	Spontaneous vaginal delivery at 40,5 weeks. Retained placenta with moderate haemorrhage (700 ml). MRP. Haemorrhage due to uterine atony. **Management:** Oxytocin, sulproston, methylergometrin, ferrous saccharate. **Substandard care:** Not identified	3500 ml 6.0 g/dl
10	29y, G1P0	Spontaneous vaginal delivery at 39.5 weeks. Haemorrhage due to retained placenta. **Management:** Oxytocin. MRP. Ferrous saccharate. **Substandard care:** Not identified	2600 ml 3.9 g/dl
11	25y, G2P1	Induction with prostaglandins at 38,5 weeks because of pre-eclampsia. Haemorrhage due to laceration of cervix and vagina. **Management:** Suturing of cervix and vagina. Oxytocin, sulproston, tranexamic acid, recombinant factor VII. Embolisation uterine arteries after persistent bleeding. ICU admission, EPO, darbepoietin alpha, ferrous saccharate. MgSO4 because of convulsions of uncertain underlying cause. **Substandard care:** No hysterectomy performed	2800 ml 3.1 g/dl
12	28y, G1P0	Bells palsy at 38,5 weeks. Hypertension. Spontaneous labour at 40,2 weeks, oxytocin because of prolonged second stage. Haemorrhage due to laceration of cervix and vagina and secondary coagulopathy. **Management:** Suturing of cervix and vagina. ICU admission. Oxytocin, sulproston, cyklokapron, desmopressin, EPO, ferrous saccharate, coagulation factors [1]. **Substandard care:** Not identified	4000 ml 3.5 g/dl
13	25y, G2P1 OH: CS	Repeat elective CS at 40,4 week. Haemorrhage due to uterine atony. **Management:** Oxytocin, sulproston. Hysterectomy after persistence of bleeding. ICU admission. EPO, ferrous saccharate, dopamin, noradrenalin. **Substandard care:** Not identified	2000 ml 2.4 g/dl
14	39y, G3P1	Emergency CS at 40,5 weeks because of prolonged second stage. Haemorrhage 1000 ml. Management: Oxytocin, ferrous saccharate. After 15 days haemorrhage of unidentified cause and shock. **Management:** Misoprostol. Hysterectomy. ICU admission,. EPO, ferrous saccharate. **Substandard care:** :Not identified	unknown 2.6 g/dl

15	32y, G1P0	Spontaneous labour at 38,0 weeks. Intended home delivery. Transfer to hospital because of prolonged first stage and maternal fever (40.3°C). VE because of poor fetal condition on CTG. Sepsis with coagulopathy. Haemorrhage 1000 ml. **Management:** Oxytocin, sulproston, amoxicillin/clavunalate potassium. ICU admission. EPO. **Substandard care:** Planned home delivery. Hospital unprepared to refusal of transfusion. No non-transfusion declaration present.	1000 ml 3.7 g/dl
16	38y, G4P3 OH: preterm labour	Cer vical cer clage because of preterm labour in OH. Spontaneous labour at 39,1 weeks. Haemorrhage 1500 ml due to uterine atony. **Management:** Oxytocin, cyklokapron. ICU admission. Accepted blood transfusion one day post partum. **Substandard care**: Not identified	1500 ml 5.1 g/dl

IA = induced abortion, SA= spontaneous abortion, IUFD = intrauterine fetal death, CS = caesarean section, VE = vacuum extraction, EPO = erythropoietin, MRP = manual removal of the placenta. 1: recombinant factor VII, recombinant factor VIII, factor II / VII / IX / X

Substandard care

Substandard care in cases of maternal mortality and serious maternal morbidity is discussed and defined by the Maternal Mortality Committee. In our case series, substandard care was identified in five patients. In three patients (patients no. 4, 6 and 11), hysterectomy was not timely performed. One woman (patient no. 15) was planned to deliver at home. The hospital she was transferred to was not informed about her attitude towards blood transfusion and therefore not prepared for the situation. The required non-transfusion declaration was not present in her medical record. In patient no. 5, a CS was performed while she was haemodynamically unstable.

Discussion

We found that women who are Jehovah's witnesses are at a six times increased risk for maternal death, at a 130 times increased risk for maternal death because of major obstetric haemorrhage and at a 3.1 times increased risk for serious maternal morbidity because of obstetric haemorrhage, as compared to the general Dutch population.

To our knowledge, only three other studies studied the obstetric risks of women who are Jehovah's witnesses, including 332, 33 and 90 women. In the two largest studies, two cases and one of maternal death, respectively, were identified, resulting in a 44-fold and 65-fold increased risk of maternal death.[5;8] In our study, we used two large nationwide enquiries of maternal mortality and serious maternal morbidity. Therefore, a relatively large number of Jehovah's witnesses experiencing maternal morbidity or serious maternal morbidity could be selected. As the study was not performed in a prospective setting, we did not have exact data on the total number of deliveries in Jehovah's witnesses. We used demographic data to give a reliable estimation instead.

In the Nationwide Enquiry into ethnic determinants of severe maternal morbidity (LEMMoN), women were included in the category of major obstetric haemorrhage if the haemorrhage required

transfusion of 4 units of red blood cells or more. Consequently, Jehovah's witnesses could not be included in this category. Instead, they were included in the category for Intensive Care Unit admission or were reported in the last category, in which cases were reported if there were other serious complications that did not meet the criteria of the other categories.

It is important to realise that in case of acute haemorrhage, red blood cell transfusion is not always immediately required. Although guidelines suggest a transfusion threshold at a haemoglobin concentration of 7.0–8.0 g/dl, concentrations of 5.0 g/dl or more are usually well tolerated if isovolaemia is maintained. In a study on healthy individuals, Weiskopf et al. found that acute isovolumetric reduction of haemoglobin concentration to 5.0 g/dl does not appear to cause inadequate tissue oxygenation.[9]

There are limited data available on outcomes at concentrations below 5.0 g/dl. Two retrospective studies on patients who declined blood transfusion, mostly Jehovah's witnesses, found that morbidity and mortality rates were extremely high below this level,[10,11] but survival has been reported at Hb rates below 2.0 g/dl and even as low as 1.4 g/dl.[12;13]

Since the first introduction of the doctrine of blood by the society of Jehovah's witnesses, the policy has been changed several times, causing confusion in clinicians when they are confronted with these issues.[14;15] A clear statement about the acceptance of different blood components was published in the society's official magazine The Watchtower in 2004: 'Though all witnesses should refuse autologous or heterologous transfusions of blood or one of its major components, the society states that each member should decide for him or herself whether or not to accept treatment with other blood products like coagulation factors and erythropoietin'.[16;17] Sometimes, the use of a cell saver during surgery is accepted because continuity with the circulatory system is maintained. These individual choices can make a big difference in management options in cases of major obstetric haemorrhage. Therefore, the exact possibilities for each patient and the available alternatives to red blood cell transfusion should be discussed early in pregnancy.

Most hospitals are rarely confronted with the care for pregnant Jehovah's witnesses and even more scarcely with obstetric haemorrhage in these women. Therefore, centralisation of care for these patients is advisable and each hospital treating Jehovah's witnesses should have a protocol for the obstetric care and the management of obstetric haemorrhage of these patients.

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Samenvatting

Dit proefschrift beschrijft de resultaten van de LEMMoN studie, een 2 jarige landelijke studie naar ernstige maternale morbiditeit ('Severe Acute Maternal Morbidity, SAMM) in Nederland. Alle ziekenhuizen met een afdeling verloskunde in Nederland participeerden in de studie, die liep van 1 augustus 2004 tot 1 augustus 2006. Voor het eerst is hiermee inzicht verkregen in de frequentie, mortaliteit en risicofactoren van ernstige maternale morbiditeit in Nederland, alsmede de factoren die wijzen op tekortschietende zorg (substandaard zorgfactoren) die daarbij een rol spelen. Wij waren speciaal geïnteresseerd in het verband tussen etniciteit en ernstige maternale morbiditeit, omdat etniciteit een significante risicofactor blijkt te zijn voor moedersterfte en ernstige maternale morbiditeit.

In **Hoofdstuk 1** wordt beschreven wat de aanleiding was voor het opzetten van de LEMMoN studie. Internationale en nationale perspectieven worden besproken. SAMM wordt in toenemende mate geaccepteerd als een nieuwe kwaliteitsparameter voor de kwaliteit van verloskundige zorg in westerse landen, in aanvulling op de maternale sterfte statistieken. Terwijl de maternale sterfte in westerse landen tegenwoordig zeer laag is, tonen verschillende studies wereldwijd dat er de laatste jaren sprake lijkt te zijn van een stijging van de incidentie van SAMM in westerse landen. In Nederland is momenteel geen registratiesysteem aanwezig voor obstetrische complicaties. Ook in de huidige Landelijke Verloskundige Registratie (LVR) worden ernstige maternale complicaties helaas niet geregistreerd, evenals bepaalde risicofactoren voor zwangerschapscomplicaties zoals body mass index en keizersnede in de voorgeschiedenis.

In **Hoofdstuk 2** worden enkele methodologische overwegingen besproken die een rol speelden bij het ontwerp van de studie. Hoewel de methodologie in het algemeen uitgebreid beschreven is in de respectievelijke hoofdstukken, waren er enkele aspecten die een meer gedetailleerde uiteenzetting verdienden dan mogelijk was in de gepubliceerde artikelen. Ook aanvullende informatie betreffende definities, inclusiecriteria en selectie van de referentiepopulatie is in dit hoofdstuk te vinden. Daarnaast wordt het daadwerkelijke beloop van de LEMMoN studie beschreven en worden enkele resultaten van subanalyses binnen Nederland besproken.

Hoofdstuk 3 beschrijft de resultaten van de LEMMoN studie in grote lijnen. Zevenennegentig procent van alle maandelijkse meldkaartjes werd daadwerkelijk geretourneerd, waardoor de LEMMoN studie 358.874 bevallingen in Nederland representeert. Er werden 2552 gevallen van SAMM gerapporteerd met een overall incidentie van 7,1 per 1000 bevallingen. Opname op de intensive care (IC) werd gerapporteerd in 847 gevallen (incidentie 2,4 per 1000), uterusruptuur in 218 gevallen (6,1/10.000), eclampsie in 222 gevallen (incidentie 6,2/10.000) en ernstige fluxus in 1606 gevallen (incidentie 4,5 per 1000). Overall case fatality rate was 1 op 53. De helft van alle gevallen betrof ernstige fluxus.

Resultaten met betrekking tot etniciteit staan beschreven in **Hoofdstuk 4**. Niet-westerse immigranten hadden een 1,3 keer zo hoog risico op SAMM (95% betrouwbaarheidsinterval 1,2-1,5). Het verhoogde risico gold voor alle vormen van SAMM, waarbij de grootste verschillen gezien werden bij vrouwen met eclampsie. Er werden grote verschillen gevonden voor verschillende etnische minderheden, variërend van een niet-verhoogd risico voor Marokkaanse en Turkse vrouwen tot een 3,5-voudig verhoogd risico voor vrouwen uit Afrika onder de Sahara. (95% betrouwbaarheidsinterval [BI]2,8-4,3). Verschillen bleven significant na correctie voor sociaaleconomische status, werkloosheid, alleenstaande moeder zijn, pariteit en keizersnede in de voorgeschiedenis in multivariate logistische regressie analyse. Dit suggereert dat er nog andere dan deze factoren een rol spelen. Met name moet men hierbij denken aan migratiegerelateerde factoren zoals korte verblijfsduur in Nederland, gebrek aan sociale netwerken en gebrek aan kennis van het Nederlandse gezondheidszorgsysteem. De uitkomsten suggereren dat er mogelijkheden lijken te zijn voor verbetering van de kwaliteit van zorg door interventies te richten op specifieke etnische minderheidsgroeperingen.

In de hoofdstukken 5-8 worden de resultaten beschreven van bestudering van de verschillende inclusiegroepen binnen de LEMMoN studie.
In **Hoofdstuk 5** worden alle IC opnames tijdens de zwangerschap en het kraambed in Nederland gedurende de studieperiode beschreven. In totaal werden 837 casus geanalyseerd, hetgeen een derde van het totaal aantal inclusies in de LEMMoN studie betrof. De incidentie van IC opname in Nederland was 2,4 per 1000 bevallingen. Er waren 29 gevallen van maternale sterfte, hetgeen een mortaliteit geeft van 1 op 29 (3,4%) vergeleken met 1 op 53 voor SAMM overall. De meest voorkomende redenen voor IC opname waren ernstige fluxus (48,6%), hypertensieve aandoeningen van de zwangerschap (29,3%) en sepsis (8,1%). Beademing was nodig in 34,8%, behandeling met inotropica in 8,8%. Vrouwen die al primair onder controle waren van de gynaecoloog, hadden een verhoogd risico op IC opname, en vrouwen die thuis waren bevallen een verlaagd risico. Geconcludeerd werd dat men door alleen naar IC opnames te kijken, twee derde van alle gevallen van ernstige maternale morbiditeit mist.
In **Hoofdstuk 6** worden alle gevallen van uterusruptuur in Nederland gedurende de studieperiode beschreven. In totaal werden 210 vrouwen geanalyseerd, 6,9% van alle inclusies in de LEMMoN studie. De populatie gebaseerde incidentie was 5,9 per 10.000 bevallingen, hetgeen vergelijkbaar was met andere westerse landen. In 183 gevallen (87,1%) was sprake van een litteken uterus. De incidentie van ruptuur met en zonder litteken was respectievelijk 5,1 en 0,8 per 10.000 bevallingen. Er waren geen gevallen van maternale sterfte en 18 gevallen van perinatale sterfte (8,7%). De meest voorkomende symptomen van uterusruptuur zijn continue buikpijn en

suboptimaal CTG. Vaginaal bloedverlies, hypertonie of atonie zijn vaak afwezig. Het overall absolute risico op uterusruptuur was 1 op 1709 bevallingen en steeg naar 1 op 198 in vrouwen met een litteken uterus en 1 op 251 in vrouwen die epidurale anesthesie hadden tijdens de partus. In univariate analyse bleek het risico op uterusruptuur tevens verhoogd na inleiding van de baring (op welke wijze dan ook), bij prematuriteit, serotiniteit, overgewicht, hogere maternale leeftijd en niet-westerse etniciteit. Het relatief risico van inleiding van de baring was 3,6 (95% betrouwbaarheidsinterval 2,7-4,8). In vergelijking met de studie van Kwee et al. in 2002-2003 was het percentage inleidingen bij vrouwen met een sectio litteken in Nederland gedaald. Hoewel in de literatuur veel aandacht wordt besteed aan de associatie van uterusruptuur met een sectio litteken en met het inleiden van de baring, vond 13% van de rupturen plaats bij vrouwen zonder uterus litteken en 72% tijdens spontane weeënactiviteit.

In **Hoofdstuk 7** worden alle gevallen van eclampsie in Nederland tijdens de studieperiode beschreven. In totaal werden 222 vrouwen geanalyseerd, 7,6% van alle inclusies in LEMMoN. We vonden een incidentie van 6,2 per 10.000 bevallingen, hetgeen twee keer zo hoog bleek te zijn als in andere westerse landen. Er waren drie gevallen van maternale sterfte (mortaliteit 1 op 74; 1,4%). Risicofactoren in univariate analyse waren meerlingzwangerschap, primipariteit, jonge maternale leeftijd, niet-westerse etniciteit en overgewicht. Substandaard zorg werd vastgesteld in de meerderheid van de casus: profylactisch magnesiumsulfaat was slechts in 10,4% van de gevallen gegeven en antihypertensiva in 39,6% van alle gevallen waarbij de bloeddruk bij opname al 170/110 of hoger was. Daarnaast werd bij 15 van 18 tijdens audit bijeenkomsten geanalyseerde casus (83%) geconcludeerd dat er sprake was van substandaard zorg. Wij concludeerden dat deze resultaten, in combinatie met het relatief hoge aandeel van hypertensieve aandoeningen in de moedersterfte, kritische evaluatie vereiste van het Nederlandse beleid bij hypertensieve aandoeningen in de zwangerschap.

Ernstige fluxus bleek de belangrijkste oorzaak te zijn van ernstige maternale morbiditeit in Nederland, verantwoordelijk voor 51,1% van alle complicaties in de LEMMoN studie. In totaal werden 1606 gevallen gemeld gedurende de studieperiode (incidentie 4,1 per 1000 bevallingen).

In **Hoofdstuk 8** worden alle gevallen van uterusextirpatie of embolisatie vanwege ernstige fluxus in Nederland gedurende de studieperiode beschreven. Deze serie van 205 patiënten representeert de ernstigste gevallen binnen de fluxus groep (12,8% van alle gevallen van ernstige fluxus). De overall incidentie van uterusextirpatie danwel embolisatie voor ernstige fluxus was 0,57 per 1000 bevallingen. Er werden 114 gevallen van embolisatie gemeld (incidentie 0,32 per 1000; mortaliteit 2,0%) en 108 gevallen van uterusextirpatie (incidentie 0,30 per 1000; mortaliteit 1,9%). Zeventien vrouwen ondergingen alsnog een uterusextirpatie na mislukte embolisatie. Keizersnede (RR 6,6; 95% BI 5,0-8,7) en meerlingzwangerschap (RR 6,6; 95% BI 4,2-10,4) waren

de belangrijkste risicofactoren in univariate analyse. De incidentie van uterusextirpatie voor ernstige fluxus in Nederland was in de lagere regionen vergeleken met de incidentie in andere landen, zoals gerapporteerd in het Peristat II rapport. Voor embolisatie zijn geen populatie incidenties bekend uit de literatuur. In 46% van de hier beschreven vrouwen kon de toekomstige fertiliteit worden gespaard door middel van succesvolle embolisatie.
Tenslotte werden 223 gevallen van 'overige maternale morbiditeit' (naar het oordeel van de behandelend arts) gerapporteerd. Een overzicht van deze casus wordt gegeven in Hoofdstuk 3.

Het is bekend dat Jehovah's getuigen een verhoogd risico hebben op ernstige maternale morbiditeit en maternale sterfte. Dit risico is gekwantificeerd in **Hoofdstuk 9** door gebruik te maken van de LEMMoN database en gegevens van de Commissie Maternale Sterfte over de jaren 1983-2006. Jehovah's getuigen hadden een absoluut risico van 1,4% op ernstige maternale morbiditeit door ernstige fluxus. De maternal mortality ratio was 68 per 100.000 levendgeborenen. Relatief hadden Jehovah's getuigen een 3,1-voudig verhoogd risico op ernstige maternale morbiditeit door ernstige fluxus en een 100-voudig verhoogd risico op maternale sterfte door ernstige fluxus, in vergelijking tot de algemene zwangere populatie in Nederland.

Onderdeel van de LEMMoN studie was een uitgebreide analyse van de onderrapportage van ernstige maternale morbiditeit. Er bleek geen mogelijkheid te zijn om onderrapportage van IC opnames landelijk vast te stellen. Onderrapportage van uterusruptuur en eclampsie, vastgesteld door vergelijking met gegevens van de LVR, bleek laag te zijn (2-3%). Onderrapportage van ernstige fluxus bleek significant te zijn en om die reden initieerden wij een grote landelijke survey waarin we transfusie data verzamelden van zo veel mogelijk bloedtransfusie laboratoria in Nederland. De resultaten van deze survey staan beschreven in **Hoofdstuk 10**. We ontvingen data van 65 van de 98 ziekenhuizen met een verloskunde afdeling in Nederland en vergeleken die met de data in de LEMMoN studie van dezelfde ziekenhuizen gedurende dezelfde studieperiode van 20 maanden. Achttien van de 65 ziekenhuizen werden geëxcludeerd omdat het niet lukte de gerapporteerde bloedtransfusiegegevens te laten verifiëren door een obstetricus om logistieke redenen. Data van de overige 47 ziekenhuizen waren beschikbaar voor analyse. Gedurende de studieperiode werden 824 casus geïdentificeerd door de bloedtransfusie laboratoria en 727 via de LEMMoN studie. In totaal werden 1018 unieke casus geïdentificeerd. Na cross-matching werd een onderrapportage van 29% gevonden. Dat betekent dat een meer realistische benadering van de werkelijke incidentie van ernstige fluxus in Nederland 5,7 per 1000 bevallingen is, in plaats van 4,1 per 1000. Onderrapportage bleek met name substantieel te zijn onder de minder ernstige gevallen van ernstige fluxus. Er waren geen gevallen van uterusextirpatie of embolisatie

in verband met fluxus gemist. Wij concludeerden dat rekening zou moeten worden gehouden met onderrapportage in alle grote multicentrische epidemiologische studies om tot een meer betrouwbare benadering van de werkelijke incidentie te komen en zodoende betere vergelijking van epidemiologische data mogelijk te maken.

Hoofdstuk 11 beschrijft de introductie van audit van ernstige maternale morbiditeit in Nederland. Sinds 2005 hebben wij zeven audit bijeenkomsten georganiseerd door het hele land. Een panel werd samengesteld, bestaande uit experts en stafleden en arts-assistenten van de betrokken ziekenhuizen. Voorafgaand aan iedere bijeenkomst werden gedetailleerde gegevens van geselecteerde casus verzonden naar alle panelleden voor individuele beoordeling. Tijdens een plenaire bijeenkomst werden vervolgens de bevindingen bediscussieerd en werden substandaard zorg factoren bepaald bij meerderheid van stemmen. Substandaard zorg werd gevonden in 53 van de 67 geanalyseerde casus (79%). Specifieke aanbevelingen werden geformuleerd voor implementatie in lokale en landelijke richtlijnen. Over het algemeen was men van mening dat de casus uit de LEMMoN studie ernstige maternale morbiditeit betroffen. Substandaard zorg bleek aanwezig in vier van de vijf casus. Voortgaande audit van gevallen van ernstige maternale morbiditeit wordt van harte aangemoedigd, zowel op landelijk/regionaal als op lokaal niveau.

Hoofdstuk 12 betreft de algemene discussie, waarin vele aspecten van ernstige maternale morbiditeit in Nederland de revue passeren.