Safe motherhood : severe maternal morbidity in the Netherlands. The LEMMoN study

Zwart, J.J.

CHAPTER 2

Methodological aspects

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2.1 Introduction

Much thinking and reading has preceded the start of the LEMMoN study. Some of the most important methodological considerations are described in the first part of this chapter. Complete description of the methods is in the respective chapters. The second part describes the actual running of the study in more detail than was possible in the published manuscripts. Special attention is paid to differences within the Netherlands.

Part 1 Methodological considerations

2.2 Considerations related to definition of severe maternal morbidity

Final inclusion criteria used in the LEMMoN study were defined after searching the literature using a pre-defined search strategy in PubMed (Figure 1).

Figure 1. Search strategy

("Morbidity"[MeSH] AND (maternal OR mother OR mothers) AND (pregnancy OR pregnant OR pregnancy complications) AND (severe OR severity) NOT (child OR infant)) OR ((maternal[title] OR mother[title] OR mothers[title]) AND morbidity[title]) OR (("intensive care"[Majr] OR "critical care"[Majr] OR (care[title] AND (intensive[title] OR critical[title]))) AND (pregnancy OR pregnant OR pregnancy complications OR maternal OR mother OR mothers) NOT (child OR infant)) OR ("Postpartum Hemorrhage"[MAJR] OR (Postpartum[title] AND (Haemorrhag*[title] OR bleeding[title] OR Hemorrhag*[title])) AND morbidity) OR ("Pregnancy Toxemias"[Majr] OR (severe[title] AND (pre-eclampsia[title] OR preeclampsia[title])) AND morbidity NOT (child OR infant)) OR (("uterine rupture"[Majr] OR "Uterine rupture"[Title Word]) AND morbidity)

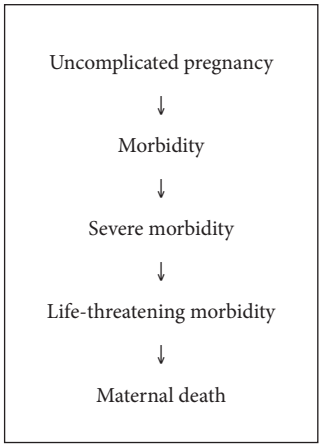
Maternal morbidity has been defined in 1989 by the World Health Organization as morbidity in a woman who has been pregnant (regardless of the site and duration of the pregnancy) from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes.[1] This definition does not take into account women who are still pregnant, and it fails to clearly define the postpartum interval. As most studies on maternal morbidity in high income countries include women up to six weeks postpartum, we included all severe acute maternal morbidity (SAMM) during pregnancy, childbirth or puerperium. Incidental and accidental cases were not excluded, but marked as such. Following the terminology used in maternal mortality

studies, this should actually be mentioned as 'Pregnancy-related morbidity' instead of 'Maternal morbidity'. Apparently, the WHO definition is not regularly used and needs to be adjusted to at least also include women who are still pregnant. This could be easily achieved by changing the first part of the definition into 'morbidity in a woman who *is or* has been pregnant…'.

The continuum of maternal morbidity

Maternal morbidity is thought to represent a continuum between two extremes: physiology and maternal mortality (Figure 2).[2]

Figure 2. Continuum of maternal morbidity



On this continuum, pregnancy can be complicated by morbidity, severe morbidity, life-threatening morbidity and maternal death. Life-threatening morbidity can result either in maternal death or in recovery or permanent disability. Life-threatening morbidity is also referred to as "near miss" maternal morbidity. This term is derived from sentinel event audit in the aviation industry. There is no universally accepted definition of a "near miss" because it is strongly influenced by local maternal health parameters. Mantel et al, who introduced the term, used the following striking definition: "a very ill woman who would have died had it not been that luck and good care were on her side".[2] It clearly expresses the factors that contribute to the difference between live and death, i.e. good care and luck. Strictly spoken, the term near-miss is incorrect: in the aviation industry, it refers to a near accident with no casualties or material damage involved. When used in the context of maternal health, there is already an 'accident' with a casualty, potentially suffering serious short and long term consequences. Therefore, we preferred to use the term severe acute maternal morbidity throughout this thesis.

Objective assessment of the severity of maternal morbidity remains difficult. When should one

consider it 'severe', and when is it a 'near miss'? A different way of selecting cases of SAMM is by using a predictive model or scoring system. Geller at al developed and tested such a system in the United States to select near-misses from a series of cases of maternal morbidity.[3;4] They used expert opinion as the gold standard and assessed the accuracy of different scoring systems in terms of sensitivity and specificity. A four-factor scoring system was recommended, including ICU admission, extended intubation, blood transfusion (>3 units) and surgical intervention. However, a two-factor scoring system with only ICU admission and transfusion (>3 units) yielded exactly the same results in their sample: 100% sensitivity and 78% specificity. The scoring systems largely used management based criteria.

Defining major obstetric haemorrhage

With respect to the definition of major obstetric haemorrhage (MOH), different options were considered: inclusion based on blood loss, transfusion need or drop of haemoglobin level. The latter was considered to be the most objective, but obviously depends on standardised assessment of pre- and post haemorrhage haemoglobin levels, which is difficult in all cases and not feasible at all in observational studies. Blood loss is known to be largely underestimated, especially in case of MOH.[5] Therefore, we considered inclusion based on transfusion need to be the best option. We thereby realised that this is a management based criterion and thus subject to local transfusion policy. Using a cut-off point of four units of packed cells, we expected not to miss cases of SAMM without including too many cases that eventually turned out to be less severe.

2.3 The reference population

Choosing the most appropriate reference population (denominator data) is crucial for calculating the most accurate incidence figures. As this study included all cases of SAMM during pregnancy, childbirth and puerperium, the ideal reference cohort would have been 'all pregnant women during the study period'. As these data were not available, we had to use alternative reference data. We could think of two possible sources for the denominator data, namely the Dutch perinatal database of the Netherlands Perinatal Registry and birth statistics from Statistics Netherlands.

Intuitively, using data from the Dutch Perinatal Database seemed to be the best choice. However, various problems were encountered, the most important being that the exact percentage of deliveries the database represents was unknown. Since deliveries under guidance of general practitioners are not included in this database, it is incomplete. This is thought to concern less than seven percent of all deliveries, but exact numbers of missing deliveries are unknown. The fact that nobody knows to what extent the Dutch Perinatal Database is incomplete, makes it less valuable as an epidemiologic tool. Furthermore, the Dutch Perinatal Database uses slightly different definitions than Statistics

Netherlands. Therefore demographic data from Statistics Netherlands could not merely be applied. For instance, there is a difference regarding the gestational age from which stillbirths are included and the assessment of ethnicity is different. Finally, there have been technical problems with uploading delivery data from a small number of hospitals for the year 2005, resulting in missing data.

Mainly due to the question of unknown representativity, we ultimately decided to use data from Statistics Netherlands as denominator data. These data were based on birth certificates for the exact study period, and we corrected them for multiple births and stillbirths of 24 weeks or over.

As complications of early pregnancy were included in the numerator but not in the denominator, the incidence we express is a ratio rather than a rate. It describes the number of cases of a specific obstetric condition in the Netherlands during the study period, divided by the number deliveries during that period.

Using the above mentioned method, we calculated the number of births this study represents as shown in Table 1. There were 371,021 deliveries in the Netherlands during the exact study period. Since the percentage of returned monthly communication cards was 96.7%, the study is thought to represent 358,874 deliveries.

Table 1. Denominator data

	2004 (last 5 months)	2005	2006 (first 7 months)	study period LEMMoN
Number of live births	81,030	187,910	106,717	375,657
Number of twins	5/12 * 3523	3027	7/12 * 3210	6367
Number of triple pregnancies	5/12 * 64	40	7/12 * 34	87
Number of stillborns ≥ 24w	5/12 * 1013	983	7/12 * 856	1904
Total number of deliveries	79,931	185,786	105,304	371,021

Source: Statistics Netherlands (CBS) 2007

Part 2 Actual performance and regional results of the LEMMoN study

2.4 Participation

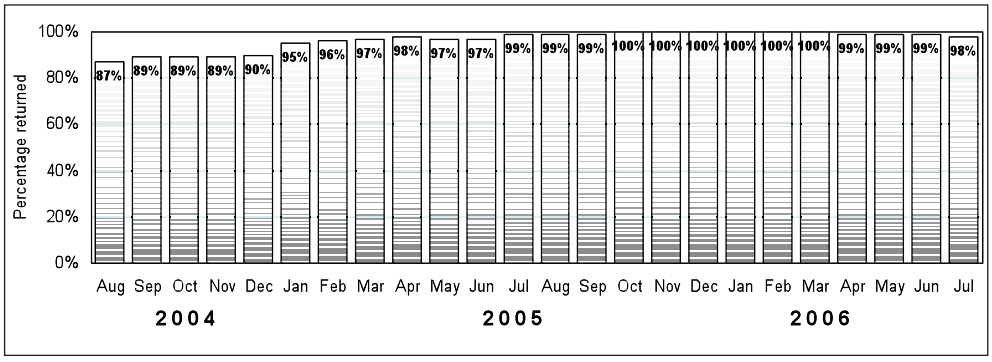
We succeeded to get participation in all 98 hospitals with a delivery ward in the LEMMoN study. Important features that brought about this universal participation included

- selection of the most dedicated clinicians to act as local coordinator of the study,
- clear and concise information delivery before initiation of the study,
- easy method of case ascertainment using the web-based system of the National Signalling Centre for Obstetrics and Gynaecology (NSCOG) provided by TNO Quality of Life, Leiden, the Netherlands,
- support with data collection on location if necessary,

- a two-monthly newsletter to keep attention to the study,
- LEMMoN cakes for the best including hospitals and
- continuous contacting of non-responders.

Response rates for every single month of the study are shown in Figure 3. Overall response rate was 96.7%. Human resources needed for data collection involved one full-time study coordinator, eight students who were part-time available for data collection and entry, an obstetrician to regularly remind non-reporting local coordinators to return their monthly response cards. We were able to run this study efficiently by making use of the National Signalling Centre for Obstetrics and Gynaecology (NSCOG), which delivered the experience and infrastructure for on-line reporting of cases of SAMM on a monthly basis. The use of this system has undoubtedly added to the high participation and response rates.

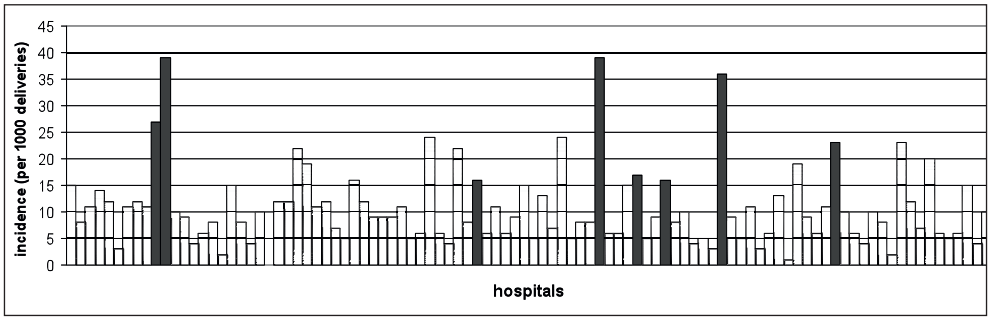
Figure 3. Monthly response rate



2.5 Incidence: local, regional and temporal differences

Incidence varied largely by hospital, as shown in Figure 4. Academic hospitals (dark bars) were likely to have a high-er incidence due to selection and referral pattern. For other hospitals, specific case mix of the hospital population may account for the differences found. Also, differences in local policy for transfusion and ICU admission likely influenced incidence, as well as eagerness to identify and report cases. After having addressed all these possible confounders, the incidence may reflect the quality of care in a specific hospital.

Figure 4. Variation of incidence by hospital*



***each bar represents a hospital in the Netherlands, dark bars represent academic teaching hospitals**

As shown in table 2, the incidence in academic hospitals was indeed about three times that of non-academic hospitals. Incidence was also higher in non-academic teaching hospitals as compared to non-teaching hospitals (relative risk 1.3; 95% confidence interval 1.1-1.5). Sub-analysis of incidence by delivery volume of hospital is shown in Table 3. A trend was observed towards increased incidence of SAMM in larger volume hospitals, also when excluding academic centres from analysis.

Table 2. Comparison of tertiary care centres: inclusion pattern, rate of SAMM and referral rate

	ICU	Uterine rupture	Eclampsia/ HELLP	MOH	Other	Reported cases (n)	Rate of SAMM	Referrals [n(%)]
AMC	29%	7%	11%	37%	**34%**	70	2.3	29 (41%)
VUMC	28%	8%	9%	48%	24%	126	**4.2**	33 (26%)
UMCG	31%	7%	**21%**	*29%*	26%	42	1.8	17 (40%)
LUMC	29%	6%	*4%*	50%	30%	105	4.0	37 (35%)
AZM	*15%*	7%	12%	51%	29%	41	1.7	6 (15%)
UMCN	41%	5%	8%	**79%**	10%	39	*1.5*	16 (41%)
Erasmus	34%	6%	*4%*	60%	19%	112	3.7	40 (36%)
UMCU	**49%**	6%	8%	62%	*4%*	84	2.1	34 (40%)

ICU=intensive care unit; MOH=major obstetric haemorrhage. Highest rates are in bold, lowest rates are in italic

A comparison was made of the inclusion pattern of SAMM between the eight academic centres in the Netherlands (Table 4). We noted large difference in the relative contributions of different subgroups to the overall SAMM incidence, except for uterine rupture. We also noted large differences in percentage of referrals from other hospitals among the SAMM cases, but these differences could not explain the differences in incidence.

Table 3. Incidence by type of hospital (2005)

Type of hospital	Number of deliveries	# LEMMoN	Incidence (/10,000)	RR (95% CI)
Non-academic teaching hospital (n=35)	54,742	595	**10.9**	1.3 (1.1-1.5)
Non-academic non-teaching hospital (n=55)	47,273	384	**8.1**	1.0
Academic centre (n=8)	11,805	327	**27.7**	3.4 (2.9-3.9)

RR=relative risk; CI=confidence interval

No marked seasonal variations were observed for SAMM overall and for different subgroups. Inclusion of cases by calendar month is shown in Figure 5. Overall incidence ranged from 77 to 133 cases per month. Trends in incidence during the study period were not noted for either of the subgroups of SAMM.

Table 4. Incidence by volume* (2005)

Volume (deliveries/year)	Number of deliveries	# LEMMoN	Incidence (/10,000)
<1000 (n=40)	29,035	233	**8.0**
1000-1500 (n=39)	42,384	402	**9.5**
>1500 (n=19)	32,077	344	**10.7**

***academic centres excluded**

We also performed a sub-analysis of SAMM by province in the Netherlands. The Netherlands is divided into 12 provinces. Although organisation and funding of health care is a nationwide issue, this analysis enabled us to study regional differences in SAMM. As shown in table 5 and figure 6, regional incidence of SAMM varied from 2.7 to 8.5 per 1000 deliveries. The incidence was clearly increased in the urbanised Western part of the country (the so-called 'Randstad') as compared to the more rural areas. To illustrate the influence of urbanisation on the incidence of SAMM, we calculated an urbanisation factor based on data from Statistics Netherlands.[6] After correction for this factor, differences in incidence appeared to have largely disappeared. This correlation could be caused by the higher rate of non-Western immigrant women and the higher rate of women with a low socio-economic position in the more urbanised parts of the country. These regional results illustrate the importance of case-mix analysis when comparing incidences between hospitals in the Netherlands.

Figure 5. Seasonal variation in number of inclusions

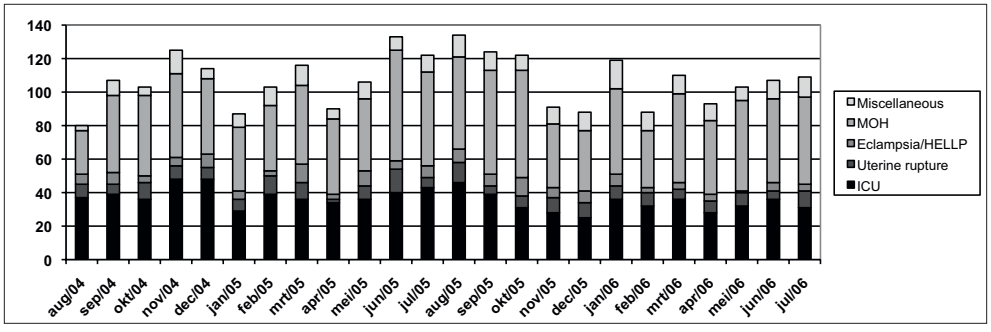


Figure 6. Distribution of severe acute maternal morbidity in the Netherlands

Table 5. Incidence of SAMM by province (arranged by urbanisation level)

	Reported cases	total births	Incidence SAMM	urbanisation factor*	Rate of non-Western women in LEMMoN
Zuid-Holland	697	81,750	**8.5**	0.76	54%
Noord-Holland	529	62,918	**8.4**	0.73	53%
Utrecht	210	30,968	**6.8**	0.65	30%
Flevoland	74	10,520	**7.0**	0.58	48%
Noord-Brabant	294	52,902	**5.6**	0.54	19%
Overijssel	138	27,789	**5.0**	0.51	10%
Gelderland	251	44,841	**5.6**	0.50	23%
Limburg	134	20,281	**6.6**	0.49	25%
Groningen	79	11,907	**6.6**	0.49	13%
Zeeland	52	7,843	**6.6**	0.40	20%
Friesland	67	14,743	**4.5**	0.40	12%
Drenthe	28	10,240	**2.7**	0.37	8%

Urbanisation factor calculated from data of Statistics Netherlands

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