Strategies to Reduce Perinatal Health Inequalities

THE HEALTHY PREGNANCY 4 ALL STUDY

AMBER A. VOS

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The Healthy Pregnancy 4 All study

Aanpak om perinatale gezondheidsverschillen te verminderen

De Healthy Pregnancy 4 All studie

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'Alles is relatief'

CONTENTS

Chapter 1

General introduction

Perinatal health inequalities

Perinatal health is a topic of growing international interest. As of 2004, two subsequent reports concluded that substantial differences in perinatal health exist within European countries.[1 2] With regards to the Netherlands, these reports demonstrated that perinatal mortality rates in the Netherlands were higher than in the surrounding European countries, and showed a slower rate of decline.[1] On top of this, further investigation revealed inequalities in adverse perinatal outcomes within the Netherlands. 'Inequality' was defined as a relevant difference in outcome according to a grouping criterion which is ethically judged to be undesirable unless this difference is biologically determined and unavoidable. The so-called PROGRESS criteria are the internationally accepted criteria set to use (Place of residence, Race/ethnicity/culture, Occupation, Gender/, Religion, Education, Socioeconomic status, and Social capital).[4 5]

Adverse perinatal outcome rates appeared to be much higher in the four largest cities (Amsterdam, Rotterdam, Den Haag, and Utrecht – the so-called G4-cities).[6 7] Additionally, inequalities were observed at neighborhood level within these G4-cities.Women with higher risk loads especially found in deprived districts and are often associated with socio-economic and ethnicity related risk factors such as low education, low-income and poor integration into society. Socio-economic status and neighbourhood deprivation are most consistently related to these adverse outcomes.[8 9]

In order to gain more insight in the causes of the situation in the Netherlands and to prioritize research at a national level, the Signalement study was performed in which the concept of 'Big 4 morbidities' was introduced.[10] This study was based on a detailed analysis of a complete perinatal registry available from the Dutch Perinatal Registry (PRN).[11 12] The analysis provided the insight that 85% of the mortality cases were preceded by four types of perinatal morbidity, called the Big 4 conditions. These Big 4 conditions include: small for gestational age (birth weight < 10^{th} percentile for gestational age), preterm birth (< 37^{th} week of gestation), congenital anomalies (list defined), and low Apgar score (<7 after 5 minutes).[10 13] At least three of these conditions (Apgar score excluded) were subject to risk factors.

Evidence from large cohort studies and the Dutch perinatal registry demonstrated that effects of non-medical risk factors on perinatal outcomes were as important as medical or obstetrical risk factors. These non-medical risk factors include lifestyle and social risk factors such as working conditions, educational level, and household income.[14-17] The contribution of these factors to pregnancy outcome inequalities was due to the prevalence of inequalities, variation in the relative risk of the risk factor itself (with more risk in for example disadvantaged women), or both.[18 19] An additional mechanism is that if risk factors are present in certain combinations, there is a cumulative effect of risk factors. The risks can be larger than the single risks of risk factors added together. This phenomenon, called risk accumulation, may enhance already existing inequalities.[16 17]

Previous studies indeed showed that non-medical risk factors and risk accumulation were particularly observed amongst women living in deprived areas (characterized by overrepresentation of low socio-economic status, single parenthood, and immigrant status.[8 9 20]

Antenatal risk assessment: medical and non-medical risk factors

Non-medical risk factors such as socio-economic status and lifestyle never received much attention in antenatal care.[21] Current antenatal risk assessment is based on the national guideline for indications for referral to a gynaecologist (in Dutch this is called 'de VIL'). In this guideline, indications for referral encompass medical and obstetrical risk factors only.[21] Risk assessment not only lacked to address non-medical risk factors, it also missed a comprehensive tool for standardized risk assessment. In response to the need, a new risk assessment instrument which also incorporated the concept of risk accumulation was developed in the Ready for a Baby program.[22] This instrument, the so-called Rotterdam Reproductive Risk Reduction score card (R4U scorecard), connects medical and non-medical risk factors in a non-invasive, standardized scorecard that can be used for routine use in antenatal healthcare. Risk factors were included in the R4U score card if they had an evidence based relation with one or more of the Big 4 conditions. The result ('score') can directly be linked to early clinical management protocols or care pathways. In addition, a risk score above a predefined cut-off point can be used to assess pregnant women multidisciplinary.

Current position of the Netherlands

Results from the Peristat III report suggested improvement of the Dutch perinatal rank.[23] Both fetal (>28 weeks of gestation) and neonatal (>24 weeks after birth) mortality rates declined between 2004 and 2010 in the Netherlands. The professional organisations of midwives and obstetricians concluded that the perinatal outcome improved in the Netherlands and that future reports should confirm whether improvement was temporarily or structural.[24]

In our view, this judgement was too optimistic.[25] Firstly, the definitions used by the Peristat group (and corresponding publications) were not in correspondence to the definition of perinatal mortality set by the World Health Organisation (WHO). The WHO defines perinatal mortality as mortality as of 22 weeks of gestation instead of 24 or 28 weeks of gestation, which was used by Peristat.[26] This might have led to an underestimation of the figures presented. Secondly, not every European country was able to present birth weights in combination with gestational age to Peristat. This made it impossible to distinguish between prematurity and dysmaturity, both important but fundamentally different risk factors for perinatal mortality.[27] Thirdly, numbers were not standardized for

population characteristics such as age or parity and countries differed in organisational aspects and quality of antenatal healthcare.

To create a more valid comparison, we compared the Netherlands with surrounding countries that are comparable in terms of precision, quality of antenatal healthcare, and population characteristics. When we carefully compared Dutch perinatal statistics to similar data from Belgium (Flanders in particular), Scandinavian countries, and Germany, the assumed improvement was less clear.[25] We created a bar graph (figure 1.1) that depicts mortality rates (in promille) assessed over pregnancies as of 22 weeks of gestation (the definition of the World Health organization). We distinguished fetal mortality (defined as mortality as of 22 weeks of gestation per 1000 births) and early neonatal mortality (defined as mortality until 7 days postpartum per 1000 births), and if combined better known as perinatal mortality as defined by the World Health Organisation (figure 1.1). This graph shows that, despite the glimmer of hope the Peristat II initially brought, we still have the highest absolute perinatal mortality rates compared to surrounding countries.

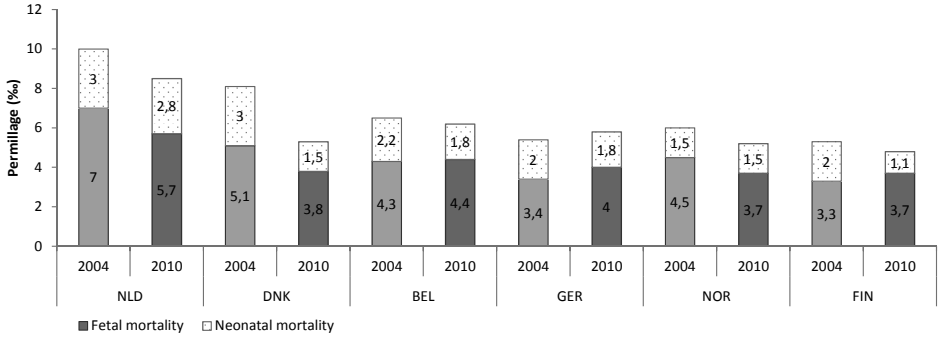

Figure 1.1 Fetal and neonatal mortality rates in the Netherlands compared to surrounding countries in 2004 and 2010.

Rates for perinatal and neonatal mortality originate from the Peristat II (2004) and III (2010) reports respectively, but an exception was made for Belgium. These rates originate from the Study centre for Perinatal Epidemiology (SPE)3 and represent Flanders only. With the addition of rates from Wallonia and Brussels in the 2010 report, these numbers were otherwise incomparable.

NLD = Netherlands, DNK = Denmark, BEL = Belgium (Flanders), GER = Germany, NOR = Norway, FIN = Finland

Adapted from Vos et al, 2014[25]

Initiatives to improve perinatal health

The perinatal mortality rate started a policy process on national level which resulted in broad new measures to improve perinatal health outcome: (a) the institution of a national Advisory Committee (Steering Group) in 2008 that organized expert panels to propose recommendations for improvement of perinatal health outcome, and (b) priority setting for perinatal research by the Netherlands Organisation for Health Research and Development (ZonMw).[28] This resulted in the initiation of local and regional programs, and the aforementioned Signalement study.[10]

The ministry of Health, Welfare and Sports provided in total 9 million euro for the entire period to effectuate the several proposed measures to intervene in perinatal healthcare. A board, the college of Perinatal Health (CPZ), was formed in 2011 to superintend the effectuation of the measures of the Advisory Committee with the perinatal healthcare field.

In Rotterdam the Ready for a Baby program was initiated in 2009 by the Rotterdam municipal council and the Department of Obstetrics & Gynaecology of the Erasmus University Medical Centre.[22] Developed instruments and gained experiences from this public health program resulted in the national Healthy Pregnancy 4 All study. This study was launched in 2011 by the Erasmus University Medical Centre in 14 municipalities in the Netherlands with support of the Ministry of Health, Welfare and Sports. It focused on preconception care and broadened risk selection during pregnancy. In the risk assessment sub-study, on which this thesis was based, we investigated the implementation of the R4U scorecard, corresponding care pathways, and multidisciplinary consultations in antenatal healthcare.

AIM OF THIS THESIS

The aim of this thesis can be summarized as follows:

- To evaluate the policy process that led to the Healthy Pregnancy 4 All study;
- To assess the influence and assessment of non-medical risk factors on perinatal outcomes;
- To study if and how neighbourhood deprivation was related to perinatal outcomes beyond the 'G4-cities'.

These aims are translated into the following research questions:

1. Why and how did the perinatal mortality problem make its way into the national political agenda? (chapter 2)
2. To what extent is it possible to implement a new method of antenatal risk assessment? (chapters 3, 4, and 5)

3. How are non-medical risk factors currently assessed during routine antenatal healthcare? (chapters 6 and 7)
4. What is the contribution of non-medical risk factors to perinatal outcomes and how is this related to risk accumulation? (chapter 8)
5. What is the contribution of neighbourhood deprivation to perinatal outcomes and are there any differences between municipalities? (chapters 9 and 10)

OUTLINE OF THIS THESIS

This thesis consists of three parts, of which each draws evidence from different sources. Part I addresses on initiatives to improve perinatal health, and consists of the chapters two through five. **Chapter two** describes a policy analysis in which we evaluated why and how the perinatal mortality problem made its way to the political agenda and which policies were formulated. **Chapter three** presents an overview of the Healthy Pregnancy 4 All study and the selection of geographical areas for the study. The design and outline of the corresponding risk assessment sub-study are described in **chapter four**. In **chapter five** the implementation of the risk assessment sub-study within the Healthy Pregnancy 4 All study is evaluated. Part II focusses on non-medical risk factors in pregnancy, and consists of the chapters six through eight. **Chapter six** reviews the literature on published risk screening instruments and provides the development of the Rotterdam Reproductive Risk Reduction (R4U) scorecard with its methodological and clinical considerations, and service response towards detected risk factors. In **chapter seven** the assessment, current antenatal policy, and referral possibilities for non-medical risk factors are described. **Chapter eight** presents the study of the prevalence of non-medical risk factors according to and the relation with socio-economic status, ethnicity and geographical areas, and their contribution to adverse perinatal outcomes and risk accumulation. Part III is based neighbourhood deprivation and perinatal outcomes, and consists of the chapters nine and ten. A study regarding the association between neighbourhood deprivation and adverse perinatal outcome is presented in **chapter nine**. **Chapter ten** presents a study which aims to identify perinatal health inequalities on neighbourhood level and the contribution of socio-demographic risk factors to pregnancy outcomes on municipal level.

To resume this thesis, **chapter eleven** elaborates on main findings, methodological considerations and implications for the clinical field and policy making.

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Part I

INITIATIVES TO IMPROVE PERINATAL HEALTH

Chapter 2

Analysis of policy towards improvement of perinatal mortality in the Netherlands

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Submitted

ABSTRACT

Relatively high perinatal mortality and morbidity rates* in the Netherlands resulted in a process which induced policy changes regarding the Dutch perinatal healthcare system. Aims of this policy analysis are (1) to identify actors, context and process factors that promoted or impeded agenda setting and formulation of policy regarding perinatal health care reform and (2) to present an overview of the renewed perinatal health policy.

The policy triangle framework for policy analysis by Walt and Gilson was applied.** Contents of policy, actors, context factors and process factors were identified by triangulation of data from three sources: a document analysis, stakeholder analysis and semi-structured interviews with key stakeholders.

Analysis enabled us to chronologically reconstruct the policy process in response to the perinatal mortality rates. The quantification of the perinatal mortality problem, the openness of the debate and the nature of the topic were important process factors. Main theme of policy was that change was required in the entire spectrum of perinatal healthcare. This ranged from care in the preconception phase through to the puerperium. Furthermore emphasis was placed on the importance of preventive measures and socio-environmental determinants of health. This required involvement of the preventive setting, including municipalities. The Dutch tiered perinatal healthcare system and divergent views amongst curative perinatal health care providers were important context factors. This study provides lessons which are applicable to health care professionals and policy makers in perinatal care or other multidisciplinary fields.

* Zeitlin, J., et al., PERISTAT: indicators for monitoring and evaluating perinatal health in Europe. Eur J Public Health, 2003. **13**(3 Suppl): p. 29-37.

** Walt, G. and Gilson, L., Reforming the health sector in developing countries: the central role of policy analysis. Health Policy Plan, 1994. 9(4): p. 353-70.

INTRODUCTION

The health issue

Several studies have revealed that the Netherlands has relatively unfavorable perinatal mortality rates.[1-3] In 2004, the PERISTAT I study showed that the Netherlands was one of the European countries with the highest perinatal mortality rates (10.5 mortality cases per 1000 births as of 22 weeks of gestation).[3] The Dutch position slightly improved in 2008 (10 mortality cases per 1000 births), but rates remained relatively high compared to other European countries.[3] In response, numerous studies were conducted to identify causes and determinants of perinatal mortality. It became clear that there were large perinatal health inequalities within the country, which were associated with low socio-economic status.[4-8]

Whilst it is widely acknowledged that poor socioeconomic circumstances affect health throughout life, it was only during the last decade that this concept was translated into actual policy regarding perinatal healthcare in the Netherlands. The numbers also brought on that the unique organization of perinatal care in the Netherlands was questioned openly for the first time.

The concern of relatively high perinatal mortality and morbidity rates triggered a policy process which resulted in intervention in the organization of perinatal health care.

The health policy environment

The policy process took place within a uniquely organized field: the Dutch perinatal health system. Figure 2.1 depicts the field that is involved in either formulating or implementing perinatal health policies.

The perinatal healthcare field

The curative care echelon: Curative care in the perinatal healthcare field is comprised of preconception care, antenatal care, labor care and postpartum care. This care is delivered by primary caregivers (midwives in the community), secondary caregivers (gynecologists in secondary hospitals) and tertiary caregivers (gynecologists in university hospitals). Inherent to the Dutch system, gynecologists are also obstetricians. Professionals within these three tiers function autonomously in accordance to their own guidelines. Co-operation between the professionals of the tiers is close because of delineation by the so-called 'List of obstetric indications', or LOI. This consensus based list provides indications to allocate women to care according to either a 'low risk' for pathology or a 'high risk' for pathology. When allocated to the low-risk category, women receive care exclusively from a community midwife and can opt for a home birth or out-patient hospital birth. High risk women are attended to by gynecologists or clinical midwives in the second or third tier, they do not have the option of a home-delivery.

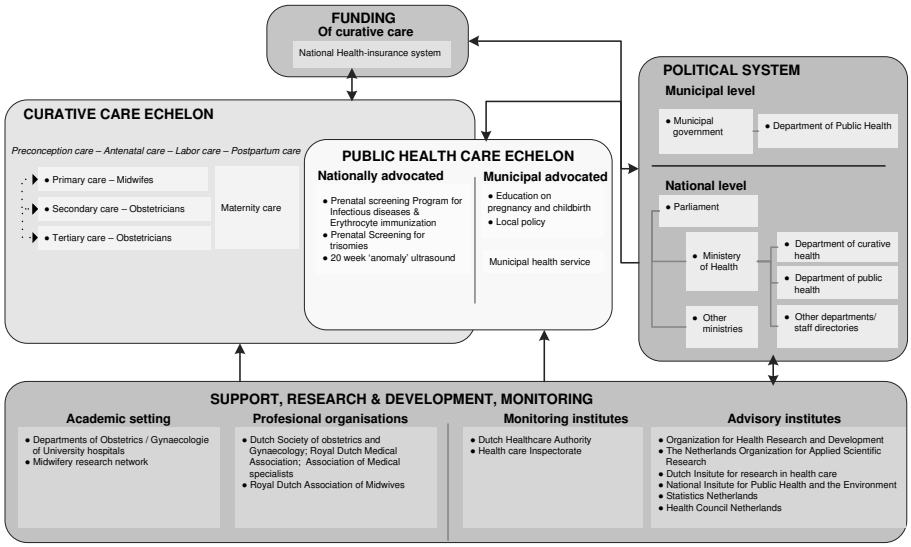


Figure 2.1 The health policy environment.
Adapted from Schafer et al. 2010[26]

The organization model of perinatal care of the Netherlands differs from other countries because of the strong and independent position of midwifery.[9 10] Firstly midwives have power because in the Dutch system they attend to the largest proportion of pregnant women. The fact that women typically start antenatal care with a midwife is driven by the Dutch culture in which childbirth is seen as a natural process. Furthermore, the 'LOI' defines indicated care in secondary and tertiary settings. The latter is only reimbursed after referral by primary care.

Secondly, the government provides favorable licensing laws, insurance regulations and government support for midwifery education.[9] Lastly, the profession organization of midwives safeguards autonomous roles of midwives.[9 10] The autonomy and the large role of midwives is seen as one of the reasons that the Netherlands is a country with relatively non-medicalized birth, with low rates of obstetric interventions (e.g. caesarean section) and high rates of home-births.

The public healthcare echelon: General public healthcare – also referred to as the preventive health care setting - is organized at a municipal level except for a few elements of preventive perinatal care, which are organized nationally (the screening of infectious diseases and erythrocyte immunization, first trimester screening for chromosomal abnormalities and ultrasound detection of fetal anomalies). At a municipal level, the public health departments are responsible for the organization of disease prevention, health promotion, and health protection. Involvement of the municipal public healthcare set-

ting in perinatal healthcare was often restricted to promotion of lifestyle in pregnancy and information about breastfeeding.

Support, research and development

The curative perinatal healthcare field has an extensive infrastructure for research and development. Besides the scientific expertise from universities, there are several private and government led institutes that independently advise the sector. Professionals in the curative perinatal healthcare field are represented by professional organizations. Midwives have their own professional organization, The Royal Dutch Association of Midwives, which aims to strengthen the independent position of midwives by promoting the quality and access to midwifery-led care. Gynecologists are represented in three professional organizations, namely the Royal Dutch Medical Association, Association of Medical Specialists, and the Dutch Society of Obstetrics and Gynecology. The latter is responsible for developing guidelines.

Funding of the system

The curative health system is funded by national health-insurance. Basic health insurance covers all essential curative care. Its content is regulated by the Health Insurance Act. Additional to basic health insurance, insurance companies provide supplementary packages.

Political system and development of health policy

In the Netherlands, health policy is made at national, provincial and municipal level.

Since 2006 the national government's role in health care policy has changed. Instead of being responsible for direct control of volumes, prices, and productive capacity, the national government fulfills a regulatory and supervisory role. Most of the tasks are delegated to independent bodies.

Public health care policy is defined by the Health Ministry, Welfare and Sports (from now on called the Health Ministry) with a national memorandum on public health. This memorandum is written every 4 years by the department of public health – a sub-department of the Health Ministry. Different institutes provide local statistics to identify health and environmental issues which need to be addressed with policy in the memorandum. To shape national policy to meet local needs of municipalities, each municipality writes an additional memorandum. This enables municipalities to deviate from the national memorandum whenever local environmental statistics point out additional needs.

Changes in perinatal healthcare policy

Before 2004, effectuation of perinatal health policy largely depended on the curative system and its own research and development field. Collaboration between policy makers of the departments of curative and public health of the Health Ministry was uncommon. Retrospectively, the perinatal mortality debate has led to policy reform, to many initiatives and to mind switches (e.g. to address socio-economic determinants) in the field. These changes are in stark contrast to the culture prior to the debate, when the way perinatal health care was organized was undisputed.

By benchmarking perinatal mortality and morbidity rates, EURO-PERISTAT has exposed that several European countries have relatively unfavourable perinatal health statistics. Ideally, this benchmarking would result in policy changes to improve perinatal health in these countries. The EURO-PERISTAT group has even formulated the goal to monitor policy initiatives over time.[3] Comparison of policies in response to high perinatal mortality and morbidity rates is informative for countries facing the challenge to improve perinatal health at a population level. This paper provides a retrospective analysis on the policy process that was brought about by publication of perinatal mortality rates by EURO-PERISTAT. To our knowledge this is the first policy analysis in the literature aiming to summarize the policy measures that have been taken after the perinatal mortality debate took flight after the EURO-PERISTAT reports.

With our policy analysis we return to the beginning of the perinatal mortality debate in 2004 and we focus on the policy process and the proposed measures to reduce perinatal mortality and inequality. The aim of this policy analysis was twofold. First, we evaluate 'why' and 'how' the perinatal mortality problem made its way onto the political agenda. Secondly, we present an overview of the overall contents of the renewed perinatal health policy. In the discussion, we elaborate about lessons which can be drawn from this policy process.

METHODS

In this evaluation we applied the Policy Triangle framework for policy analysis by Walt and Gilson (see Supplementary Figure 2.1).[11,12] The variables of this policy triangle (actors, content, context and process) formed the basis for our data collection and organization. Data collection was conducted retrospectively (AV, SVV). The timeframe of the analysis is from 2004 to 2011.

- Document analysis: An electronic search was performed in the database of the Dutch government to identify documents about perinatal mortality.[13] The search was performed for the period of January 2004 to January 2012. Keywords were: Pregnancy,

Perinatal Health and Preconception care. Documents that reported high perinatal mortality rates or about interventions to reduce perinatal mortality were eligible for the document analysis. Two authors (initials removed) assessed eligibility of identified documents. They performed citation tracking; meaning they collected the grey literature (e.g. newspaper articles or scientific publications) cited by important documents. The document analysis provided potential actors and key content of the policy triangle.

- Stakeholder analysis: We defined stakeholders as those individuals or organizations with an interest in an issue or policy, those who might be affected by a policy and those who may play a role in making the policy.[14] A list of stakeholders, their positions and interests with respect to perinatal mortality mas made, based on recollection of the authoring team and the document analysis. Key informants were selected by consensus of the authoring team.
- Interviews: The key informants identified in the stakeholder analysis were interviewed in order to investigate the policy process. Additional interview candidates were identified during the process. The candidates varied from scientists in the curative sector to representatives of the professional organizations to delegates of the national Health Ministry and the Dutch House of Representatives. Interviews were performed according to a semi-structured topic list consisting fixed format and open questions. The interview item list consisted of the following domains: (1) inquiry regarding position and interests to verify the stakeholder analysis, (2) agenda setting and (3) intervention selection. Across these domains questions were formulated to identify elements of the policy triangle (actors, content, context and process factors). The interviews were transcribed verbatim. Fragments of the interviews were coded into elements of the policy triangle (actors, context, content or process) by two authors (initials removed). Interview candidates provided consent for the use of citations.

Elements of the policy triangle (fragments or summaries of interviews or documents) were extracted and classified as 'actor' (individuals or organizations that affect policy), 'content' (substance of a particular policy which details its constituent parts), 'context' (political, economic, social or cultural factors which may have an effect on health policy) or 'process' (the way in which policies are initiated, developed or formulated, negotiated, communicated, implemented and evaluated). These items were organized chronologically in a data spreadsheet. This coding approach was piloted after which the two data extractors (AV, SVV) had consensus on the approach. This allowed us to make a chronological reconstruction of the policy process structured by the elements of the policy process.

RESULTS

The search of our document analysis identified 437 relevant hits of which 64 hits were included in the document analysis (379 hits were excluded after retrieval of the document in case of duplicates or because the topic was not related to perinatal mortality).

The results of the stakeholder analysis are provided in Supplementary Table 2.1. All (delegate(s)) of the identified organizations in were approached. All approached individuals agreed to participate in the interviews. In total 12 interview candidates were interviewed in 9 sessions varying from 30 – 90 minutes.

The identified content of governmental policy was organized in a chronologic time line (Figure 2.2). This formed the basis for the chronologic headings according to which we described the policy process in this section. Actors, content, context and process factors of this chronologic reconstruction were summarized graphically in the policy triangle in Figure 2.3.

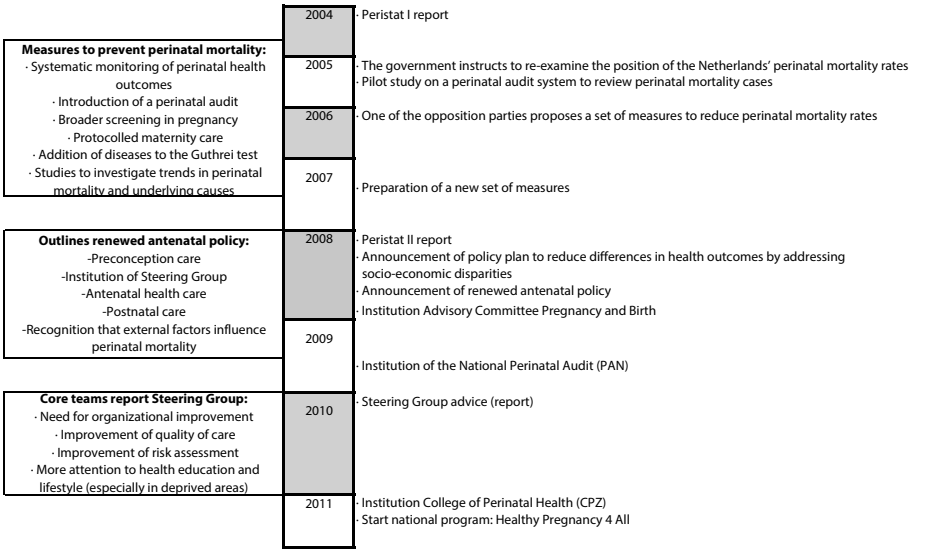
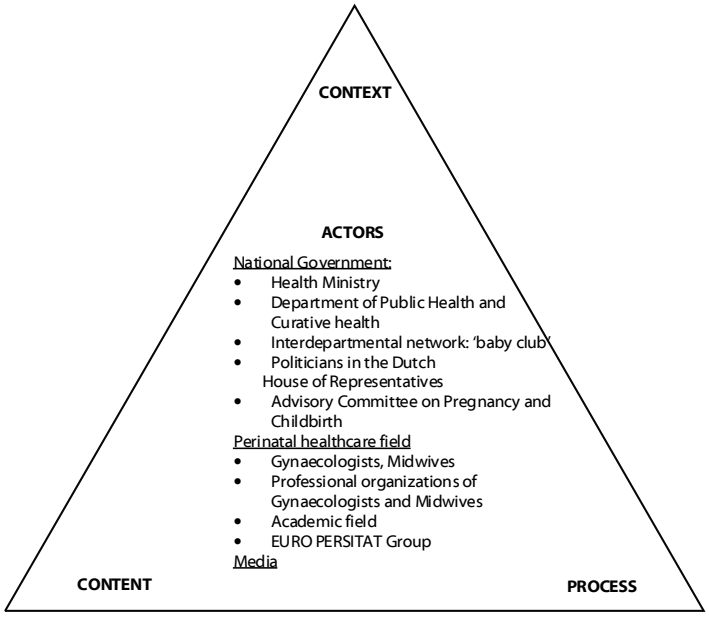


Figure 2.2 Time line: governmental measures to improve perinatal outcomes in the Netherlands in 2004-2011.

First political measures: 2004 – 2008

Up until 2008, perinatal health care was a low priority file to the department of curative care (within the Health Ministry). The file was dormant as there were no large issues within the perinatal health field until the perinatal mortality rates became apparent. According to the interviewed candidates, policy makers were surprised with the perinatal mortality statistics. They perceived that the Netherlands had one of the best perinatal health care systems of Europe. All interviewees confirmed that the results of the first PERISTAT report received little attention from politicians, the professional organizations and health care providers. Interview candidates explained that at first the perinatal mortality statistics were not perceived as a problem because the credibility of the data was debated. The general opinion of the field was that the unfavorable perinatal mortality rates of the Netherlands in comparison to other countries were due to underreporting of perinatal mortality and morbidity rates in other countries. Furthermore, explanations were sought in specific characteristics of the Dutch population (e.g. the relatively older age of future mothers).[15] In 2005 the Minister of Health asked the National Institute for Public Health and Environment to verify the outcomes of the first PERISTAT report.[13] They concluded that the increased perinatal mortality was at least partly explained by factors that can be improved by more effective prevention (i.e. preconception care, smoking cessation). The Health Ministry remained expectative. This led to parliamentary questions. One member of the House of Representatives was particularly dedicated to midwifery-led perinatal care. Perinatal health issues were often directly associated to this member. In the absence of measures from the Health Ministry, the political party of this representative proposed a set of measures to improve perinatal mortality rates in the Netherlands in 2006.[13] In response the Health Ministry introduced an initial set of measures to lower perinatal mortality rates and to improve perinatal health (see Figure 2.2) for the contents of the measures).[13] These measures were largely similar to the measures proposed by the political party of the aforementioned representative. In the meantime this party had become a governing party rather than an opposing party. This provided them with more power. The first preventive measures which were introduced up to 2007 included: 1. systematic monitoring of perinatal health outcomes by a national perinatal database; 2. introduction of a perinatal audit; 3. increased screening in pregnancy; 4. protocolled maternity care; 5. adding diseases to the neonatal screening program (Guthrie test) and 6. commissioning the Netherlands organization for Health Research and Development to set up a research program to investigate trends in perinatal mortality and underlying causes. This came to be the Perinatal Audit. They started to audit term perinatal mortality cases as of January of 2010.

NATIONAL POLICY TRIANGLE



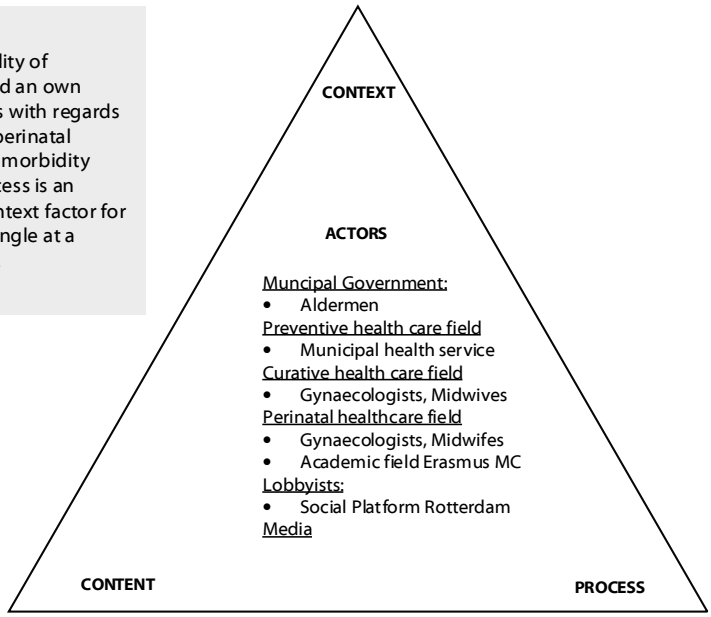
Key elements of the National Policy Triangle

Content	Process	Context
First measures before 2008		
• Expectant management towards Peristat I report • Suggestion of measures by a dedicated member of House of Representatives • Plan to found the first collaborative platform for obstetric care. • Plan to found the Perinatal audit • Plan to found the Dutch Perinatal Registry (PRN) • First policy measures (see Figure 2)	• Peristat I • Reconsideration of Dutch Perinatal mortality rates • Resistance by the political opposition party to the expectant management of the Health Ministry	• Nature of the subject • Obstetrics was a low priority topic for the department of Curative Health .
Renewed perinatal healthcare policy and translation to practice 2008 - 2011		
• Formation of the Steering Group • Allocation of financial resources • Renewed antenatal policy: intervention in care (curative and preventive health care) throughout the whole range of perinatal health care. • Formation of College of Perinatal Health to monitor effectuation of measures proposed by the Steering Group • Commissioning of the 'Pregnancy and Childbirth' research program • Commissioning of the Healthy Pregnancy 4 All program	• Pivot point: recognition of the perinatal mortality problem after Peristat II • Political interference: parliamentary questions required rapid actions • Incontrollable media attention • Founding of the 'Babyclub' • Mind shift from curative to preventive care, emphasis on municipal involvement, as the directory of preventive care picks up the perinatal mortality problem. • Participation of different professionals in the Steering Group to select interventions thought the whole spectrum of perinatal care. • Collaboration between the Department of Public Health and the Erasmus MC to develop an intervention approach	• Unique organization of perinatal health care in the tiered Dutch Health care system • Different key principles between Gynecologists and Midwifes gave friction. • Perinatal health was not embedded as a responsibility of the public health care field. • Trend in community based intervention approaches and effects of physical and social environment on health. • Exemplary intervention program: Ready for a Baby (see Municipal policy triangle). • Repetitive demission of cabinet resulting in shifts in political coalitions from left to liberal wing parties.

Figure 2.3 Policy process.
The policy triangle was used to summarize the policy process according to the policy triangle.

MUNICIPAL POLICY TRIANGLE

The Municipality of Rotterdam had an own policy process with regards to their high perinatal mortality and morbidity rate. This process is an important context factor for the policy triangle at a national level.



Key elements of the Municipal Policy Triangle

Content	Process	Context
• Allocation of resources to effectuate the proposed initiatives to reduce perinatal mortality • Commissioning of the Ready for a Baby program	• Urban perinatal health inequalities and need of organizational change in perinatal health care was recognized by the academic department of Obstetrics. • Bridging between research field and a social lobby platform towards municipal policy makers brought the perinatal mortality problem on the agenda. • Creating engagement amongst curative and preventive sector to collaborate in a municipal based intervention program. • Selection of interventions in different phases of perinatal health care • Transparent program out roll and the novelty of the approach promoted that the program was noticed by national policy .	• High urban perinatal mortality rate and concomitant problem: safety and capacity problems in the midwifery field • Perinatal health (care) became a concern for municipal policy makers • Media attention for municipal problems and solutions • Fast translation from science to care due to the nature of the problem

Renewed perinatal healthcare policy (2008 – 2010)

The PERISTAT II report was a turning point in perinatal health care policy.[1] The Netherlands was confronted with its disadvantaged position in Perinatal Health compared to other European countries for a second time. As a consequence, the Dutch PERISTAT project group and both professional organizations consciously decided to inform the media to achieve political agenda setting. The media eagerly joined the debate. All respondents provided that this was due to the nature of the topic. One respondent stated: "The media invented the term 'baby mortality' instead of 'perinatal mortality', since that is a term that the public is not familiar with. The problem with baby mortality is that is has connotations of healthy babies dying, instead of premature or intra-uterine death." Furthermore, perinatal health is an accessible topic: "almost everybody has an opinion about the topic: birth. Everybody knows somebody who has had a baby, even if they haven't had one themselves. Everybody can condemn a 'baby death rate." Although the media attention appeared to be a useful tool in the beginning, it was felt that the attention became incontrollable and the nuances in the perinatal mortality debate were lost: "the debate took on a life of its own, and then of course you cannot get the genie back into the bottle." The debate diverted to looking at causes for perinatal mortality within the care system – as the way perinatal care is organized in the Netherlands is the most obvious difference with other European countries.

An intense debate between the professional organizations and the step to agenda setting

Whilst professional organizations were paralyzed by disagreement when they were first confronted with the perinatal mortality statistics in 2008, they were forced to agree to work together to reduce perinatal mortality. Interviews confirmed that from this time on both professionals organizations gave the perinatal mortality issue a high priority. However, collaboration between the two was complicated because of the historical incongruous visions of how perinatal health care should be organized optimally. Proposed solutions concentrated on the integration of antenatal care.[13]

The risk approach of gynecologists is not always accepted by midwives. Midwives believe the proactive approach of gynecologists to risk in childbirth leads to unnecessary obstetric interventions. This medicalization of pregnancy is in direct contradiction with the philosophy that birth is a natural process and with client centeredness. According to midwives "A pregnant woman is not a patient to a midwife, for the midwife the pregnant woman is a client: a woman that happens to be pregnant rather than a pregnant patient that happens to be a woman." Aspects regarding risk assessment are a classic dispute between midwives and gynecologists in the Netherlands. According to gynecologists, risk assessment was failing and the dichotomous categorization into high and low risk was failing. "In practice the difference between high-and low-risk patient is difficult to

preempt: in the end somebody in the low-risk compartment can have complications and it occurs that somebody in the high-risk category does not have complications."

Altering the approach to risk assessment touches concepts of 'professional autonomy of midwives' and medicalization ("an increase of 'risk thinking' legitimates more medicalization") and client centeredness.

Another factor that contributed to incongruous visions was the different perspectives on issues of the professional organizations due to their different goals. The professional organization of gynecologists is primarily tasked with providing evidence based guidelines while the safeguarding of the professions interests is delegated to a different organization. In contrast, the professional organization of midwives has both of these roles. They were originally founded to safeguard the position of the midwifery profession. Later they also became responsible for the development of guidelines. Interviews confirmed that this provided an unequal position in the discussion, as this resulted in the questioning of their objectivity in the debate.

Another factor in the policy process was the high public profile of the debate. Both professional organizations stated that attention form the media initially had a positive effect. It provided urgency to address the debate and achieve a consensus regarding the need to intervene in perinatal health. However, later in the debate, the same attention from the media was reported as an impediment. The professional organization of midwives stated that the speed and negativity of the media required a defensive stance, in which they lost time to gain a proactive mode to formulate measures.

Contrary to what one would assume, it was not the professional organizations themselves or the Health Ministry that raised the urgency of addressing the perinatal mortality issue. Rather it was parliament that once again insisted upon a rapid response to resolve the perinatal mortality problem. Due to 17 parliamentary questions (the way to get items on the political agenda and initiate actions by departments), perinatal mortality became a 'key priority' at the Health Ministry.[13] Meanwhile, the aforementioned Representative remained to represent the interest of community midwives. Due to the urgency of the problem a so-called 'Baby club' was initiated at the Ministry of Health. This unique interdepartmental network provided a platform to discuss solutions with policy makers from different departments of the ministry. This enabled them to answer the parliamentary questions rapidly. The functioning of the interdepartmental network was even referred to by one respondent as "disaster command center."

The National Institute for Public Health and the Environment used the national perinatal database to confirm the PERISTAT II data and to reveal potential underlying causes of adverse outcomes. They identified causes within four categories: 1. organization of perinatal care (e.g. travel time to a hospital, collaboration between community midwives and gynecologists or risk assessment), 2. maternal factors (e.g. ethnicity or education level) 3. fetal factors (e.g. congenital anomalies) and 4. socio-demographic

factors (e.g. deprived area).[13] Recognition of these potential causes shed the light on two main themes. Firstly, interventions were necessary within the entire perinatal health care system from the preconception period through to and including the puerperium. Secondly, the role of non-medical risk factors and the influence of neighborhood deprivation on perinatal mortality was recognized to be more important than previously thought.[16 17]

Box 2.1 Renewed perinatal policy

1. **Preconception care:** stimulating folic acid intake; explore the efficacy of general perception and eventually integrate this in the health care system.
2. **Institution of Advisory Committee**: advice on quality-enhancing measures for the entire obstetric chain (from preconception care to maternity care), with special attention to deprivation, organization of care and development of guidelines.
3. **Antenatal health care:** introducing quality indicators, investigation hospital performance at off business hours, special attention to care in deprived neighborhoods (safety and supplementary tariff).
4. **Postnatal care:** evaluating the current effectiveness of maternity care, more extensive screening in the neonatal screening program (the Guthrie test).
5. **External factors:** reducing socio-economic related health inequalities

The Minister of Health needed to come up with rapid measures due to the urgency of the issue created by the House of Representatives by means of parliamentary questions. The Health Ministry presented five main intervention themes (based on prior inquiries) in 2008 which are presented in Box 2.1 and planned to install a Steering Group to refine the strategy to intervene in the organization of perinatal health care the Steering Group was installed in 2008.[13] Specific aims of the Steering group were: to investigate whether the PERISTAT results were correct, to identify potential causes for the higher perinatal mortality rates and to propose specific measures. The Health Ministry placed particular value on the advices forthcoming from this committee and postponed actions until this committee completed its investigation.[13] Two years after its installation, the Steering Group presented a comprehensive report which was widely accepted by the field.[18] The key recommendations of this report were largely in line with the previous policy changes (see box 2.1), but translated into more practical measures: the need for organizational improvement, improvement of quality of care (in particular care in acute situations), improvement of risk assessment, and more attention to health education and lifestyle in and before pregnancy with a focus on deprived areas.[13]

The Minister of Health adopted the plans. However, when the cabinet fell, effectuation of the advices was delayed. This is when the department of public health and the Ministry of Living, Work and Integration became involved to implement the advices of the

Steering Group. From this point on, the direction of curative care of the Health Ministry took a step back.

Simultaneous actions at a municipal level

A local policy process took place in the municipality Rotterdam (see right triangle in Figure 2.3). This process was a contextual factor for the national policy process. Rotterdam had a perinatal mortality rate far above the country's average. The local department of Obstetrics and Gynecology approached a local social platform (an advisory board for societal issues towards politics) to discuss the municipality's inequality in perinatal health and potential solutions with the local Alderman. Once it was realized at municipal level that "you need a healthy start in life to have a healthy society" the agenda was set. Policy makers took on this vision and wrote a memorandum in which they stated the intention to reduce perinatal mortality and morbidity rates to the national level within 10 years.[19] The municipality provided budget to effectuate the proposal which resulted in the 'Ready for a Baby program' as of 2009.[20] The perinatal mortality problems and solutions in the 'Ready for a baby' program caught attention from the Ministry of Health and the House of Representatives. Later it proved to be exemplary in the effectuation of urban perinatal health policy.

From policy to practice (2010 – 2011)

In this period, the department of public health (of the Ministry of Health) became engaged in the perinatal mortality debate. Prior to 2010, perinatal mortality was predominantly seen as a topic for the curative sector and not seen as an item for the public health sector. However, the department of public health persuaded the Health Minister that improvement of perinatal mortality required their involvement. They had the vision that health care should be delivered locally and that "health should be seen in relation to the social and physical environment." This was taken up in the national policy memorandum. It was seen as a challenge to spread this message and to make perinatal health a key priority amongst municipal health policy makers. Furthermore, to intervene in perinatal health collaboration between curative and preventive domains within local municipalities was needed. The department of public health identified the need for a dedicated project to effectuate their vision.

The department of public health persuaded the Minister of Health to allocate extra budget to develop evidence based interventions to reduce perinatal morbidity and mortality rates. In agreement with their vision that policy should address socio-environmental health factors, the intervention would require implementation of preventive measures at municipal level. They recognized that they needed a field partner to engage municipalities in effectuating their vision and evaluating their vision with research. They identified the 'Ready for a Baby' program in Rotterdam. Having approached its executors,

namely the Department of obstetrics of the Erasmus University Hospital, they discussed a national program. This resulted in a research proposal and grant to facilitate what later became the Healthy Pregnancy 4 All program. Two interventions were selected: 1) a preconception care program in which both curative and preventive professionals participate and 2) systematic risk assessment with an antenatal risk assessment tool addressing medical and non-medical risk factors and associating care pathways.[21 22] The program was launched in the deprived neighborhoods of 14 municipalities with the most adverse perinatal outcomes, compared to the national average.[5] The effectiveness of the implementation of two interventions in the local municipal setting was to be assessed by research parallel to the program.[5]

In total, the Health Ministry provided 9 million euro for the entire period to effectuate the proposed measures to intervene in perinatal healthcare. A board, namely the College of Perinatal Health, was formed to superintend the effectuation of the measures of the Advisory Committee.[13]

Perinatal mortality debate: a catalyst to innovate

Retrospectively, this policy process in response to perinatal mortality provided several side effects that resulted in additional events and interventions in the perinatal healthcare field. A selection of these additional events is presented in Box 2.2.

Box 2.2 The catalyzing effect of the perinatal mortality debate: additional events in the perinatal health field

Research field:

- setting of a research agenda (Signalement study)
- calling attention for more funding for research in perinatal healthcare: appointment of the Netherlands organization for Health Research and Development – Pregnancy and Childbirth program
- forming of research consortia

Training:

- accelerated training of more maternity nurses to compensate for shortages
- expansion of the number of training places for midwives and to professionalize the training

Financial:

- additional tariff for midwives in disadvantaged neighborhoods
- debate about personal contribution for outpatient deliveries

Organizational:

- founding of Birth centers
- debate about integrated care

DISCUSSION

Main findings

The Perinatal mortality was a health issue which resulted in a national policy process. In this study we performed a retrospective analysis regarding the agenda setting and formulation of policy to intervene in the perinatal mortality rate between 2004 and 2011.

Attention for the topic resulted in the creation of a new network of policymakers consisting of policymakers from both the department of curative and preventive health, politicians, researchers and practitioners. This resulted in the review of the organization of perinatal health care and formulation of renewed perinatal health care policy. A broad network of actors resulted in the formulation of diverse measures. Policy emphasized preventive care and measures throughout the full spectrum of the perinatal period: from preconception health through to and including the puerperium. It was acknowledged that perinatal health is not solely influenced by biological factors but by social and environmental factors as well and that perinatal health affects health outcomes in adult life.[23] This resulted in the policy that intervention in perinatal mortality requires municipal involvement. The policy process occurred in a relatively short period. The most important process factors where the nature of the topic and the fact that perinatal mortality rates and the public profile of the debate. This promoted that a broad scope of professionals was engaged in the policy process. In contrast, prior to the debate, only policy makers of the department of curative health were involved. Important contextual factors were the organization of perinatal health within the tiered health care system and divergent views amongst perinatal health care providers.

Key elements in the agenda setting

Firstly, the topic could be targeted because the perinatal mortality problem had been quantified by PERISTAT and by additional research. It was this quantification of perinatal health data that created urgency to act amongst politicians, Aldermen, and the preventive sector. Prior to the debate, the organization of perinatal health had not been evaluated. The system was deemed to be infallible by the majority of policy makers (and society).

Secondly, the nature of the topic was engaging to all actors in the debate. The fact that the topic of perinatal mortality concerns a relatively large group in society made this a subject of interest to politicians, policy makers, health care professionals and the public. The media was eager to be an intermediary and fueled the debate. Especially the involvement of politicians and the media set the speed of the debate. Gynecologists and midwives could not agree upon the ideal organization of perinatal care. However, the high public profile and the speed of the debate forced them to agree that the perinatal health statistics required changing in the organization of perinatal healthcare. Whilst

the whole debate was fiery, there was agreement that rapid interventions were necessary amongst all actors involved.

A key result of the agenda setting was the founding of a new network at a national policy level that committed to identify solutions to intervene in perinatal health. Two actors in these networks (or subnetworks in the perinatal mortality policy process) should be mentioned specially. Firstly the Baby Club, that consisted of policy makers from different departments of the Health Ministry. This network promoted that the department of public health became involved and that measures reflected a more socioeconomic environment oriented approach. Secondly, the Health Ministry appointed a Steering Group which promoted that interventions were selected after input from a multidisciplinary range of actors.

Key elements in the formulation of policy

The relatively unfavorable perinatal mortality rates caused a broad multidisciplinary network to recognize that change in the organization of perinatal health care was required. Prior to these numbers, perinatal health policy was restricted to the department of curative health of the Health Ministry. It can be said that the multidisciplinary scope of actors that arose during the agenda setting was the foundation for the diversity of the contents of policy. Firstly there was a shift in actors involved in policy making: where first policy was only made by the department of curative care, the department of public health became an important actor in policy making. This was enabled by the fact that budget was allocated to the department of public health. They had formulated that policy should incorporate that more attention should go out to non-medical risk factors and that local municipalities should be involved in effectuation of community based health care. The Perinatal health issue became an icon project to effectuate this vision. The academic field became involved in the selection and effectuation of interventions. Secondly, with regards to the key concept to intervene throughout the whole range of perinatal chain from preconception care to care in the postpartum period. The Steering Group should be mentioned. The Steering Group functioned as a bridge between the research field (providing evidence to point out the rationale and the evidence for interventions), midwives and gynecologists and the policy field. This promoted collaboration and the acceptance of measures by the curative field.

Strengths and limitations

To our knowledge this is the first policy analysis aiming to summarize the policy process that took flight after the EURO-PERISTAT reports. This limits comparison to what extent policy measures to reduce perinatal mortality have been taken in other European countries and why they were taken. This is one of the aims of EURO-PERISTAT.[3]

There are many frameworks for the evaluation of policy processes. The policy triangle provided a suitable framework for our policy analysis. It was specifically designed to identify the multitude of factors (content, process, context and actors) that affected policy. In this model context and process factors are equally as important as the actors. We did not investigate changes in the roles of actors or stakeholders, because we deemed these roles as fairly consistent within the relative short period of our study. Therefore this study is of limited value to identify stakeholders for future advocacy of policy. In order to identify stakeholders for future advocacy we would recommend a prospective policy analysis.

Strength of this policy analysis is the triangulation of methods, which provided the opportunity to cross-verify findings from different sources. With the brief stakeholder analysis and snow-ball sampling we aimed to identify key informants for interviews. Triangulation of data from these data sources provided grounds for a coherent policy analysis. However, while triangulation provides the opportunity to verify data, it does not exclude subjective interpretation. The authors of this manuscript are active in the perinatal healthcare field and were involved in the Healthy Pregnancy 4 All project, one of the initiatives that came out of the policy process evaluated in this article. As researchers within the field we noticed policy changes and new bridges amongst professionals in the perinatal health care field, which provided grounds to conduct this study. However, being members of the perinatal health care field can also introduce subjectivity in interpretation of findings. We tempted to limit any potential bias by having the first authors (who were not involved in any of the events prior to 2011) conduct the analysis and the other two authors verify findings. To avoid bias in observations it would have been ideal to objectivize verify findings with an external observer, without any involvement in the policy process. However, to our knowledge everybody with enough authority to verify findings, would by definition have a role in the perinatal field and thus per definition have a potential bias due to their position.

Many countries have highly specialized obstetric care systems and underdeveloped collaboration between curative and public health care like the Netherlands.[24] We believe this study can generate thought regarding contents of policy, as it is largely based on current literature (e.g. importance of socioeconomic determinants in health), which is applicable regardless of system factors.

Practical implications and recommendations

The implications and recommendations for health care professionals and policy makers confronted with health issues in a similar fragmented field can be summarized as follows:

- Demonstrating the importance of the problem (numbers are essential) can help to bring policy issues to the agenda.

- Placing the problem in a multidisciplinary context can result in identification of new solutions. Collaboration between the academic field (knowledge) and politics (money and policy), and between the curative and preventive sector resulted in new measures. This is an example of how investing time in the identification of the stakeholders with whom you share a problem can be rewarded with better collaboration in the selection of interventions.
- Urgency and fast actions can be enforced by engaging the political field and the media. However, this should be done with caution as it can polarize discussions in such a way that they which may become incontrollable.
- Finding a network that is aware of your problem or related problems can increase the likelihood that resources are allocated to solve your problem. In this policy process the perinatal mortality debate proved to be a catalyst for solutions to related problems.
- Reducing perinatal mortality and inequalities in perinatal health requires integration of care from the curative and the preventive sector. National governments need to collaborate with municipalities to deliver perinatal health care that addresses socio-environmental determinants in a tailored fashion.

CONCLUSIONS

Over the past decade politicians and policy makers have acknowledged that the high perinatal mortality rates were a national health issue over the past decade. This resulted in new policy. Regarding content of formulated policy, we observed that prior policy policies were related to care within the curative setting. Key features of new policy were firstly that intervention was necessary throughout the full range of perinatal care (from the preconception care period to the postnatal period. Secondly, interventions would have to address socio-demographic factors that influence perinatal health. This shift to addressing socio-environmental determinants of perinatal health requires municipal involvement.

The broad range of actors led to the diversity of interventions. Where there was disagreement regarding intervention selection at first, agreement and interventions selection was enforced by political pressure and mediated by the Steering Group. However, according to politicians, future debates should reveal the role of the perinatal healthcare field in further solutions of the problem: "From now on the ball is in their court." This policy analysis focused on formulated policy. Future research needs to evaluate the extent to which policy has been implemented and been effective in reducing perinatal mortality.

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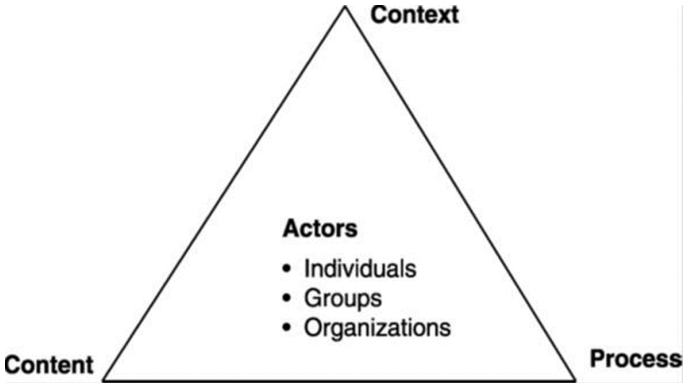
SUPPLEMENTARY FILES



Supplementary Figure 2.1 The policy framework by Walt and Gilson.
This figure depicts Walt and Gilson's Policy Triangle framework which was applied for this policy analysis.11 12 Central in this triangle are the actors. The term 'actors' refers to individuals in a particular system or organization. These actors have a role in the policy process by interplay with context, content and process. 'Context' refers to systemic factors as political, economic, social, and (inter)national factors which may have an effect on health policy. They can be classified into structural, situational, cultural or exogenous factors.25 'Process' refers to the way in which policies are initiated, developed or formulated, negotiated, communicated, implemented and evaluated.12 Process can be classified into phases in different ways. Buse et al. propose the following stages: problem identification and issue recognition, policy formulation, policy implementation and policy evaluation. The triangle connects these variables: actors, content, context and the process influence and interact with each other.12

Supplementary Table 2.1 Stakeholder analysis: Involvement, interests, power, position regarding the issue and influence of the issue on the actor.

Stakeholders	Involvement	Interests	Power/ Influence	Position	Impact of issue on actor
Erasmus Medical Center - Department of Obstetrics and Gynaecology	Provision of information regarding the health issue and potential interventions and evaluation of these interventions (from a clinical and scientific point of view).	HIGH	MEDIUM	SUPPORTIVE	LOW
Ministry of Health, Welfare and Sport	Accountancy regarding the Health system and signaling of problems in the Health system, inequalities - from a policy makers point of view.	HIGH	HIGH	SUPPORTIVE	HIGH
Member of chamber	Committing to decrease perinatal health inequalities amongst ethnic minorities from a political - socialistic point of view.	HIGH	HIGH	SUPPORTIVE	HIGH
Municipal Health Service of Rotterdam	Provision of experiences in identification of the need to intervene in Perinatal health and to seek collaboration between municipal parties, academic hospitals and community health care providers.	HIGH	MED/ LOW	SUPPORTIVE	MEDIUM
The Royal Dutch Organisation of Midwives	Accountancy regarding midwives and their practices (guidelines and education) in the field and advocacy of midwives.	HIGH	HIGH/ MED	SUPPORTIVE	HIGH
Dutch Society of Obstetrics and Gynaecology	Accountancy regarding professionals and their practices (guidelines and education) in the field and advocacy of gynecologists.	HIGH	HIGH/ MED	SUPPORTIVE	MEDIUM
Netherlands Organization for Applied Scientific Research	Delivery of knowledge and evaluation of interventions regarding perinatal health.	MEDIUM	HIGH	SUPPORTIVE	LOW
Institute for public health and environment	Delivery of knowledge and evaluation of interventions regarding perinatal health.	MEDIUM	HIGH	NEUTRAL	LOW

This table presents the results of the stakeholder analysis performed to assist the actual policy analysis in the identification of key informants in the policy process. Characteristics of each of these stakeholders were identified based on pre-knowledge before the policy analysis.

Chapter 3

The Healthy Pregnancy 4 All Study: Design and cohort profile

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ABSTRACT

Background Promotion of healthy pregnancies has gained high priority in the Netherlands because of the relatively unfavourable perinatal health outcomes. In response a nationwide study Healthy Pregnancy 4 All was initiated. This study combines public health and epidemiologic research to evaluate the effectiveness of two obstetric interventions before and during pregnancy: (1) programmatic preconception care (PCC) and (2) a systematic antenatal risk assessment (including both medical and non-medical risk factors) followed by patient-tailored multidisciplinary care pathways. In this paper we present an overview of the study setting and outlines. We describe the selection of geographical areas and introduce the design and outline of the preconception care and the antenatal risk assessment studies.

Methods/design A thorough analysis was performed to identify geographical areas in which adverse perinatal outcomes were high. These areas were regarded as eligible for either or both sub-studies as we hypothesised studies to have maximal effect there. This selection of municipalities was based on multiple criteria relevant to either the preconception care intervention or the antenatal risk assessment intervention, or to both. The preconception care intervention was designed as a prospective community-based cohort study. The antenatal risk assessment intervention was designed as a cluster randomised controlled trial – where municipalities are randomly allocated to intervention and control.

Discussion Optimal linkage is sought between curative and preventive care, public health, government, and social welfare organisations. To our knowledge, this is the first study in which these elements are combined.

BACKGROUND

Perinatal mortality rates in the Netherlands are high and decline slower than in other European countries.[1-3] Furthermore, an inequality in adverse perinatal outcomes is seen as more risks and a higher risk load for adverse outcomes were found for women living in socially deprived areas.[4] Population-based cohort studies, e.g., the Generation R[5] and ABCD[6] studies have contributed to our knowledge of various health problems in pregnancy and childhood and their lasting impact on health in later life. Studies using a large national Dutch database (The Netherlands Perinatal Registry) showed increased adverse pregnancy outcome in large urban areas, in particular in deprived neighborhoods.[7,8] Analyses of this database provided recognition that four specific morbidities precede perinatal mortality in 85% of cases, the so-called 'Big4' morbidities.[9,10] These are: congenital anomalies (list defined), preterm birth (<37th week of gestation), small for gestational age (SGA, birth weight <10th percentile for gestational age) or low Apgar score (<7, 5 minutes after birth).

Taking prior research into account, a nationwide study focusing on deprived areas with a higher than average perinatal mortality and morbidity rate was designed. Our strategy was to perform a thorough epidemiological analysis to identify areas in which interventions would theoretically have the highest impact in improving perinatal health.

Healthy Pregnancy 4 all

With the support of the Ministry of Health and Welfare a nationwide study called 'Healthy Pregnancy 4 All' (HP4All), was initiated. Several municipal pilot studies in the city of Rotterdam provided its framework.[11] The main objective of HP4All is to evaluate the effectiveness of the interventions and their associated preventive strategies in either the preconception period or the antenatal period to reduce adverse pregnancy outcome. Accordingly, two sub-studies are designed: a population-based prospective cohort study focusing on the effectiveness of customized preconception care (PCC) and a systematic antenatal risk assessment score-card including both medical and non-medical risk factors followed by patient-tailored multidisciplinary care pathways.

The rationale of the PCC sub-study originates from increasing evidence showing the critical influence of embryonic development and placentation during early pregnancy on pregnancy outcome.[12-14] Risks influencing this early pregnancy phase can be modified optimally in the preconception period.[14-16] The Dutch Health Council recommended (2007) to integrate general PCC in the health care system.[17] The Minister of Health, however, advised to evaluate the utilization and effectiveness of PCC for high risk groups first, before collective reimbursement of PCC in Dutch obstetric care would be (re)considered.

The second sub-study concerns a cluster randomized controlled trial, focusing on the early detection of risks for adverse pregnancy outcomes with a score card including both medical and non-medical risks. The unique Dutch system of obstetric care system has three risk-based levels of care: primary care (indicated for low risk pregnancies and deliveries, provided by independently practicing midwives), and secondary/tertiary care (indicated for high risk pregnancies, provided by obstetricians).[18] As the level of care depends on the distinction between low risk and high risk pregnancies, antenatal risk assessment is an important part of Dutch obstetric care.[18] Although social deprivation has been shown to contribute to adverse perinatal health in the Netherlands, standard risk assessment does not include the assessment of non-medical risks of perinatal health.[4,7,19,20] In addition, subsequent patient-tailored pathways are lacking. Therefore, in the new antenatal risk assessment tool ('R4U score card') both medical and non-medical risk factors are explicitly taken into account as part of the HP4All study.

The aim of this paper is to present an overview of the HP4All study. Below, we first describe the selection of geographical areas most eligible for the interventions. Next we introduce the design of the preconception care and the antenatal risk assessment sub-studies.

METHODS/DESIGN

Identification and selection of the eligible geographical areas for the interventions

The first step was the identification of the geographical units in which the aforementioned sub-studies would preferably be carried out. We used a national Geographic Information System (GIS) to divide The Netherlands into 62 municipalities, being the 50 municipalities with > 70.000 inhabitants and the 12 provinces (excluding the 50 previously selected municipalities). The second step involved the selection of municipalities in which to carry out the sub-studies, based on multiple criteria which are relevant to either the preconception care intervention or broadened antenatal risk assessment.

Of the 50 cities with >70.0000 inhabitants, we selected municipalities according to socio-demographic parameters associated with high risk load (maternal age, parity, ethnicity, and socioeconomic status) and perinatal outcome data (overall 'Big4' and perinatal mortality prevalence). Before the municipalities could be selected, specific parameters that make delivery of PCC or antenatal risk assessment relevant were applied.

For the PCC sub-study these criteria were (1) proportion of women having their first antenatal booking visit at ≥14 weeks of gestational age, and prevalences of (2) congenital anomalies and of (3) SGA. The moment of the first antenatal booking is important because it is a condition for timely intervention upon present risk factors. The effective-

Table 3.1 Demographic characteristics of the study population by yes/no 'G4-cities' (the four largest cities) with percentages in brackets

	G4-Cities	NETHERLANDS MINUS G4-CITIES	TOTAL
No.of pregnancies during study period	245445 (100.0)	1338420 (100.0)	1583865 (100.0)
Parity			
Primiparous	121592 (49.5)	607953 (45.4)	729545 (46.1)
Multiparous	123853 (50.5)	730467 (54.6)	854320 (53.9)
Ethinicity			
Western	139786 (57.0)	1186772 (88.7)	1326558 (83.8)
Non-Western	105659 9(43.0)	151648 (11.3)	257307 (16.2)
Maternal age			
< 20 years	6987 (2.8)	19861 (1.5)	26848 (1.7)
20-24 years	34864 (14.2)	127013 (9.5)	161877 (10.2)
25-29 years	61354 (25.0)	395138 (29.5)	456492 (28.8)
30-34 years	85444 (34.8)	535927 (40.0)	621371 (39.2)
≥ 35 years	56796 (23.1)	260481 (19.5)	317277 (20.0)
Socioeconomic 'status score'			
<p20	145367 (59.2)	254607 (19.0)	399974 (25.3)
p20-p80	58641 (23.9)	853074 (63.7)	911715 (57.6)
>p80	41437 (16.9)	230739 (17.2)	272176 (17.2)
Neighbourhood			
Non-deprived	165658 (67.5)	1320392 (98.7)	1486050 (93.8)
Deprived	79787 (32.5)	18028 (1.3)	97815 (6.2)
Perinatal outcomes**			
Congenital anomalies	5233 (2.1)	33159 (2.5)	38392 (2.4)
Preterm birth	15673 (6.4)	81646 (6.1)	97319 (6.1)
Small for gestational age	27724 (11.3)	125175 (9.4)	152899 (9.7)
Apgar score <7	3385 (1.4)	14818 (1.1)	18203 (1.1)
(5 minutes after birth)			
Any Big4**	50267 (20.5)	242697 (18.1)	292964 (18.5)
Fetal mortality†	1478 (0.6)	6718 (0.5)	8196 (0.5)
Intrapartum mortality	458 (0.2)	2126 (0.2)	2584 (0.2)
Neonatal mortality††	761 (0.3)	3547 (0.3)	4308 (0.3)
Perinatal mortality‡	2697 (1.1)	12391 (0.9)	15088 (1.0)

** Individual 'Big4' morbidities do not add up to 'any Big4'.
as women can have >1 'Big4' morbidity.
† From 22 weeks of gestational age.
†† 0–7 days postpartum.
‡ Total of fetal, intrapartum and neonatal mortality.

ness of these interventions is larger in an early fetal stage. Congenital anomaly and SGA prevalences are considered to be indicative for a region's periconceptional health status.

For the antenatal risk assessment sub-study, additional criteria were (1) overall perinatal mortality rates, (2) perinatal mortality amongst women with 'Big4' pregnancies ('case-fatality'), and (3) prevalence of SGA and prematurity. For each specific indicator we present the absolute rate, the standardised rate and the so-called inequality-rate, the latter being expressed as the relative risk of the outcome for low SES (socioeconomic status) pregnant women compared to high SES pregnant women, after direct standardisation for maternal age, parity and ethnicity. Standardisation[21] is needed because a region with, e.g. a high number of non-Western women or a high number of teenage pregnancies will generally have a higher prevalence of adverse perinatal outcomes.

Data sources

The division of The Netherlands into 62 municipalities was based on 4-digit postal codes areas. Data were provided by the Falk company (www.falk.nl), the National Public Health Authority, and the Statistics Netherlands organisation (CBS, www.cbs.nl). Information on socioeconomic status (SES, determined in 2006) per postal code area was obtained from the Social and Cultural Planning Office (SCP, www.scp.nl). Data on pregnancy and perinatal outcome were derived from The Netherlands Perinatal Registry (2000–2008). This database contains information of more than 97% of all pregnancies in The Netherlands.[21] The data are routinely collected by 94% of midwives, 99% of gynaecologists and 68% of paediatricians including 100% of Neonatal Intensive Care Unit paediatricians.[21]

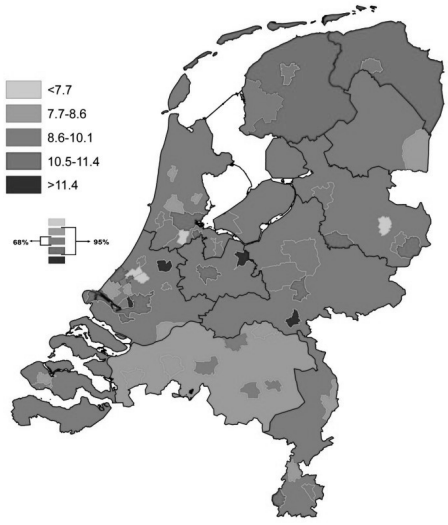

Figure 3.1 Absolute prevalence of perinatal mortality per 1000 births.

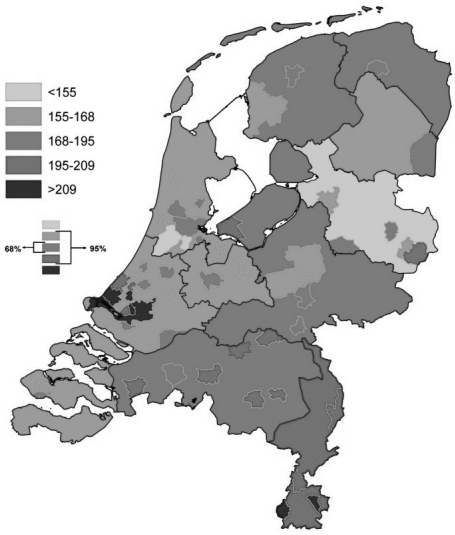

Figure 3.2 Absolute prevalence of 'Big 4' morbidities per 1000 births.

Table 3.1 shows the demographic characteristics of the so-called 'G4-cities', i.e. the four largest cities: Amsterdam, Rotterdam, The Hague, Utrecht, and the rest of the Netherlands. Compared to the rest of The Netherlands, the 'G4'-cities have a larger proportion of non-Western women (43% vs. 11.3%), more teenage pregnancies (2.8% vs. 1.5%), and more women in low SES neighbourhoods (59.2% vs. 19.0%). Considerably more women live in deprived neighbourhoods (32.5% vs. 1.3%) and the overall adverse perinatal outcome is worse in 'G4-cities', as illustrated by a 'Big4' prevalence of 20.5% compared to 18.1%.

Perinatal mortality and 'Big4' prevalence

Figures 3.1 and 3.2 illustrate the geographical distribution (50 municipalities and 12 provinces) of perinatal mortality rates, and the prevalence rate of 'Big4' (per 1,000), respectively. Various shades of red represent the different prevalence classes, the darker the shade the more prevalent the adverse outcome. The classes are based on the distribution of the rates: the middle three classes comprise 95% (2 standard deviations) of the outcome levels; the middle class comprises 68%. Both figures show large geographical inequalities in adverse perinatal outcomes on the national level.

Comparison municipalities

We additionally compared these outcomes across areas after direct standardisation[22] for population differences by maternal age, parity, ethnicity, and SES. Standardisation is needed because a region with, e.g. a high number of non-Western women or a high

Table 3.2 Selection criteria* for the preconception care experiment with scoring in deciles; the higher deciles represent a more likely qualification for inclusion

		DEMOGRAPHICS				1ST ANTENATAL BOOKING ≥14W			CONGENITAL ANOMALIES			SGA			RANK
#	*CITIES*	% PREG	AGE <20	NW ETHN	LOW SES	ABS	STND	INEQ	ABS	STND	INEQ	ABS	STND	INEQ	
1	Amsterdam	10	8	10	10	10	10	3	3	2	7	8	6	9	96
2	Rotterdam	10	10	10	10	10	10	3	6	7	4	10	9	6	105
3	Den Haag	9	10	10	10	10	10	2	9	8	4	10	9	8	109
4	Utrecht	9	3	10	6	10	10	4	10	10	7	3	2	7	91
5	Eindhoven	8	7	9	7	9	9	6	8	9	8	9	9	5	103
6	Tilburg	8	8	9	9	5	4	10	4	4	5	10	10	3	89
7	Almere	8	7	10	3	10	9	1	7	7	6	9	8	8	93
8	Groningen city	7	9	5	9	2	2	5	2	2	4	5	3	5	60
9	Breda	7	6	6	5	3	1	9	9	9	3	6	7	4	75
10	Nijmegen	7	5	6	9	3	3	9	4	5	6	8	8	6	79
11	Enschede	6	8	8	10	4	4	2	5	5	3	9	7	6	77
12	Apeldoorn	6	5	3	2	6	7	4	1	1	9	5	4	10	63
13	Haarlem	7	3	7	6	8	7	3	1	2	7	4	4	7	66
14	Arnhem	6	9	9	8	8	5	7	6	6	3	7	7	5	86
15	Zaanstad	6	4	8	6	7	7	1	2	3	2	5	4	8	63
16	Amersfoort	7	2	7	4	9	9	7	5	6	6	3	2	4	71
17	Haarlemmermeer	7	1	4	1	4	5	4	1	1	2	2	2	7	41
18	's-Hertogenbosch	5	3	3	4	1	2	10	9	9	4	8	8	4	70
19	Zoetermeer	5	6	8	3	1	1	6	4	4	1	7	6	10	62
20	Zwolle	6	7	3	4	2	3	7	2	1	7	2	1	10	55
21	Maastricht	4	9	4	6	4	3	10	10	10	10	10	10	1	91
22	Dordrecht	6	10	9	7	9	8	3	2	1	3	7	7	8	80
23	Leiden	5	4	7	6	8	8	6	8	7	10	6	5	3	83
24	Emmen	4	6	1	10	4	5	10	2	2	7	6	4	9	70
25	Ede	5	6	3	5	5	6	6	7	8	2	1	1	5	60
26	Venlo	3	7	8	7	3	2	8	6	6	5	9	10	1	75
27	Westland	4	1	1	1	5	7	6	10	10	8	1	1	10	65
28	Deventer	5	6	6	8	7	8	7	7	7	2	7	7	2	79
29	Delft	3	7	9	9	7	5	7	10	10	10	5	5	6	93
30	Sittard-Geleen	3	8	3	7	1	2	10	5	4	4	9	8	1	65
31	Leeuwarden	4	10	4	9	5	4	8	8	8	2	5	3	10	80
32	Alkmaar	4	4	6	5	6	6	8	5	5	10	2	2	2	65
33	Heerlen	2	10	5	10	3	4	8	10	10	3	10	10	2	87
34	Helmond	5	5	7	6	6	5	4	8	8	5	9	10	1	79
35	Hilversum	1	5	5	3	9	9	1	1	1	8	3	5	1	52
36	Súdwest Fryslân	3	5	1	8	2	2	9	2	2	10	1	1	3	49
37	Amstelveen	2	1	8	2	8	8	1	1	1	10	2	1	10	55
38	Hengelo	4	6	4	7	5	6	1	4	3	1	4	4	5	54
39	Purmerend	2	4	6	4	9	10	1	3	5	1	4	6	9	64
40	Roosendaal	2	5	9	1	2	1	8	9	9	8	8	10	1	73
41	Oss	2	2	4	3	1	1	7	5	4	9	10	10	2	60
42	Schiedam	1	10	10	10	10	10	2	7	6	4	10	9	7	96
43	Spijkenisse	1	9	7	4	3	2	5	3	3	1	6	9	4	57
44	Leidschendam-Voorburg	2	2	7	3	8	7	5	5	4	9	3	5	5	65
45	Alphen a/d Rijn	1	2	5	1	4	4	9	7	8	1	4	4	6	56
46	Almelo	3	8	5	8	2	3	1	1	1	9	7	6	1	55
47	Vlaardingen	1	8	10	5	7	4	8	6	5	9	8	8	4	83
48	Gouda	3	3	8	8	3	1	9	1	3	3	4	3	3	52
49	Middelburg	1	9	4	7	6	6	4	8	6	6	4	3	3	67
50	Vlissingen	1	10	6	5	8	6	5	6	8	1	8	9	3	76
#	*PROVINCES*														
51	Groningen	8	7	2	9	7	9	5	3	2	8	5	6	7	78
52	Friesland	9	4	1	8	9	9	3	10	10	8	2	3	9	85
53	Drenthe	9	3	1	5	6	8	6	4	4	2	3	5	8	64
54	Overijssel	9	1	1	2	5	7	2	3	3	6	1	2	9	51
55	Gelderland	10	2	2	2	1	3	3	10	9	9	2	3	6	62
56	Utrecht	10	1	3	1	2	3	5	9	9	5	1	1	7	57
57	Noord-Holland	10	1	2	2	7	8	2	6	6	5	1	1	8	59
58	Zuid-Holland	10	2	2	1	4	5	4	8	7	7	1	2	9	62
59	Zeeland	8	3	1	3	10	10	2	4	5	1	3	5	4	59
60	Noord-Brabant	10	1	2	1	1	1	9	7	7	5	6	7	2	59
61	Limburg	9	4	2	2	1	1	10	9	10	6	7	8	2	71
62	Flevoland	8	9	5	4	6	6	6	3	3	9	6	6	7	78

10% highest score
10-20% highest score
10% lowest score

* '% PREG':% pregnant women in the general population / 'AGE <20':% teenage pregnancies / 'PRIMI':% primiparous women / 'NW ETHN':% non-Western pregnant women / 'LOW SES':% women in neighbourhoods with a socioeconomic status score < p20 / 'ABS': Absolute% / 'STND': Standardised% / 'INEQ': Inequality as measured by the relative risk of prevalences between women from neighbourhoods with socioeconomic status score < p20 compared to > p80.

Table 3.3 Selection criteria* for the risk selection experiment with scoring in deciles; the higher deciles represent a more likely qualification for inclusion

		DEMOGRAPHICS					PERINATAL MORTALITY / ALL WOMEN			PERINATAL MORTALITY / BIG4 MORBIDITIES			PERINATAL MORTALITY / START LABOUR IN PRIMARY CARE			RANK
#	*CITIES*	% PREG	AGE <20	PRIMI	NW ETHN	LOW SES	ABS	STND	INEQ	ABS	STND	INEQ	ABS	STND	INEQ	
1	Amsterdam	10	8	10	10	10	8	6	9	8	7	7	7	5	8	113
2	Rotterdam	10	10	7	10	10	10	10	3	6	7	3	10	9	5	110
3	Den Haag	9	10	7	10	10	9	8	7	6	7	4	10	8	9	114
4	Utrecht	9	3	9	10	6	9	9	2	9	10	2	7	6	5	96
5	Eindhoven	8	7	9	9	7	5	5	4	2	2	2	9	8	6	83
6	Tilburg	8	8	7	9	9	8	8	6	4	5	8	9	9	3	101
7	Almere	8	7	4	10	3	8	10	3	5	8	3	6	7	7	89
8	Groningen	7	9	10	5	9	7	9	1	8	9	3	2	1	7	87
9	Breda	7	6	6	6	5	3	4	7	2	4	6	7	8	3	74
10	Nijmegen	7	5	8	6	9	10	10	4	10	10	2	6	6	7	100
11	Enschede	6	8	5	8	10	9	9	4	8	6	3	9	8	3	96
12	Apeldoorn	6	5	4	3	2	8	8	8	9	8	8	3	4	10	86
13	Haarlem	7	3	9	7	6	4	6	8	5	6	9	3	2	7	82
14	Arnhem	6	9	10	9	8	9	4	9	9	6	8	5	2	8	102
15	Zaanstad	6	4	6	8	6	2	1	1	2	1	4	5	6	4	56
16	Amersfoort	7	2	6	7	4	10	10	5	10	10	7	1	1	8	88
17	Haarlemmermeer	7	1	5	4	1	4	3	7	7	6	7	1	1	6	60
18	's-Hertogenbosch	5	3	10	3	4	6	5	3	4	4	5	6	7	5	70
19	Zoetermeer	5	6	6	8	3	1	1	2	1	1	1	6	7	10	58
20	Zwolle	6	7	6	3	4	6	2	5	8	4	2	4	1	10	68
21	Maastricht	4	9	8	4	6	8	7	8	3	2	6	10	9	6	90
22	Dordrecht	6	10	4	9	7	2	1	3	2	1	5	7	4	10	71
23	Leiden	5	4	10	7	6	4	2	9	3	2	9	4	5	3	73
24	Emmen	4	6	4	1	10	2	2	1	3	3	1	8	6	10	61
25	Ede	5	6	1	3	5	7	4	9	9	5	10	1	3	2	70
26	Venlo	3	7	5	8	7	3	2	10	3	1	10	10	10	2	81
27	Westland	4	1	1	1	1	1	2	8	1	1	8	8	7	9	53
28	Deventer	5	6	6	6	8	9	9	3	7	5	4	9	10	3	90
29	Delft	3	7	8	9	9	1	1	5	1	1	1	10	10	8	74
30	Sittard-Geleen	3	8	9	3	7	3	1	7	1	1	9	9	9	1	71
31	Leeuwarden	4	10	9	4	9	5	5	10	5	5	10	5	5	5	91
32	Alkmaar	4	4	7	6	5	2	2	10	4	3	10	3	4	1	65
33	Heerlen	2	10	10	5	10	7	8	6	1	2	8	10	10	4	93
34	Helmond	5	5	4	7	6	5	4	8	4	3	10	8	8	2	79
35	Hilversum	1	5	10	5	3	7	5	2	10	8	6	3	3	4	72
36	Súdwest Fryslân	3	5	2	1	8	7	7	10	10	10	10	1	1	7	82
37	Amstelveen	2	1	3	8	2	1	1	10	7	5	9	1	1	10	61
38	Hengelo	4	6	3	4	7	5	7	5	6	6	7	4	4	4	72
39	Purmerend	2	4	8	6	4	2	3	9	5	4	9	7	9	5	77
40	Roosendaal	2	5	5	9	1	2	5	2	1	2	5	9	10	1	59
41	Oss	2	2	5	4	3	3	4	7	1	2	7	8	7	6	61
42	Schiedam	1	10	9	10	10	10	10	9	6	4	8	5	1	4	97
43	Spijkenisse	1	9	8	7	4	10	8	6	9	8	4	6	7	7	94
44	Leidschendam-Voorburg	2	2	7	7	3	1	1	10	4	3	10	2	3	8	63
45	Alphen a/d Rijn	1	2	8	5	1	10	10	1	10	10	5	4	3	5	75
46	Almelo	3	8	3	5	8	1	3	2	2	5	1	6	6	1	54
47	Vlaardingen	1	8	7	10	5	7	10	3	6	10	3	10	10	2	92
48	Gouda	3	3	1	8	8	6	3	10	7	6	9	2	2	3	71
49	Middelburg	1	9	1	4	7	1	3	1	3	4	2	2	2	2	42
50	Vlissingen	1	10	4	6	5	6	9	1	4	7	1	8	10	1	73
#	*PROVINCES*															
51	Groningen	8	7	3	2	9	9	8	6	10	9	6	5	5	4	91
52	Friesland	9	4	2	1	8	10	9	5	9	9	4	4	6	9	89
53	Drenthe	9	3	2	1	5	6	6	2	8	8	2	4	5	9	70
54	Overijssel	9	1	1	1	2	5	7	4	8	9	1	1	3	9	61
55	Gelderland	10	2	1	2	2	5	6	4	5	7	4	3	4	6	61
56	Utrecht	10	1	2	3	1	4	5	4	6	7	3	3	4	6	59
57	Noord-Holland	10	1	3	2	2	4	6	7	7	9	6	1	2	8	68
58	Zuid-Holland	10	2	2	2	1	4	6	1	5	8	1	2	2	9	55
59	Zeeland	8	3	2	1	3	8	7	8	10	10	5	2	3	1	71
60	Noord-Brabant	10	1	3	2	1	3	3	6	3	3	7	7	8	2	59
61	Limburg	9	4	5	2	2	3	4	5	2	3	6	8	9	1	63
62	Flevoland	8	9	1	5	4	6	7	6	7	9	5	5	5	10	87

10% highest score
10-20% highest score
10% lowest score

* '% PREG':% pregnant women in the general population / 'AGE <20':% teenage pregnancies / 'PRIMI':% primiparous women / 'NW ETHN':% non-Western pregnant women / 'LOW SES':% women in neighbourhoods with a socioeconomic status score < p20 / 'ABS': Absolute% / 'STND': Standardised% / 'INEQ': Inequality as measured by the relative risk of prevalences between women from neighbourhoods with socioeconomic status score < p20 compared to > p80.

number of teenage pregnancies will generally have a higher prevalence of adverse perinatal outcomes.

Tables 3.2 and 3.3 show the socio-demographic parameters and the specific criteria for the PCC and the antenatal risk assessment sub-studies. For each specific indicator we present the absolute rate (ABS), the standardized rate (STND) and the inequality-rate (INEQ, the relative risk of the standardised outcome for low SES pregnant women compared to high SES pregnant women).[8] Next, to facilitate comparisons, we assigned decile scores to regions, varying from one (the region is one of the 10% areas with best outcomes) to 10 (the region belongs to the 10% worst outcomes). The sum of the decile scores for the various indicators by region is shown in the last column ('RANK'); higher scores imply unfavourable ranking. For clarity, colors are used to differentiate between favourable and unfavourable outcomes: green represents the first decile (with the best outcome), pink the 10th decile (10% with the most adverse outcomes), the 10th-20th decile. Based on the sum of the decile scores for the PCC sub-study (table 3.2), the pink and amber municipalities have the most adverse outcomes, i.e. 1. The Hague; 2. Rotterdam; 3. Eindhoven; 4. Amsterdam; 5. Schiedam; 6. Almere ; 7. Delft; 8. Utrecht; 9. Maastricht; 10. Tilburg; 11. Heerlen; 12. Arnhem; 13. Friesland. According to the sum of the decile score for the risk assessment sub-study (table 3.3) the following municipalities show the most adverse outcomes: 1. The Hague; 2. Amsterdam; 3. Rotterdam; 4. Arnhem;

Figure 3.3 Participating municipalities in the 'Healthy Pregnancy 4 All' project.

5. Tilburg; 6. Nijmegen; 7. Schiedam; 8. Utrecht; 9. Enschede; 10. Spijkenisse; 11. Heerlen; 12. Vlaardingen; 13. Groningen; 14. Leeuwarden.

Final selection municipalities

After the epidemiological selection of the candidate municipalities the list was first presented to the Ministry of Health. The next step was to inform the Alderman and municipal health authorities about their perinatal health status. They were invited to commit to the HP4All study. Criteria to participate were: a) active involvement by a local Policy Officer (>one day per week for the duration of the study), b) local political support for the study (e.g. financial support, involvement in health related policy, local resources, involvement of local networks).

The following municipalities agreed to participate (see figure 3): in the province of Groningen, Appingedam / Delfzijl / Menterwolde / Pekela and Groningen city, the municipalities of Enschede, Nijmegen, Heerlen, Tilburg, Schiedam, Utrecht, The Hague, Amsterdam, and Almere.

All municipalities decided to participate in both sub-studies. As a separate municipal program on reducing perinatal mortality was already being carried out in Rotterdam[5], this city was not selected for participation in the HP4All study.

In these participating municipalities, general practitioners, midwives, and obstetricians were approached for provision of the interventions. Additional to the identified municipalities, the province of Friesland best qualified for the PCC sub-study and the province of Groningen for the risk assessment sub-study.

INTRODUCTION TO THE SUB-STUDIES

The preconception care sub-study

This sub-study is a prospective cohort that aims to evaluate the effectiveness of individual Preconception Care Consultations and the effectiveness of the employed recruitment strategy for the PCC consultation services. Preconception care consultations are delivered by primary caregivers (General Practitioners and midwifes) in the community. These consultations consist of two sessions. Prior to the first session the woman fills in a questionnaire (www.zwangerwijzer.nl). This questionnaire screens risk factors across the following domains: background, lifestyle, medical history, obstetric/ gynecologic history, family, work/environmental. Thus, risk factor screening is performed in a uniform way before the consultation. During the consultation a history is taken regarding the presence of potential risk factors and a intervention plan is made with the women/ couple to reduce/ eliminate risk factors. Three months later a follow-up consultation is planned to evaluate adherence to the intervention plan.

Uptake of individual PCC is known to be low. Thus additional efforts seem necessary to promote uptake of the consultations.[23] For this purpose a 4-tiered recruitment strategy is employed. Women are informed about the PCC consultations by: (1) an invitational letter from the municipal health service or municipality, (2) invitational letter from the family doctor, (3) referral by the youth health care service, (4) referral by a perinatal health peer educator.

The study population consists of women aged 18 – 41 years old. Participation is voluntary.

There are several primary outcomes. Firstly, the effectiveness of the PCC consultations in terms of behavioral changes (use of folic acid supplements, smoking cessation, cessation of alcohol consumption and illicit substances besides individual risk factors (e.g. obesity). Secondly, the effectiveness of the recruitment strategy is assessed. We address this effectiveness by measuring the extent to which each recruitment arm results in visitation of the PCC service and by the characteristics of women that these recruitment strategies reach.

Women are enrolled in the cohort study after they have made an appointment for the PCC consultation. When they participate they are asked to fill in a questionnaire and consent to laboratory tests before each visit to the PCC health service. Biomarkers are tested to vouch self-reported behavioral change of primary outcomes (erythrocyte folate, %carbohydrate transferrin (CDT), serum cotinine levels and urinary drug tests). Furthermore anthropometric measurements are collected at these two visits by the PCC provider. This data collection provides data for pre- and post-measurements regarding PCC behaviors. Characteristics of women that visit the peer education sessions are measured by questionnaires.

The antenatal risk assessment sub-study

In this cluster randomised trial (Trial registration: Dutch Trial Registry: NTR-3367) midwifery practices in participating municipalities ('clusters') were randomly assigned to either the use of a score card ('R4U') based antenatal risk assessment, care pathways and multidisciplinary consultation (intervention group) or conventional risk assessment (control group).

The 70-item 'R4U' score card consists of six risk domains (social status, ethnicity, care, lifestyle, medical history and obstetric history). Corresponding care pathways to both medical and non-medical services will support health care professionals to encounter complex (non-)medical risk factors. A predefined weighted sum risk threshold, based on weighted single risk factors, is derived from the 'R4U' score card. If a pregnant woman's individual sum risk score exceeds the threshold, her case will be assessed in a multidisciplinary setting with community midwives, obstetricians, and other care providers.

Score card based systematic risk assessment will be performed with the 'R4U' score card at the first antenatal booking visit followed by (provided that informed consent is given), if necessary, a specific referral to, e.g. a higher level obstetric care (gynaecologist), or psychosocial care in case of medical or non-medical high risk using risk-specific care pathways. Additionally, these women at increased risk will be reviewed in a multidisciplinary team of caregivers concerning tailored antenatal care. We aim to assess 20% of all pregnant women in this multidisciplinary setting.

Participating midwives and obstetricians receive personal instructions in planned sessions by the project team for the practical use of the web-based 'R4U' score card. Besides, an e-learning program is available for all caregivers. The project team has developed 28 templates of care pathways for all risk factors in the 'R4U' score card. Together with local healthcare professionals in perinatal care, municipal services, community health services, and other services, these templates will be adapted in organised meetings to local setting, taking the availability of local facilities, agreements, and guidelines into consideration.

Pregnant women's risk status in the control group is assessed conventionally, i.e. according to the elaborate so-called 'List of Obstetric Indications' (in Dutch: Verloskundige Indicatie Lijst)[24] which lists all conventional (>140) high risk indications (for referral or consultation). In each control municipality care 'as usual' will be provided until 700 participants have been included or until 2/3 of the study period (2 years) has passed. After that moment, the implementation of the risk assessment intervention will start.

Primary outcomes are the prevalence of preterm birth and SGA, and the efficacy of 'R4U' implementation (measured by the number of 'R4U' score cards completed by the health care professional against the number of booking visits, the development and use of care pathways following 'R4U' scores, actual performed multidisciplinary consultations, and patient and healthcare professional satisfaction).

Organisation and time schedule

The study is rolled out by the national HP4ALL staff of the Erasmus Medical Center in Rotterdam and by the local HP4ALL project managers. The staff consists of 2 junior researchers, research assistants and 2 project managers (1 for each sub-study) and 2 program directors. The local project managers are either allocated from the municipality or from the municipal health services. Organisation and logistics regarding out roll of the two sub studies is presented in the specific design papers.

The HP4All study was initiated in April 2011. The HP4ALL research team was organised by May 2011. Municipalities had committed to participation in September 2011. Within the municipalities local health care providers eligible to participation in the sub-studies were invited to participate as of November 2011. At time of writing, the study is ongoing.

Ethical considerations

The two The HP4All sub-studies have been approved by the Institutional Board Review of the Erasmus Medical Centre Rotterdam (Preconception Care sub-study: MEC 2012–425; Antenatal risk assessment trial: MEC 2012–322). Participants in both studies will receive written and oral information about the study after which informed consent will be obtained. Participation in either sub-study is voluntary and no extra incentives will be provided. Health care providers participating in both studies do not receive incentives. However in the PCC sub-study, providers will receive reimbursement from the HP4All project, as PCC consultations are currently not covered by (most) health care insurances.

DISCUSSION

In this study we described the set-up of the 'Healthy Pregnancy 4 All' study in which high perinatal risk regions are targeted with two interventions based on preconception care and antenatal care. The foundation of this study lies in the scientific and systematic analysis of the perinatal health problem in the Netherlands. The study meets the current evidence to intervene early (before or in pregnancy) upon risk factors associated with these perinatal health outcomes. By selection of geographical areas, the study will intervene in potentially high risk populations that potentially will benefit the most. We hypothesise that both strategies will contribute to the promotion of perinatal health. In this project, optimal linkage is sought between curative and preventive care, public health, government, and social welfare organisations. To our knowledge, this is the first study in which these elements are combined.

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Chapter 4

Effectiveness of score card-based antenatal risk selection, care pathways, and multidisciplinary consultation in the Healthy Pregnancy 4 All study

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ABSTRACT

Background Promotion of healthy pregnancies has gained high priority in the Netherlands because of relatively unfavorable perinatal outcomes. In response, a nationwide study, 'Healthy Pregnancy 4 All' (HP4ALL), has been initiated. Part of this study involves systematic and broadened antenatal risk assessment (the Risk Assessment sub-study). Risk selection in current clinical practice is mainly based on medical risk factors. Despite the increasing evidence for the influence of nonmedical risk factors (social status, lifestyle or ethnicity) on perinatal outcomes, these risk factors remain highly unexposed. Systematic risk selection, combined with customized care pathways to reduce or treat detected risks, and regular and structured consultation between community midwives, gynecologists and other care providers such as social workers, is part of this study.

Methods/Design Neighborhoods in 14 municipalities with adverse perinatal outcomes above national and municipal averages are selected for participation. The study concerns a cluster randomized controlled trial. Municipalities are randomly allocated to intervention (n = 3,500 pregnant women) and control groups (n = 3,500 pregnant women). The intervention consists of systematic risk selection with the Rotterdam Reproductive Risk Reduction (R4U) score card in pregnant women at the booking visit, and referral to corresponding care pathways. A risk score, based on weighed risk factors derived from the R4U, above a predefined threshold determines structured multidisciplinary consultation. Primary outcomes of this trial are dysmaturity (birth weight <p10), prematurity (birth <37 weeks), and efficacy of implementation.

Discussion The 'HP4ALL' study introduces a systematic approach in antenatal health care that may improve perinatal outcomes and, thereby affect future health status of a new generation in the Netherlands.

BACKGROUND

Perinatal mortality rates in the Netherlands are higher than in other European countries and are showing a slower rate of decline.[1] The latest confirmed statistics describe a perinatal mortality rate (deaths from 22 weeks of gestation up to 7 days postpartum) of 8.5 per 1,000 births.[2] In addition, higher risks for adverse outcomes were found for women living in socioeconomically deprived areas, particularly in the four largest cities in the Netherlands.[3] The adverse perinatal health outcome in the Netherlands has triggered debates and initiatives to study and intervene in possible causes for these adverse outcomes.

More than 85 percent of all causes of perinatal mortality in the Netherlands are associated with four adverse perinatal outcomes, namely congenital disorders, small for gestational age (birth weight <10th percentile for gestational age), premature delivery (birth <37 weeks), and/or a suboptimal start at birth (Apgar score <7 after 5 minutes); these are defined as the 'Big 4' outcomes. [4] Poor outcomes were especially observed in deprived districts and are often associated with socioeconomic and ethnicity related risk factors such as low education, low income and poor integration into society.[5,6]

The Dutch system

The Dutch antenatal healthcare system is divided into three levels of care in which a distinction is made between low-risk and high-risk pregnancies. The primary level of care, antenatal health care, is provided by independently practicing midwives who deliver care to pregnant women with an uncomplicated pregnancy, childbirth and the postpartum period. These women are estimated to be 'low risk'. If complications (threaten to) occur, midwives refer the women to a gynecologist at the secondary level of care.[7] The tertiary level of care takes place in centers for perinatology with a neonatal intensive care unit and an obstetric 'high-care' department. The latter is reserved for severely ill women or threatened pregnancies.[8]

Current practice of risk selection

Current risk selection during the antenatal period focuses on medical risk factors.[9,10] A list of obstetric indications, for which referral from primary to secondary care is prescribed, has been composed by professionals involved in the field. On this list, the most frequently occurring medical conditions and prior obstetric complications are allocated to the different levels of care. The composition of this list was based on best evidence or best practices. Since the last update in 2003, there has been an increase in evidence of the influence of nonmedical risk factors (social status, lifestyle or ethnicity) on adverse perinatal outcomes.[11] These risk factors are usually not considered in current risk screening practices. Moreover, it was shown that an accumulation of these risk factors

can even further harm the chances of a good pregnancy outcome. This phenomenon implies that the presence of a number of smaller risk factors, rather than a single greater one, increases the risk on adverse perinatal outcomes. [4,11,12]

Initiatives to improve perinatal health

To improve perinatal health, especially in socially deprived districts, the Rotterdam municipal council and health scientists of the Erasmus University Medical Centre initiated a city-wide perinatal health program 'Ready for Baby' in 2009. [5] The 'Ready for Baby' program provided the framework for this national study. It was within this program that scorecard-based risk screening and corresponding care pathways were developed and piloted. Within the context of this program, the Rotterdam area served as a testing ground for a number of experiments, including the development and piloting of the R4U (Rotterdam Reproductive Risk Reduction) scorecard for antenatal risk screening.[13] These former experiences were used to further improve and implement these tools in other municipalities with high perinatal mortality and morbidity in the Healthy Pregnancy 4 All study. The Healthy Pregnancy 4 All study was launched in 2011 by the Erasmus University Medical Centre in 14 municipalities in the Netherlands. It focuses on preconception care and broadened risk selection during pregnancy.[14]

In the risk assessment substudy, we will implement and investigate the Rotterdam Reproductive Risk Reduction (R4U) scorecard, corresponding care pathways and multidisciplinary consultation. This score card focuses on both medical and nonmedical risk factors, including psychological, social, lifestyle, obstetric and nonobstetric care-related risks. During the first antenatal visit, the R4U scorecard will be assessed by a midwife or gynecologist. The aim of this study is to investigate the effectiveness of this new approach in antenatal health care on perinatal outcomes.

METHODS/DESIGN

Outline

The study design concerns a cluster randomized controlled trial at the municipality level. Selected municipalities are randomly allocated to intervention and control groups. The intervention comprises systematic risk selection with the R4U scorecard in pregnant women at the booking visit and referral to the corresponding care pathways. A risk score, based on weighed risk factors derived from the R4U, above a predefined threshold determines consultation among community midwives, gynecologists, and other care providers, such as social workers in a multidisciplinary setting.

The study aims 1) to investigate the effectiveness of systematic approach in antenatal health care on adverse pregnancy outcomes (primarily lowering prematurity and small

for gestational age outcomes) and 2) the efficacy of implementation (measured by the number of R4Us filled out by the healthcare professional, the performance of multidisciplinary deliberations and patient and healthcare professional satisfaction).

Participants/eligibility criteria

The selection of neighborhoods is based on the presence of an elevated incidence of adverse perinatal outcomes (above both the national and municipal average). Municipalities are extracted after a selection process in which zip codes with high adverse perinatal outcomes are identified in a thorough analysis. For this analysis, data from all singleton pregnancies in the Netherlands over the period of 2000 to 2008 were obtained with permission from the Dutch Perinatal Registry (PRN).[15] The detailed selection process of the municipalities and geographical areas are described elsewhere.[14]

All midwives and gynecologists providing care to women living in these zip codes will be invited to participate in the Healthy Pregnancy 4 All study. All pregnant women living in these selected areas are eligible for this trial. All municipalities deal with an above-average perinatal mortality rate and many disadvantaged neighborhoods. Exclusion criteria include an acute obstetric situation during the booking visit (for example, ectopic pregnancy) and women in labor during this initial visit.

Study design

To prevent contamination, we have randomized on the level of municipalities instead of (1) on the level of midwife practices or (2) on the level of hospitals or obstetric collaborations.

Randomization at the level of the individual patient is not possible because of contamination to a healthcare professional: a care provider will not be able to distinguish between intervention and control participants within their practice.

Many midwife practices are cooperating with hospitals in so-called obstetric collaborations (OC's). Randomization on the level of OC's was also not an option: hospitals are always involved in one particular OC, but midwife practices can participate in more than one OC. This is especially the case in municipalities with more than one hospital.

Intervention and control

Use of the R4U scorecard, corresponding care pathways, and multidisciplinary consultation will be compared with conventional antenatal health care. In municipalities allocated to the intervention group, midwives and gynecologists will use the R4U scorecard during every first antenatal visit (provided that informed consent is given). The R4U scorecard consists of six domains (social status, ethnicity, care, lifestyle, medical history and obstetric history), subdivided into 70 items. The R4U scorecard is proposed to facilitate improved coordination of antenatal care through systematic and uniform

risk screening for medical and nonmedical risk factors. A risk score, based on risk factors derived from the R4U, above the predefined cut-off point implies follow-up action. This follow-up action includes multidisciplinary consultation between obstetric caregivers and non-obstetric caregivers (for example, social workers) and prioritization of risk factors. For each cluster, this cut-off point will be calculated after a pilot of 50 R4U scorecards have been completed in a municipality. We strive to assess 20% of all pregnant women in this multidisciplinary setting. Healthcare professionals determine when and how to organize these meetings, with a minimum frequency of once a month. A standardized format is available to discuss a patient in such meetings. The purpose of these meetings is to assess a customized antenatal policy for each individual pregnant woman.

We developed 28 templates of care pathways for all risk factors incorporated in the R4U score card. Care pathways consist of steps a caregiver could follow to meet specific needs for pregnant women. Together with local healthcare professionals from both the perinatal care, community health services (called the GGD), and other services, these templates will be adapted to local circumstances. Local facilities, agreements, and guidelines will be incorporated. Depending on local availability, care pathways will developed for all items as presented in the R4U scorecard. These created care pathways will support the individual healthcare professional to encounter complex (non-) medical risk factors. They can also facilitate the collaboration among different healthcare professionals and professionals within the community health services.

Pregnant women in the control group will receive conventional antenatal health care. After the inclusion of 700 participants or after two-thirds of our study period (2 years), we will end the control group in a particular municipality and will start with the implementation of the R4U scorecard and corresponding care pathways. As mentioned in our introduction, several studies revealed a disadvantaged position of the Netherlands regarding perinatal mortality. For the first time, the unique organization of antenatal care in the Netherlands was openly questioned. In response, health care professionals and policy makers were urged to undertake interventions. The fact that we made municipalities aware of their perinatal health statistics and allocated them to be 'a control' was contradictory to ambitions to intervene, as the control status was felt to be the negligent attitude of local health authorities.

We are lenient to this aspect and will offer them the opportunity to start with the intervention after they have reached a certain amount of included subjects or at two-thirds of the way through the study. Therefore, we aim to implement and facilitate this new approach in all 14 municipalities at the end of the study period. This implies that the study design remains a parallel trial in which only pregnancy outcomes from regular antenatal health care in control municipalities will be analyzed. Pregnancy outcomes of women enrolled after the 'cross-over' in control municipalities (that is, women in control municipalities that were exposed the intervention) will not be analyzed for this purpose.

Procedures, recruitment, randomization, and collection of baseline data

Randomization took place in January 2011 by an independent statistician who was not involved in executing the study. In order to decide whether matching was necessary, in each cluster, the adverse perinatal outcomes (Big 4 and perinatal mortality) were stratified according to socioeconomic status and ethnicity. Since clusters were not considerably different in terms of these characteristics, we decided that matching of clusters for socio-economic status and ethnicity was unnecessary.

As stated before, midwife practices participate in OC's. Due to merging plans between OC's in the north of the Netherlands, four small municipalities and one large municipality were combined and form one cluster (named Groningen). Thus, ten municipalities were randomly assigned to the intervention (n = 5) or the control group (n = 5).

In the randomization procedure, municipalities were numbered according to the expected number at risk. Hereby, we ensured that both arms of the experiment were comparable in size. Five random numbers were drawn from the uniform distribution between zero and one. If the number was below 0.5, the first of the pair would be assigned to the intervention, otherwise to the control group. The clusters Amsterdam, Tilburg, Groningen, Enschede and Nijmegen are allocated as intervention municipalities. The clusters for The Hague, Schiedam, Heerlen, Almere and Utrecht are control municipalities.

The logistics are carried out in close collaboration with participating local program coordinators, midwives, gynecologists, and, if available, research midwives in the 14 participating municipalities. Eligible women will receive participant information, and they will be asked for written consent to collect data on their pregnancy outcomes by the participating healthcare professionals. These healthcare professionals will register all participating women anonymously by a study number in a web-based database. We will ask to register the 4-digit zip code, maternal age, gestational age at booking visit, and certain items of the obstetric history. All women participating in the risk assessment study within the HP4ALL study will receive either one or two questionnaires. The first questionnaire contains questions regarding baseline characteristics, such as marital status, household composition and income, education level, ethnicity, lifestyle (smoking, alcohol, and drug use), use of folic acid, medical history, and use of medication. This questionnaire will be completed around the first antenatal visit (depending on local logistics). The second questionnaire focuses on satisfaction. In this questionnaire, we will investigate patient satisfaction regarding their first antenatal visit. We compare satisfaction in participants in the intervention group with participants receiving conventional antenatal health care. This questionnaire will be completed by a selection of study participants. We will ask all participating practices/hospitals to distribute this questionnaire in a predefined time period of 3 months to all study participants having their third antenatal visit. This visit is before the so-called 20-week ultrasound. With this

timing, we try to avoid bias in answering the questionnaire due to outcomes resulting from this ultrasound.

To provide baseline characteristics from participating healthcare professionals, an interview will be performed with one healthcare professional from each participating midwifery practice and hospital. In this structured interview, we will collect data on the number of patients and employees, the current use of risk-selection instruments, collaboration with hospitals and (other) midwifery practices in OC's, and work processes in their antenatal healthcare (for example, counseling for prenatal screening, or ultrasound facilities). This will be repeated at the end of the study. We will use the Relational Coordination survey to measure the coordination performance of healthcare professionals. Gittell's theory of Relational Coordination has been developed for measuring coordination performance among different professions. The healthcare professionals will be surveyed about their communication and relationships with other healthcare professionals during the antenatal phase. This will allow us to observe the effect of our intervention on the coordination performance of healthcare professionals.[16] Table 4.1 provides an overview of the planned assessments within the risk assessment sub-study including variables, methods and outcomes.

Outcome

The primary outcomes are small for gestational age, preterm birth, and efficacy of implementation. Small for gestational age is defined as birth weight below the 10th percentile for gestational age. Preterm birth is defined as birth before 37 weeks of gestation.

Efficacy of implementation will be measured by the number of R4Us completed by the healthcare professional against the number of booking visits, the development and use of care pathways, actual performed multidisciplinary consultations, and patient and healthcare professional satisfaction. Primary outcomes, except for patient satisfaction, will be recorded by healthcare professionals or the project team after delivery on case record forms in an electronic database.

Secondary outcomes are perinatal mortality (from the 22th week of gestation until 7 days postpartum), undetected small for gestational age and unexpected preterm births (babies born in the first level of care), and prevalence and accumulation of medical and nonmedical risk factors.

Other outcome parameters are: detection and prevention of impaired growth and preterm birth during pregnancy, delivery modus, place of delivery, involved healthcare professionals, congenital anomalies, neonatal admission, asphyxia, maternal morbidity (such as pre-existing chronic disease, pregnancy complications, and positive booking bloods) and maternal mortality.

Table 4.1 Planned assessments of the risk selection experiment: variables, methods and outcomes

Patients		
Variables	**Methods**	**Outcomes**
1. INTERVENTION GROUP		
Nonmedical risk factors: 39 items from the risk scorecard, categorized into the domains of social, ethnicity, care, and lifestyle.	R4U scorecard + registration form 'Obstetric history'	Primary outcomes: - Preterm birth - Small for gestational age
Medical risk factors: 30 items from the risk scorecard, categorized into the domains of general history and obstetric history	Questionnaire 'Baseline characteristics'	Secondary outcomes - Undetected small for gestational age and unexpected preterm births (babies born in the first level of care)
Baseline characteristics: Age, zip code, ethnicity, onset of care, household composition, family income, employment, education level, smoking, alcohol, drugs, folic acid use, medication use, pre-existing chronic diseases, and sexually transmitted diseases.	Case Record Form 'pregnancy and delivery data'	- Prevalence of risk factors - Risk accumulation - Involved healthcare professionals during pregnancy - Detection and prevention of impaired growth and preterm birth during pregnancy - Perinatal mortality - Congenital anomalies - Delivery modus - Place of delivery
2. CONTROL GROUP		
Baseline characteristics: Age, zip code, ethnicity, onset of care, household composition, family income, employment, education level, smoking, alcohol, drugs, folic acid use, medication use, pre-existing chronic diseases, and sexually transmitted diseases.	Registration form 'Obstetric history' Questionnaire 'Baseline characteristics' Case Record Form 'pregnancy and delivery data'	- Asphyxia - Neonatal admission - Maternal morbidity (such as pre-existing chronic disease, pregnancy complications, positive booking bloods), and maternal mortality.
Patient satisfaction in both groups	Questionnaire 'Patient experiences during the first antenatal visit'	- Which topics were discussed (10 examples)? - What was your experience? - Do you think this was important to ask?
Care providers		
Variables	**Methods**	**Outcomes**
General characteristics participating midwives practices and hospitals in both groups	Interview-based questionnaire	- Current status number of patients and employees - Use of risk selection instruments - Collaboration with hospitals and (other) midwifery practices - Work processes (for example, counseling for prenatal screening, or ultrasound facilities).
Care provider satisfaction in both groups	Questionnaire	- Feasibility - Efficacy of implementation - Collaboration - Continuation of intervention

Follow-up

The follow-up period consists of 6 weeks. Details of pregnancy, delivery, and maternal follow-up will be recorded after 6 weeks in a case record form. If necessary, medical records of newborns will be requested (if consent is provided).

Ethical considerations

This study has been approved by the Ethics Committee of the Erasmus Medical Center Rotterdam (Ref. No. MEC-2012-322) and by the management of participating hospitals that requested an extra review.

All participants will receive written and oral information about the study, after which informed consent will be obtained. Participation is voluntary and no extra incentives will be provided.

STATISTICS

Sample size

The sample size is determined by focusing on the primary objective of the trial: the effectiveness of systematic antenatal screening on adverse small for gestational age (<10th percentile) and preterm birth (gestational age below 37 weeks). In this cluster-randomized trial, sample size depends on (1) the average risk of small for gestational age and preterm birth without the intervention (π_o); (2) the expected effect of the intervention (π_1); (3) the inflation factor reflecting the partial similarity/dependency of women's outcomes or responses within the same cluster; (4) the α; and (5) power (1-β) of the test.

Based on data from the Dutch perinatal registry[15], the average prevalence in our selected zip code areas in the years 2000 to 2008 was 16.7%. In the intervention group, we expect a prevalence of 13% at the end of the study period. The average prevalence of both primary outcomes in the Netherlands was 12% for the years 2000 to 2008[15], and we expect a decline towards this prevalence during our study period. The inflation factor was estimated to be 2.06.[18] This factor reflects the design effect of a cluster trial, and takes into account the degree of similarity among responses within a cluster. With five municipalities in each group (a total of ten clusters) and an alpha of 0.05 (two-sided test), 7,000 participants (3,500 per arm) should provide power in excess of 80%. This means 700 women are needed per cluster. It is assumed that a difference of 150 to 200 participants between the larger and smaller clusters has no implications for the outcome.[17]

Data analysis

Data will be analyzed according to the intention-to-treat principle. The effectiveness of the R4U scorecard, corresponding care pathways and multidisciplinary consultation versus conventional antenatal healthcare (measured as the difference in small for gestational age and preterm birth between both groups) will be assessed by using multilevel logistic regression with random effects. Results will be presented as effect estimates with a measure of precision (95% confidence interval). Data will be analyzed anonymously on two levels: the maternal and the municipal level. To guarantee anonymity, we will not analyze the data on community practice or at the hospital level. Study participants, municipalities, and community practices or hospitals will not be traceable. Other analyses related to our intervention are based on differences in other birth outcomes (for example, Apgar score), the number of referrals between community midwives and gynecologists, adequacy in risk assessment (for example, detection of growth restriction in the antenatal phase), and the contribution of nonmedical risk factors to adverse birth outcomes between the intervention and control group. These outcomes will be assessed with univariate and multivariate regression analysis with 95% confidence intervals.

DISCUSSION

The main objective of this trial is to investigate the effectiveness of a new systematic approach in antenatal healthcare on adverse pregnancy outcomes and efficacy of implementation. We will implement and investigate the Rotterdam Reproductive Risk Reduction (R4U) scorecard and corresponding care pathways in 14 municipalities.

The study meets the current evidence to intervene early in pregnancy upon (modifiable) risk factors associated with adverse perinatal health outcomes. We aim to target a population that potentially will benefit the most with the use of selected geographical areas. With the use of care pathways, optimal linkage is sought between curative and preventive care, such as public health, government, and social welfare organizations.[14]

To our knowledge, this is the first approach in antenatal healthcare whereby systematic risk selection for both medical and nonmedical risk factors, variable thresholds, tailor-made care pathways, and structured consultation between midwives, gynecologists and other care providers are combined. This study will introduce a systematic approach in antenatal health care, which may improve perinatal outcomes and, thereby, future health status of a new generation in the Netherlands.

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Chapter 5

Implementation of score card-based antenatal risk selection, care pathways, and interdisciplinary consultation (the Healthy Pregnancy 4 All study)

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ABSTRACT

Objective The aim of this process evaluation was to evaluate the implementation the risk assessment (RA) sub-study within the national Healthy Pregnancy 4 All (HP4All study. The HP4All study was a complex programmatic intervention within a municipal setting in which optimal linkage was sought between curative and preventive antenatal healthcare. The RA intervention consisted of the implementation of a systematic scorecard-based risk screening in pregnancy during the first antenatal visit in 11 municipalities, in case risks were detected then subsequent patient-tailored care pathways and consultation of professionals from different medical and social disciplines were put in place.

Methods To evaluate adoption and implementation of the RA approach in an antenatal healthcare setting, we used an existing framework for the development of a program implementation monitoring plan with specific attention to the setting and context of the program. We performed triangulation of data from multiple data sources and applied pre-specified criteria for evidence of implementation to examine the evidence for implementation.

Results Six out of 11 municipalities (54%) met our criteria of implementation for the entire risk assessment program, whereas 3 of 11 (27%) met the criteria if the three components of implementation (scorecard-based risk screening, care pathways and multidisciplinary consultations) were analysed separately into more depth.

Conclusions The results of this process evaluation will be used to assess program implementation of HP4All for summative and formative purposes, and to get a better understanding of the associations between specific program elements and program outcomes.

INTRODUCTION

After the European PERISTAT-1 study showed that perinatal mortality was substantially higher in the Netherlands in comparison to other European countries [1], practitioners, researchers, politicians and the Ministry of Health, Welfare and Sports have undertaken numerous actions to improve perinatal outcomes. Research revealed that in 85% of all cases mortality was preceded by perinatal morbidity (e.g. preterm birth, small-for-gestational age, suboptimal start or congenital anomalies). [2] Besides our relatively unfavourable position compared to surrounding countries, large inequalities within the Netherlands were observed.[3] Poor outcomes were more prevalent in deprived areas and were often associated with socio-economic and ethnic minority related risk factors such as low-income or less integration into society.[3 4] This information made perinatal mortality an important political and social issue, which led to many national and local initiatives in the Dutch antenatal healthcare field (obstetric and midwifery system).

The Healthy Pregnancy 4 All (HP4All) study was initiated in 2011 by the Erasmus University Medical Centre with support of the Ministry of Health, Welfare and Sport to implement strategies to improve perinatal outcomes with special focus on deprived areas. The selection of neighborhoods was based on the presence of an elevated incidence of adverse perinatal outcomes (above both the national and municipal average).[5] The 'Ready for a baby' program, a prior program in the city of Rotterdam, provided the framework for this national study.[4] It was within the Ready for a baby program that several instruments for the HP4All study were developed and piloted.[6] These former experiences were used to further improve and implement the tool in other municipalities with high perinatal mortality and morbidity in the HP4All study.

The main purpose of the HP4All study was to evaluate the effectiveness of two interventions in 14 municipalities to prevent and reduce adverse pregnancy outcomes; (1) the preconception care sub-study, a population-based prospective cohort study focusing on the feasibility and effectiveness of customized preconception care, and (2) the risk assessment sub-study, a cluster randomized trial to investigate the effectiveness of scorecard-based antenatal risk assessment to identify women early in pregnancy at risk for adverse pregnancy outcomes.[5]

This paper focuses on the risk assessment (RA) sub-study. Despite increasing evidence for the association between non-medical risk factors (e.g. single parentship, employment status, education level, or financial debts) and adverse pregnancy outcomes [3], current risk assessment in the antenatal period focuses on medical risk factors mainly.[7 8] Furthermore, the presence of multiple (non-medical combined with medical) risk factors could have an accumulative effect, known as risk accumulation. This effect warrants comprehensive risk assessment including non-medical risk factors which is the key-principle of the RA sub-study.[9 10]

A complex structural intervention such as the RA sub-study depends on the participation of local healthcare professionals in the participating municipalities. These differences in context and setting make implementation monitoring essential. The aim of this process evaluation is to monitor and document the program implementation and to get a better understanding of the associations between specific program elements and outcomes.

This process evaluation was designed to answer the following questions: (a) Were all elements of the RA intervention delivered by the HP4All team (dose delivered)? (b) To what extent were the interventions within RA program implemented by healthcare professionals (dose received)? (c) To what extent did local caregivers and local project coordinators provide support for the new approach in risk assessment (fidelity and completeness)? (d) How many local health care professionals were involved throughout the project, and how many study participants were reached (reach)? (e) Will midwives and gynaecologists continue with the intervention as implemented (participant responsiveness)?

METHODS

To evaluate the process of implementation of the RA sub-study in an antenatal healthcare setting we used guidelines by Saunders et al. on the development of a program implementation monitoring plan.[11 12] A process evaluation for a complex intervention cannot provide a detailed understanding of all activities as this is not feasible because of variability in organizational aspects and environmental targets of changes. Rather, this implementation monitoring plan was used to identify patterns that provide evidence for implementation by triangulation data from multiple data sources.[12]

The seven steps methods by Saunders et al. was used to analyse and report implementation dose, reach, and fidelity and completeness of the implementation. These steps are based on guidelines for developing a program implementation monitoring plan [12], and methods for assessing implementation at an organizational level.[13] Saunders' steps describe the 1) setting, context, and program; 2) complete and acceptable delivery of the program; 3) development of implementation monitoring methods; 4) development of criteria for evidence of implementation; 5) collecting and organizing data during program implementation; 6) applying criteria for evidence of implementation; 7) and use of implementation data.

Step 1: Setting, Context, and Program

The setting for the RA sub-study within the HP4All study was the Dutch antenatal healthcare field (obstetric and midwifery system). The Dutch antenatal healthcare field

is unique in that it is divided into three levels ('tiers') with a distinction between low- and high risk pregnancies. The first provides care to low risk pregnancies and care is provided by community midwives or occasionally by general practitioners. The second tier is meant for pregnancies with one or more predefined risk factors and care is provided by gynaecologists. [7 8] The third tier is reserved for severe maternal or fetal morbidity and (threatening) prematurity (<32 weeks of gestation). It is provided in tertiary centers with an obstetric 'high-care' department and neonatal intensive care unit.[14] Classification into low and high risk pregnancy and indications for referral from the first tier to the second tier are described in the "List of Obstetric Indications".[7 8 15] It describes general medical and obstetric risk factors. Since the last update in 2003 there is increasing evidence for the influence of non-medical risk factors (socio-economic status, lifestyle or ethnicity) on adverse perinatal outcomes, [10 16 17] but these risk factors are usually not considered in current antenatal risk assessment.[18]

In 2009 the Ministry of Health, Welfare, and Sports established a Steering Group on 'Good care during pregnancy and child birth' to report a set of recommendations to improve the Dutch antenatal healthcare system.[19] Shortly afterwards a scientific report presented a comprehensive analysis of national perinatal data, an overview of knowledge gaps and a proposition for a research agenda in perinatal care and health.[20] Both reports underscored the need for closer collaboration between community midwives and gynaecologists. This was also emphasized by the Dutch Foundation for Perinatal Audit. [21]

The Risk Assessment sub-study in HP4All

The RA sub-study was designed as a cluster randomized controlled trial on municipal level.[22] The intervention in the RA sub-study consisted of systematic scorecard-based risk selection using the R4U (Rotterdam Reproductive Risk Reduction) scorecard in pregnant women at the first antenatal visit. Subsequent patient-tailored care pathways and consultation of professionals from different medical and social disciplines were offered in case risks were detected. The R4U scorecard covers 70 items divided into six domains (social status, ethnicity, care, lifestyle, and medical and obstetric history. The R4U scorecard gives a weighted score to every pregnant woman. If the score exceeded a predefined cut-off point, her risk profile was discussed in a multidisciplinary consultation (MC) between community midwives, gynaecologists and other invited non-obstetric care providers (e.g. social workers).[23] This cut-off point is adaptable to local availability of resources, but we aimed to have at least the upper 20% of all cases being discussed. The MC provides the opportunity to utilize a multidisciplinary view to customise antenatal policy in order to meet the individual pregnant woman's need.

All community midwives and gynaecologists providing care to women living in the selected zip codes were invited for participation in the RA sub-study. Initially, 14 mu-

nicipalities participated in the HP4All study. Due to extensive collaboration between obstetric caregivers in the north of the Netherlands, four small municipalities and one large municipality were combined to form one cluster of randomisation. Thus ten clusters were randomly assigned to either the intervention (n = 5) or the control group (n = 5). The use of the R4U scorecard and corresponding care pathways in the intervention group were compared to regular antenatal healthcare in the control group. In municipalities allocated to the intervention group, midwives and gynaecologists used the R4U scorecard during every first antenatal visit (provided that informed consent was given by the pregnant woman). Care pathways were designed for each risk factor in the R4U scorecard (i.e. a separate pathway for housing problems, financial issues and illicit drug use). They are flowcharts with instructions and contact details for referral in case a specific risk factor is detected. Local healthcare professionals from both perinatal care, municipal health services, and other services, adapted templates of care pathways to the local setting for all risk factors in the R4U scorecard. The availability of local facilities, agreements, and guidelines were incorporated.[6 22]

Pregnant women in the control group received regular antenatal health care. After the inclusion of 700 participants or after two-third of our study time was completed (2 years), the control group in each particular municipality also started implementation of the intervention. At the end of the study period, we aimed to have implemented this new approach in all 14 municipalities. Supplement 5.1 depicts the proposed strategy for rollout of key elements and corresponding timeframe of the RA sub-study.

In this process evaluation of the RA sub-study we focus on the effectiveness of implementation in terms of effect of implementation on individual behavior of midwives and gynaecologists and the organizational outcomes in the antenatal care as specified in the logic model (Supplement 5.2). To assess actual implementation in the RA sub-study the extent to which the R4U scorecard was used, care pathways were applied, risk profiles were brought into MC's, and project meetings were attended was assessed according to the predefined implementation criteria.

Implementation approach

The overall implementation goal of the RA sub-study was to introduce systematic antenatal risk assessment using the R4U scorecard, facilitated with the introduction of corresponding care pathways and MC's in the HP4All municipalities. The project team and local municipal project coordinators served as organizational 'change agents' as they implemented the intervention within their respective municipalities.[24] Change agent capacity is needed to create a sustainable environment (e.g. care pathways and MC's) and resources (availability of supporting organizations as social workers, financial resources) to secure the antenatal risk assessment as planned.

Two key elements of the implementation approach were 1) the local municipal project coordinators, community midwifes and gynaecologists working in partnership, and 2) design of the RA intervention as a standardized process within routine antennal healthcare to facilitate the organizational change in antenatal risk assessment. This design included training, technical assistance and availability of support to develop change agent capacity.

These criteria resulted in targeted goals for optimal RA implementation for the HP4All staff and local project coordinators (see step 2 below). Changes by local healthcare professionals were expected to improve the perinatal health by improving quality of antenatal health care - specifically by systematic risk screening and multidisciplinary collaboration between healthcare professionals. Initially this effect on perinatal health and delivery of antenatal care was proposed to occur within the geographic study areas. However as the care system evolves and best practices can be passed on by care providers, eventually more pregnant women living in these municipalities can benefit from the project.

We used a logic model to describe the purpose, strategies, and expected impacts and outcomes of the intervention (supplement 5.2).[11 25] The logic model is a framework to provide understanding of the program and to form a basis for its evaluation. It describes the logical relationships between the resources and activities (inputs), the outputs and impacts, and the (organisational) outcomes of a program related to a specific situation.[26] The logic model was developed at the beginning of the project and describes how the implementation process was expected to create optimal RA implementation and facilitate behavior change among healthcare professionals (row 1 in supplement 2). It was also used to organize the evaluation and implementation monitoring plan (rows 2 and 3 in supplement 5.2).

Ethics

The HP4All study has been approved by the Medical Ethical Committee of the Erasmus Medical Centre Rotterdam (MEC 2012-322), and by the management of all participating caregivers. Pregnant women receive written and oral information about the study. Participants are asked for their written informed consent. Informed consent was obtained from all individual participants included in the study.

Step 2: Complete and acceptable delivery of the program

The elements fidelity, dose, and reach are recommended to evaluate the completeness and acceptability of the program implementation.[12] Fidelity is a measure for quality of implementation, and describes to what extent the intervention was implemented as planned in the original program. In the RA sub-study, fidelity corresponds to the extent in which the implementation of the R4U scorecard, care pathways and MC's were car-

ried out by program implementers (midwives and gynaecologists). Dose of a program is divided into two elements: dose delivered and dose received. Dose delivered (completeness) describes to what extent all elements of the program were implemented. Dose received (exposure or satisfaction) explains to what extent program implementers are receptive to the program implementations. In our study, we measured satisfaction among midwives and gynaecologists and study participants as a proxy for dose received.[12] Program reach refers to the rate of involvement and representativeness of program implementers.[27] In the RA sub-study, we registered the number of participating midwives and gynaecologist, and the number of pregnant women living in one of the selected zip-code areas that participated in our study.

For the process evaluation we were also interested in participant responsiveness. Participant responsiveness refers to the degree in which the program stimulates the interest and creates persistent attention of program implementers.[27] In the RA sub-study, this reflects the intention of caregivers to continue with the different aspects of risk assessment in our program after the study period.

Step 3: Implementation Monitoring Methods

Implementation of RA included three components: the R4U scorecard, care pathways, and MC's. The development of implementation monitoring methods, as presented in table 5.1, involved 1) developing detailed questions to evaluate the process; 2) determining methods for process evaluation: data sources, instruments, and data collection procedures based on these questions; and 3) considering program resources, characteristics and context.[12] This planning process resulted in the final process evaluation plan with multiple data sources and organizational levels (administrative, health care professionals involved, local project coordinators, social services) with a variety of data collection tools and procedures. The use of multiple data sources enabled us to triangulate information from different levels and perspectives in order to generate a more complete understanding of the effects of project activities on implementation and perinatal outcomes.[11]

The final RA sub-study process evaluation and implementation monitoring plan, organized by the logic model (rows 2 and 3 in supplement 5.2) [28], included fidelity and completeness, dose, reach and patient responsiveness. The instruments (data sources) used for the process evaluation included 1) a project logbook recorded during the whole study period in which contact moments with project coordinators, midwives, gynaecologists municipal, and local social services were listed (often in project meetings), 2) a study logbook in which each practice and hospital recorded all eligible pregnant women during the study period, 3) number of completed R4U scorecards, 4) an end-of-intervention assessment to monitor the implementation results at the end of the intervention on caregiver level, 5) a caregiver satisfaction survey at the end of the

Table 5.1 Instruments, Data Sources, Variable descriptions, rating scale, and Implementation criteria to assess risk assessment implementation

Sample Item	Instrument (Data Source)	No.of items	Variable (Summary)	Rating Scale / Coding	Implementation criteria
Part 1: entire risk assessment program					
Were all three components, the R4U scorecard, care pathways and multidisciplinary consultation, implemented during the project period?	Project observation (investigator)	1	Implementation (item value)	3 = completely (3/3); 2 = largely (2/3), 1 = partially (1/3); 0 = no	Rated 2
How many contacted local health care professionals were involved throughout the project?	Project logbook (investigator)	2	Implementation (item value)	3 = excellent; 2 = moderate; 1 = needs improvement	Rated $\geq$ 2.5
Will midwifes and gynaecologists continue with the intervention as implemented?	End-of-intervention survey part 4 (caregivers)	1	Implementation (item value)	3 = completely (3/3); 2 = largely (2/3), 1 = partially (1/3); 0 = no	Top ~1/3 score
How where local project coordinators involved in the risk assessment program?	End-of-project (investigator)	8	Implementation (mean of items)	3 = excellent; 2 = moderate; 1 = needs improvement	Top ~2/3 score

Table 5.1 Instruments, Data Sources, Variable descriptions, rating scale, and Implementation criteria to assess risk assessment implementation (continued)

Sample Item	Instrument (Data Source)	No.of items	Variable (Summary)	Rating Scale / Coding	Implementation criteria
Part 2: three components separately					
R4U scorecard					
Number of pregnant woman that have been approached to participate in the study.	Study logbook (investigator)	1	Percentage of antenatal visits (coded value)	>75% of visits (3); 50% to 75% of visits (2); 25 – 50% of visits (1); < 25% of visits (0)	Rated ≥ 1.5
Number of fully completed R4U scorecards (all items answered)	R4U scorecard (investigator)	1	Percentage of fully completed R4U scorecards (coded value)	>75% of scorecards (3); 50% to 75% of scorecards (2); 25 – 50% of scorecards (1); < 25% of scorecards (0)	Rated 3
How midwifes and gynaecologists rated the R4U scorecard to support antenatal risk assessment, e.g. general satisfaction	Satisfaction survey (caregiver)	3	Satisfaction (mean of items)	3 = excellent; 2 = moderate; 1 = needs improvement	Top ~2/3 score
Completeness of implementation, e.g.: caregiver that completed the R4U scorecard	End-of-intervention survey part 1 (caregivers)	4	Implementation (mean of items)	3 = excellent; 2 = moderate; 1 = needs improvement	Rated > 5

Table 5.1 Instruments, Data Sources, Variable descriptions, rating scale, and Implementation criteria to assess risk assessment implementation (continued)

Sample Item	Instrument (Data Source)	No.of items	Variable (Summary)	Rating Scale / Coding	Implementation criteria
Care pathways					
Development of care pathways in organized meetings	Care pathway observation (investigator)	2	Total development (value of items)	3 = excellent; 2 = moderate; 1 = needs improvement	Rated $\geq$ 2
How midwifes and gynaecologists rated the care pathways to support antenatal risk assessment	Satisfaction survey (caregiver)	2	Satisfaction (mean of items)	3 = excellent; 2 = moderate; 1 = needs improvement	Top ~2/3 score
Completeness of implementation, e.g.: appropriate use	End-of-intervention survey part 2 (caregivers)	5	Implementation (mean of items)	3 = excellent; 2 = moderate; 1 = needs improvement	Top ~1/3 score
Multidisciplinary consultation (MC)					
Proportion of study participants that scored above pre-defined cut-off point were discussed in MCs	MC observation (investigator)	1	Implementation (value of item)	3 = (nearly) everyone; 2 = more than half; 1 = less than half; 0 = almost no one	Rated $\geq$ 2.5
How midwifes and gynaecologists rated the MC to support antenatal risk assessment	Satisfaction survey (caregiver)	2	Satisfaction (mean of items)	3 = excellent; 2 = moderate; 1 = needs improvement	Top ~2/3 score
Completeness of implementation, e.g.: scheduled meeting	End-of-intervention survey part 3 (caregiver)	5	Implementation (mean of items)	3 = excellent; 2 = moderate; 1 = needs improvement	Top ~1/3 score

project, 6) a care pathway development observation, 7) observation of the formation and functioning of MC's by the investigators, and 8) observation of the involvement of local project coordinators. All process items were assessed according to a predefined rating scale and were completed by the investigators at the end of the 3-year RA sub-study.

The evaluation of the RA sub-study is divided into two parts: the risk assessment program in its totality (part 1), and the three components of the RA sub-study separately (part 2). Part 2 was introduced to observe the extent of implementation in more detail, allowing the ability of tailored recommendations on municipal level. The instruments, data sources, numbers of items, variable descriptions, sample items, rating scales or coding, and implementation criteria variables are presented in table 5.

Step 4: Criteria for Evidence of Implementation

To determine the evidence of implementation, we set criteria for per data source and with regards to how many data sources provided evidence. These criteria were specific to each instrument within the RA sub-study and depended on the response scale and the range of responses (table 5.1).[11] As in the ENRICH program of Saunders, we decided to see an implementation rate of 70% or higher, or the top 2/3 score as evidence for implementation, depending on the rating scale used for a particular data source. The implementation criteria were adapted from the results from a review by Durlac and DuPre on implementation work, indicating that 60% implementation produces positive results and that implementation above 80% is rare.[27] As they did, we based their criterion on the extent to which findings were confirmed by multiple data sources. Our implementation criterion was that at least 3 out of 4 data sources confirmed findings within the entire RA program evaluation (part 5.1), and at least 8 of out 10 data sources confirmed findings within the three separate implementation elements (part 2). The "Implementation Criteria" are presented in table 5.1.

For overall implementation of RA at municipal level, a municipality was classified as "high implementers" if they met the criteria in both part 1 and part 2 (a sum score of 2 out of 3 in the column 'risk assessment', and a sum score of 5 out of 8 in the other columns) and as "medium/partial implementers" if they met the criteria in either part 1 or part 2. Initially, we combined 4 small municipalities and 1 large municipality as one unit of randomisation because of announced extensive partnerships between caregivers. However, during the project we reconsidered this decision because these municipalities went through strictly different processes during the project. As a result, two separate groups were formulated for the implementation of care pathways and MC's. This resulted in the evaluation of 11 municipalities instead of the above mentioned 10 municipalities.

Step 5: Collect and Organize Data

Data for the assessment of implementation were collected by the investigators, research midwives, and healthcare professionals. This data was recorded in Excel spread sheets and analyzed with SPSS version 20 to create scores based on variable definitions.

The establishment of implementation criteria was often the result of a combination of items, which in turn had their own rating scale. For example, the implementation criterion 'completeness of the implementation' was achieved by the combination of 4 items: primary user, time periods in which the R4U scorecard was used, eventual prolongation of the scheduled booking visit, and potential external influencing factors. For each of these items, an individual rating scale was determined. For example, for the item 'primary user' 3 points were rated in case a midwife or physician was the primary user, 2 points in case of research nurse, 1 point in case of practice assistant, and 0 points if an external person (e.g. a medical student) filled out the R4U scorecard. All these ratings were allocated on practice level, and then the municipal average of all participating practices was calculated to determine if the implementation criterion was achieved on municipal level (as presented in table 5.1). An overview of all variables, items, rating scales and allocation of scores per data source is available upon request.

RESULTS

Step 6: Criteria for Evidence of Implementation

In table 5.2 we present the evidence for implementation for the overall HP4All Risk Assessment program (part 1) and the three components of this sub-study (part 2) separately. Evidence for implementation is presented for each item, considering multiple data sources. The two summary columns indicate the number of data sources that meet the overall criteria for implementation.

In total, 6 of the 11 municipalities (54%) met our criteria of implementation for the entire risk assessment program (part 1). These include four 'intervention' and two 'control' municipalities. If we look in more detail to the extent of implementation of the three components separately, 27% of the municipalities met the criteria of implementation if the three components were analysed into more depth. In supplement 5.3 we present a summary of implementation based on the entire program (part 1) and the three components separately (part 2). Three municipalities (27%) were indicated as 'high implementers' as they met the criteria for part 1 and part 2. These were all 'intervention' municipalities. Three municipalities were classified as 'medium implementers' (27%) and the remainder (46%) did not meet the criteria for implementation.

Table 5.2 Risk assessment implementation in participating municipalities

	Part 1: entire program					Part 2: three components separately										
						R4U scorecard				Care pathways (CP)			Multidisciplinary consultation (MC)			
Municipality	Observation	Project logbook	End-of-intervention	End-of-project	Sum score	Study log book	R4U score card	End-of-intervention	Satisfaction	CP observation	End-of-intervention	Satisfaction	MC observation	End-of-intervention	Satisfaction	Sum score
A	2	2.5	2.6	3	4/4	1.8	3	6	3.8	2.4	7.8	3.4	3	6	2.2	10/10
B	2.2	3	2.5	3	4/4	2.2	3	6.8	4.5	2	8	2	3	4	2.5	8/10
C	3	3	3	3	4/4	2	3	5.7	5	1.9	8.3	3.3	2	7	2	7/10
D	1.8	2	0.8	2	1/4	1.4	3	3.6	2.8	1.5	5.4	2.6	0	NA	NA	2/10
E	2	2	2	2	2/4	1.3	2	4	3	2.2	3	3	3	7	2	6/10
F	3	3	3	1	3/4	2	2.7	7.1	3.7	2.5	5	2	3	6	2	7/10
G	1.3	2.5	1	2	2/4	1.7	2.5	4.6	4	2	4	2	0	NA	NA	3/10
H	2.5	3	2	3	3/4	1.5	3	5.3	4.3	2.5	8	2.7	3	7	2	9/10
I	1.1	2	2	2	2/4	0	NA	NA	NA	2	6.6	3.8	0	NA	NA	4/10
J	2	3	2.7	2	4/4	0	NA	NA	NA	2	1.3	3	0	3	2.3	3/10
K	0	2.5	0	1	1/4	0	NA	NA	NA	1	NA	NA	0	NA	NA	0/10
Criteria	Rated 2	Rated $\geq$ 2.5	Top ~1/3 score	Top ~2/3 score	3 or 4/4	Rated $\geq$ 1.5	Rated 3	Top ~1/3 score	Top ~2/3 score	Rated 2	Top ~1/3 score	Top ~2/3 score	Rated $\geq$ 2.5	Top ~1/3 score	Top ~2/3 score	8, 9, or10/10

A shaded score indicates evidence for implementation based on above described cut-off points. Municipalities meeting these overall criteria for implementation are shaded as well.

A – F: intervention municipalities, G – K: control municipalities

NA: not available. Not implemented, so data was not available.

Note that the 'entire program' part mainly displays the intention of practices to implement the RA sub-study. It appeared that some practices agreed to participate, attended all project meetings and were ready to start (i.e. received all information, education and study materials), but did not use the instruments in daily practice. This might have led to an overestimation of our level of implementation in terms of the inclusion of study participants and actual use of the R4U score card. Part 2 was introduced to capture this observation and reflects upon the actual use of the provided instruments.

Step 7: Use of Implementation Data

The present data can be used to group municipalities by level of implementation. By comparing municipalities with high implementation rates with the municipalities with low implementation rates, contextual factors can be identified that can provide understanding for the level of implementation and the effects on pregnancy outcomes (which await assessment). Furthermore they can be useful for formative purposes: how implementation in the future can be improved in similar or comparable contexts. The process evaluation was designed to evaluate the completeness and acceptability of a program evaluation including dose, fidelity, reach and patient responsiveness.

Reach and dose delivered

All municipalities agreed to participate in the HP4All study and only 3 midwifery practices opted not to participate in the RA sub-study. In total 36 community midwife practices and 15 hospitals participated.

Due to the design of the study, the degree of implementation differed considerably between 'intervention' and 'control' municipalities. Although control interventions were offered the opportunity to implement the intervention after they had included a maximum number of subjects for the study, implementation rates were the highest amongst municipalities that had been allocated to the intervention from the beginning of the program. Within 8 municipalities (6 intervention and 2 control municipalities) caregivers used the R4U scorecard at the end of the project. Two control municipalities intend to implement the R4U scorecard in the near future. They delayed this as they were facing other organizational changes within their practices. Care pathways have been developed in in all except one municipality. This is a high rate, especially as control interventions did not have access to the R4U scorecard until they had included the agreed number of subjects that had undergone routine care.

At the onset of the study, multidisciplinary consultations between community midwives and hospital caregivers already existed in 6 municipalities. In 2 municipalities, these consultations were implemented by the project team. In the remainder, implementation of such consultations failed due to various reasons which we will elaborate in the discussion. Within each municipality resources were allocated at the start to appoint a local project coordinator to support implementation during the project period. However, in 3 municipalities there was a lack of continuity in the availability of project coordinators. This was because it took time before a project coordinator was allocated or because project coordinators shifted (due to maternity leaves or reorganizations). Furthermore they were not always available for the requested amount of hours. The degree of availability seem to play a role since almost all 'high implementers' had an excellent score on the availability of project coordinators.

Dose received and participant responsiveness

All except one municipality rated the RA sub-study satisfactory to excellent. Caregivers were the most satisfied about the implementation of care pathways. They often reported that the project had resulted in new collaborations with partners in the 'non-medical' field such as social workers and the municipal health services. We tried to reduce 'organizational hassle' by providing caregivers with direct contact details of appointed responsible partners in the organization included in care pathways. This was evaluated positively by almost all caregivers. The MC's were also evaluated positively by all caregivers. Both community midwives and hospital caregivers indicated that the MC's were a good way to discuss patients and they often reported that they felt it had improved collaboration. In the used version (in which the scorecard was integrated in a webbased application) the R4U scorecard was perceived as cumbersome and time-consuming as caregivers had to impute patient information twice: in the application and in their own software system. They were motivated to do this during the program as they acknowledged the importance and advantages of systematic risk screening. However, integration of the R4U scorecard with their own administrative systems would be a requirement to proceed with such risk screening in the future.

Fidelity

Fidelity and completeness are illustrated in part 2 of table 5.2. The R4U scorecard was filled oud completely in almost most cases. The primary user was the intended user (midwife or hospital caregiver) in most cases. However in some hospitals they delegated the task to impute the R4U to research midwives. Women were asked at their booking visit to participate, but < 50% of all women participated in the study (written consent). The most important reasons were 1) women refused to participate in the RA sub-study (41%), 2) women did not live in the selected neighbourhoods (22%) or 3) there was a lack of time to ask women for their participation as the outpatient consultation clinics were too busy (15%). The majority of caregivers prolonged the time of the first antenatal visit to complete the R4U scorecard (70%). In one municipality, caregivers did not complete the R4U itself but only registered those risk factors from the R4U which were not included in their routine booking procedure. They received weekly assistance form project members to complete the scorecards itself.

All but one municipality started with the development and implementation of care pathways. Overall, 63% of the participating practices indicated that they used the care pathways daily or weekly. Where MC's were available, most cases where the R4U score exceeded the threshold were discussed. In some municipalities even all new pregnant women were discussed. Overall both community midwives and hospital caregivers discussed their cases. However data obtained from different collaborating practices in one municipality was conflicting. One practices stated that cases from both tiers were

discussed, while other practices mentioned that only cases from midwifery practices were discussed.

DISCUSSION

In this process evaluation we aimed to evaluate the implementation of a novel risk assessment strategy within the RA sub-study of the HP4All study. The intervention is introduced into the existing antenatal healthcare setting that serves the local potential high-risk population with regard to non-medical risks in particular. Therefore, it is a complex structural intervention in which optimal linkage is sought between curative and preventive care, such as community midwives, gynaecologists and professionals in the public healthcare echelon as well as social welfare originations.[29] For this process evaluation we applied the seven-step process described by Saunders et al to the RA intervention. They advocate their method to be particularly applicable to 'complex interventions to change organizational policies, practices, procedures or environments to improve services or outcomes in diverse settings ' such as our intervention.[12] In this study we focused attention on an intervention in the antenatal healthcare field whereby implementation of a systematic risk assessment approach was evaluated according to a predefined implementation monitoring plan. In accordance to previous studies on implementation monitoring, we found large differences in implementation rates between municipalities.[12 27] In our study, 3 municipalities met the criteria for complete implementation. The prior mentioned studies revealed that this variability can be due to constant variability in contextual factors such as organizational characteristics, availability of resources, complexity of the setting, and time required for organizational uptake of our new approach in antenatal healthcare.[12 30] Additionally, our Dutch antenatal health care system provides some specific contextual challenges. Community midwives in the primary level of care and gynaecologists in secondary and tertiary care are autonomous professionals operating in their own tiers of care in the antenatal system. This fragmented organization can be challenging.[31] The implementation of our new approach in risk assessment and collaboration primarily required a mind shift in the approach of antenatal risk assessment amongst healthcare professionals, policy makers and the public health sector in each municipality. The realisation that change is needed has shown to be an important success factor for implementation.[6] We therefore might have benefitted from the fact that we conducted our study in a period of time in which antenatal healthcare and perinatal health were a high priority file for policy makers. The current system and collaboration between community midwives and gynaecologists was scrutinized when it became clear that the Netherlands had a disadvantaged position in perinatal health

compared to its surrounding countries.[6] This led to many projects and studies to identify underlying causes and best practices.[19]

As happened in the two municipalities with the lowest implementation rates, it was easy for healthcare professionals to be overwhelmed with all these (often competing) initiatives that required their participation and collaboration. The abundant number of initiatives made that it took a long time before caregivers in these two municipalities would agree to adopt and integrate our intervention into their daily care. As a consequence of this delay and the circumstances these two municipalities (eventually) agreed to only develop care pathways but to postpone the use of the R4U scorecard and integration of care pathways. This also explains why all care pathways have already been developed, but that the R4U scorecard not yet had been used in these municipalities.

Other external factors that may have influenced the level of implementation are competition between healthcare professionals to reach their target number of pregnant women for competing (financial reasons), pre-existing impeding collaboration between the first and second tier of care or between midwifery practices, or unforeseen organizational circumstances such as reorganisations. In cases where the competition between practices was high and there were other impediments to collaboration, we saw that the R4U scorecard was only used within the practice, but subsequent actions such as the discussion of high risk cases in multidisciplinary consultations did not occur. Unforeseen organizational circumstances often resulted in temporary use or discontinuation of the R4U scorecard.

It is also essential to note that until recently the delivery of obstetric care was seen as a responsibility of the curative sector (healthcare professionals such as community midwives and gynaecologists), whereby the involvement of the preventive sector (public health) was restricted to occasional lifestyle promotion and provision of information. At the beginning of the Healthy Pregnancy 4 All study, close collaboration between both sectors was very uncommon. Surprisingly, the different care echelons started to collaborate in almost all of the municipalities to developed and implement care pathways. Prior to the study, these collaborations were virtually non-existent. Caregivers indicated that – although often faced with non-medical risk factors – it is still not their core business. Participating in the HP4All study gave professionals from different echelons an opportunity and a motive to get acquainted with one another and each other's potential roles in antenatal risk assessment and intervention. Perhaps this was a large unforeseen benefit of the program, with benefits for the future if networks are sustained locally.

Strengths and limitations

Time restraints contribute to the variability in our implementation rates. It was quite challenging to achieve organizational change in such a relatively short period of time. This process was complex because it included the initiation of a whole new concept

of risk assessment and intervention including collaboration with new partners from another sector, in a healthcare system exposed to political interference. However, we achieved that all municipalities agreed to participate in our study, that they invested in local project coordinators and that extra resources were allocated where necessary. In municipalities new partnerships between the curative and preventive sector arose or were intensified, and almost 3000 pregnancies were subjected to our novel risk assessment intervention. Although complete implementation was not reached in all municipalities, the sub-study triggered all involved professionals that risk assessment in early pregnancy is important and that identified risks need intervention because of detrimental local perinatal mortality and morbidity rates.[5] That the program had succeeded in creating an urgency to innovate in risk assessment was visible in local participation, attendance of project meetings and in the commitment of social welfare organizations, and support of local and national authorities.

The study also had unintended positive effects that will support future implementation. Three municipalities embedded the project goals in their formal local health policy. The requirement of care providers that the R4U would need to be integrated into existing software systems was met to stimulate continuation of the risk assessment strategy after the project. Lastly, a follow-up study is planned for the next three years (Healthy Pregnancy 4 All 2) allowing us to maintain, improve, and further promote sustainability of the achieved outcomes in risk assessment and collaboration investments of the last three years. With this project we also identified the need to examine other factors that might influence the levels of implementation, such as which moment in care would be optimal for risk scoring and which multidisciplinary agreements would be valuable to align collaboration and responsibilities of involved professionals.

Our study also faced some limitations. Contextual factors were challenging and could not have been foreseen when the project was planned. For the implementation of such a new approach in antenatal risk assessment, professionals from obstetric care, social welfare, and community health services should agree on the comprehensive risk concept as a starting point to collaborate. However, in some municipalities this was a challenge due to existing inter-professional communication barriers. This could not always be mitigated by the project team or local project coordinators acting as our change agents. Contextual factors such as these are difficult to foresee in the phase that intervention programs are designed, perhaps such complex interventions warrant longer project duration. The design of our study formed a complexity for implementation. The fact that we had made municipalities aware of their local perinatal health statistics and allocated them to be 'a control' seemed contradictory to ambitions to intervene. The control status was felt as a negligent attitude by local health authorities. To them, participation in the control arm of the study seemed to demand a large effort without direct benefit. We were lenient to this aspect and offered them the opportunity to cross-over to use of

the R4U after they had reached a certain amount of included participants. However, whilst doing so it seems that we did not succeed to the fullest in engaging 'control' municipalities to implement our strategy, as implementation rates after the cross-over in 'control' municipalities were still considerably lower compared than implementation rates in intervention municipalities. Perhaps the concept of a RCT is in contradiction to other motives of local health authorities. The scientific component in our program also provided other limitations. Our aim was to reach women in deprived areas – which are known to be challenging to reach. [32] Our trial was subjected to medical-ethical requirements (e.g. informed consent) which we experienced to be a barrier for participation of this particular population. Lastly, we decided to evaluate the RA sub-study in two parts: the risk assessment program in its totality (part 1), and the three components of the RA sub-study separately (part 2). This was a deliberate choice to be able to observe the extent of implementation in more detail. However, findings of part two might be overinflated for some municipalities because findings from midwifery practices and hospitals are pooled. In two municipalities, there was a practice which implemented to such a low degree that we could not extract data for our study. We excluded them from our analysis, but these municipalities remained 'high implementers' because all other practices did meet the criteria.

Conclusion and implications for practice

The complex intervention in the RA sub-study within the HP4All study makes implementation monitoring essential. The intervention as implemented provides the opportunity to act upon the growing evidence on the association of non-medical risk factors and pregnancy outcomes. However, for the implementation of such a new approach in antenatal risk assessment, a couple of conditions need to be fulfilled. First of all, caregivers need to recognize the benefit of a non-medical risk screening. This required a mind switch amongst healthcare professionals. Identification of barriers might contribute to the optimization of risk screening. Secondly, we observed that some modifications in daily practice are required (e.g. prolongation of the time schedule of the first antenatal visit and extra time for multidisciplinary consultations). Health insurance reimbursement schemes could provide resources for these modifications.[6] Thirdly, care pathways should be further developed and adapted to local circumstances after first experiences. In our study, this process promoted the collaboration between both obstetric caregivers and non-obstetric caregivers as those from social welfare, psychiatric and community health services. Finally, caregivers – especially in the first tier of care – should be supported in the additional tasks associated with research logistics.

The intervention provides a vehicle for new partnerships between antenatal healthcare between the curative and preventive sector. The results of this process evaluation will be used to fine-tune implementation of the R4U scorecard and to get a better

understanding of the associations between specific program elements and program outcomes.

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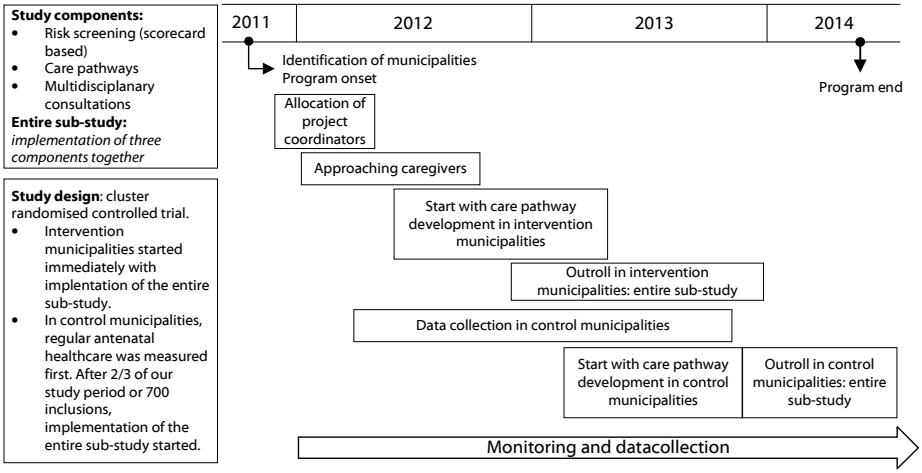
SUPPLEMENTARY FILES



Supplementary Figure 5.1 Strategy for rollout of the key elements and proposed timeframe of the Risk Assessment sub-study.

Supplementary table 5.2 HP4All Logic model and overview of measurement

	1.Input	2.Immediate impact	3.Short-term impact	4.Organizational outcome	5.Individual behavior outcome
Logic model	Development of effective working relationships among community midwives, gynaecologists, center for youth health; social services, municipal health services; Provision of training and consultation in the use of the R4U scorecard; Facilitation of access to local resources for the development of care pathways in meetings; Facilitation of (the introduction of) multidisciplinary consultation; Securing logistic support from the local project coordinators will (see 2)…	…all facilitate the development of skills and confidence among caregivers to identify and deal with both medical and non-medical risk factors, which with supportive organisational resources (see 3)…	…which will result in the development and implementation of (1) systematic and early antenatal risk assessment with the R4U scorecard among pregnant women, (2) customized care pathways on municipal level, and (3) multidisciplinary consultation with midwives and gynecologists (see 4)…	…resulting in an environment that promotes and supports a healthy pregnancy by (1) providing more opportunities for early detection and care for (non-) medical risk factors; (2) strengthening collaboration between caregivers, social services and community health services through care pathways and MCs; (3) enhance the accessibility of care for (non-) medical risk factors through the use of care pathways and organized project meetings with caregivers, social services and the municipality; (4) developing, strengthening, and/or enforcing policies supporting antenatal risk assessment; (5) strengthening organizational structures to support these changes (see 5)…	…which will result in caregivers giving more attention to non-medical risk factors in pregnancy, having increased knowledge on the existence and accessibility of social services, and enhanced collaboration between caregivers, social services and the municipality. (1) Use of R4U scorecard (2) Development and implementation of care pathways (3) Assessment of pregnant women in MCs

Supplementary table 5.2 HP4All Logic model and overview of measurement (continued)

	1.Input	2.Immediate impact	3.Short-term impact	4.Organizational outcome	5.Individual behavior outcome
Measurement component	Process: Dose delivered Assess to which extend elements of the RA intervention were implemented by the HP4All project team 1.creating a team of participating care givers 2.training of participating care givers 3.logic support of the use of tools 4.local project managers (0.2 FTE) 5.organizing project meetings	Process: Dose received Assess risk assessment formation, composition, functioning; risk assessment confidence and skills: 1.participation of caregivers 2a.use of R4U scorecard by caregivers 2b.development and use of care pathways by HP4All team and caregivers 2c.multidisciplanry consultation by caregivers 3.satisfaction among caregivers	Process: Fidelity and completeness Assess extent to which caregivers developed and carried out plans to create environments supporting a new approach in risk assessment by embedding of the R4U scorecard, care pathways, and MC's in daily practice.	Outcome: Organizational behaviour change Assess the effects of level of risk assessment implementation on availability of systemic risk assessment, care pathways and MCs, and related policies in municipalities. (1) collaboration with other caregivers (2) collaboration with local authorities and local health (3) complementary use of the R4U scorecard next to existing software programs for antenatal intake (4) counselling out financial barriers (5) adaptions in daily clinical practice to facilitate implementation (6) continuation and embedding of implementation of the three components in daily practice	Outcome: individual behaviour change Assess the program impact on antenatal risk assessment in pregnant women
Measures	• Documentation of staff activities (log book) • Documentation of records	• Evaluations (project meetings and surveys) • Review of records and other documents • Number of filled out R4U scorecards / number of intakes.	• Evaluations (project meetings) • Review of records and other documents • Project logbook	• Reach of pregnant women • Reach of caregivers and social services • Environmental observations • Collaboration	• Pregnancy outcomes • Number of completed R4Us compared to number of booking visits • Frequency of use of care pathways • Number of women discussed in MCs • Number of attended project meetings by caregivers

*caregivers were defined as midwifes and gynaecologists, HP4All: Healthy Pregnancy 4 All, MCs: multidisciplinary consultations.

Supplement 5.3 Summary of implementation based on the entire program (part 1) and the three components separately (part 2).

Municipality	Entire program	Three components separately	Implementation summary
A	High	High	High/ complete
B	High	High	High/ complete
C	High		Medium/partial
D			Low
E			Low
F	High		Medium/partial
G			Low
H	High	High	High/ complete
I			Low
J	High		Medium/partial
K			Low
	6/11 = 54%	4/11 = 36%	3 / 11 = 27%
			3 / 11 = 27%
			5 / 11 = 46%

Part II

NON-MEDICAL RISK FACTORS IN PREGNANCY

Chapter 6

An instrument for broadened risk assessment in antenatal healthcare including non-medical Issues

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ABSTRACT

Introduction Growing evidence on the risk contributing role of non-medical factors on pregnancy outcomes urged for a new approach in early antenatal risk selection. The evidence invites to more integration, in particular between the clinical working area and the public health domain. We developed a non-invasive, standardized instrument for comprehensive antenatal risk assessment. The current study presents the application-oriented development of a risk screening instrument for early antenatal detection of risk factors and tailored prevention in an integrated care setting.

Methods A review of published instruments, complemented with evidence from cohort studies. Selection and standardization of risk factors associated with small-for-gestational-age, preterm birth, congenital anomalies, and perinatal mortality. Risk factors were weighted to obtain a cumulative risk score. Responses were then connected to corresponding care pathways. A cumulative risk threshold was defined, which can be adapted to the population and the availability of preventive facilities. A score above the threshold implies multidisciplinary consultation between caregivers.

Results The resulting digital score card consisted of 70 items, subdivided into 4 non-medical and 2 medical domains. Weighing of risk factors was based on existing evidence. Pilot-evidence from a cohort of 218 pregnancies in a multi-practice urban setting showed a cut-off of 16 points would imply 20% of all pregnant women to be assessed in a multidisciplinary setting. A total of 28 care pathways were defined.

Conclusion The resulting score card is a universal risk screening instrument which incorporates recent evidence on non-medical risk factors for adverse pregnancy outcomes and enables systematic risk management in an integrated antenatal healthcare setting.

INTRODUCTION

Perinatal health is a topic of growing international concern. Two subsequent reports on perinatal health concluded that within European countries impressive inequalities exist in perinatal outcomes.[1 2] Evidence from large cohort and registry studies clearly demonstrated an equally high impact on perinatal outcomes of non-medical risk factors (e.g. social of lifestyle) compared to medical and obstetrical risk factors.[3 4]

These etiological studies also showed that the cumulative presence of a set of heterogeneous risk factors of moderate importance - rather than the presence of a single large risk - underlies most adverse outcomes. This so-called risk accumulation is especially observed in deprived geographical areas characterized by overrepresentation of women with low socioeconomic status, single parenthood, migrant status, and numerous associated risks (medical, non-medical or both).[5-7]

More than 85 percent of all cases of perinatal mortality are associated with only four adverse perinatal outcomes, either single or combined. These so-called Big 4 outcomes include congenital disorders, small for gestational age, preterm birth and / or suboptimal start at birth (low Apgar score).[8] Big 4 outcomes are in general closely related to medical and non-medical risk factors. They represent the link between increased perinatal mortality rate and their associated risk factors. Many of these risk factors are already present at onset of pregnancy.

This new evidence on risk pathways invites to more interdisciplinary collaboration, in particular between the clinical working area and the public health domain when non-medical play an essential role (horizontal integration). In this respect, a comprehensive risk model with associated integrated care delivery could underlie the antenatal health-care system.[9] Integrated care aims to 'deliver services across providers with minimal duplication and disruption, and with high-quality outcomes and patient experience'.[10] When translated to antenatal health care with a comprehensive risk model, this implies a shared risk, shared management, and shared care provision concept. This comprehensive risk models pays equal attention to medical and non-medical risk factors, both in the assessment of risk levels and the therapeutic and preventive measures.

The relatively unfavourable position of the Netherlands regarding perinatal mortality[1], in particular in urban areas [11], resulted in the development of shared care as the model for antenatal health care.[9] This comprehensive model acknowledges the relevance of accumulation of heterogeneous risks by introducing universal, broad antenatal risk assessment including medical and non-medical risk factors. Broad risk assessment is followed by multidisciplinary responsibility to reduce high risk cases.[8 12]

However, risk assessment lacked a comprehensive tool as the available routine antenatal screening instruments focus mainly on medical factors [13-17] and do not consider

risk accumulation as mechanism. The few instruments available are rarely used beyond the research setting [16], and not embedded in integrated care settings.

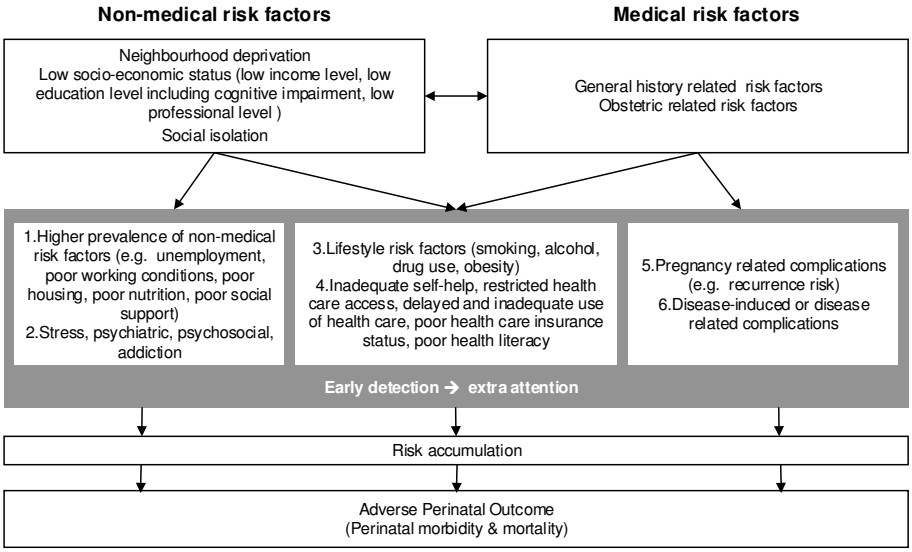
In response to the need for a comprehensive tool which connects medical and non-medical risks to integrated pathways, we developed a non-invasive, standardized score card for routine use in antenatal health care. The 'Ready for a baby' program, a prior antenatal healthcare program in the city of Rotterdam [5], provided the framework to develop and pilot this instrument in the antenatal healthcare setting.[18] The main purpose of this universally applicable score card is early identification of women with an increased risk for common adverse pregnancy outcomes, notably small for gestational age and prematurity. It offers tailored preventive and curative options for both conventionally detected risk factors (e.g. cocaine use), and for non-medical risk factors (e.g. domestic violence or financial debts). Following the current 'developmental origin hypothesis of adult disease', it is in the interest of the future health and development of the child to maximize efforts to reduce avoidable (non-) medical risk factors at the earliest possible stage.[19]

The aim of this study is to present the further application-oriented development of this risk screening instrument for early antenatal detection of risk factors and tailored prevention in an integrated care setting. This paper presents an overview of published risk assessment instruments, the methodological and clinical considerations of associated with the development of our instrument, and the application-oriented step from a score card risk profile to an integrated risk modifying approach of detected risk factors with the use of so-called care pathways in a multidisciplinary setting.

BACKGROUND

In box 6.1 we provide the conceptual framework which illustrates the interaction of non-medical and medical risk determinants and their influence on adverse perinatal outcome. Not all underlying mechanisms are revealed. Frequently factors are bidirectional related, as has been pointed out by researchers in the area of deprivation research.[11] Regarding non-medical risk factors, socio-economic status and neighbourhood deprivation are most consistently related to adverse perinatal outcome. Socio-economic status can induce adverse perinatal outcome though multiple pathways, most importantly through low education and low income levels.[20] Previous studies showed that decreased wealth and poor housing increase physiological stress.[21] Low income levels and deprivation are also associated with poor housing, nutritional deficiencies, and impaired health care access.[7 11 22] However, to date it is unknown to what extent the effect of deprivation goes beyond the effect of poor individual level of socio-economic status of citizens in deprived neighbourhoods.[23 24]

Box 6.1 Pathways of medical and non-medical determinants leading to adverse pregnancy outcome.



Regarding medical risk factors, several diseases or disease-related pharmaceuticals directly affect perinatal outcome. Effects are induced by the disease itself (e.g. increased risk for growth restriction in some auto-immune diseases) or can be more indirectly related (e.g. the increased risk for still birth in poorly regulated diabetes mellitus). Most obstetric adverse outcomes show an increased recurrence rate in subsequent pregnancies.

Lastly, non-medical risk factors also act indirectly through their general adverse health effects: low socio-economic status is associated with a higher prevalence and poor prognosis for most common diseases, and may decrease life expectancy up to 10 years in developed countries.[25 26]

METHODS

General

Our risk assessment instrument, the so-called Rotterdam Reproductive Risk Reduction (R4U) score card, was designed as a professional based risk assessment instrument applicable during the first antenatal visit. The first antenatal visit takes normally takes place before the 12th week of gestation. It focused on risks associated with the occurrence

of Big 4 outcomes at birth, and with perinatal mortality. Risks may have a medical or a non-medical background. [18] The R4U scorecard can be used as stand-alone or combined with other tests. The latter means that the scorecard could also be combined with other (pre-existing) screening tests if more extensive screening on specific risk factors is necessary (triage purpose). The final aim of the scorecard was to link responses to clinical management protocols.

Risk factors selection for the score card

The initial selection of risk factors for the first version included a review of existing risk assessment instruments, and a selected literature research for specific domains and items.[18] In view of the pilot success in terms of feasibility and acceptability of the pilot score card, the present study repeated the literature underpinning through a formal design, and adding some additional features of interest. Attention was restricted to published instruments from western countries from 1990 onwards. Score cards published until 1990 were described by other studies and therefore excluded for this purpose.[13 15-17] We performed a broad electronic literature search December 3st 2012 in Medline, Embase and Web of Science from inception to December 2012. A search strategy was developed based on antenatal risk screening and its synonyms such as 'antenatal risk assessment', 'antenatal risk screening', 'scorecard' which were also combined with 'pregnancy', 'prenatal' and 'obstetric'. Although we hand searched reference lists from main articles and relevant reviews for additional eligible studies, the synonyms were numerous. No language restrictions were applied. The remaining risk assessment instruments related to antenatal healthcare were included.

Each published instrument was structurally reviewed along the following topics: predicted outcome (e.g. low birth weight, or adverse outcome as whole), timing of screening (e.g. first antenatal visit, or selected gestational trimester), population (e.g. whole population, low income women), registration (item selection, e.g. social items, obstetrical items), scoring (summation of items, weighing of items; use of cutoffs), practical disadvantages, validation, discriminative power, and current practical use. At the second stage we complemented this review with detailed epidemiological information (prevalence and risk estimates) from well documented large birth cohort studies which have published risk factor analysis for various birth outcomes.[27-30] At a third stage we completed the candidate list with risk factors suggested by published (inter)national guidelines on prenatal assessment.[31 32]

Design of the score card

Item selection

Risk factors were selected if unequivocal evidence pointed to an association with small for gestational age, preterm birth, and congenital anomalies ('Big 3'), and perinatal mortality. While we initially aimed to detect pregnancies prone to a delivery with a low Apgar score, we excluded this aim as insufficient evidence exists on its suitability to predict in such an early stage. Initial selection of risk factors incorporated in the R4U score card took place in five expert meetings within the project group.[18] All selected risk factor questions ('items') were standardized. To increase uniformity, we defined a so-called 'script' text for each separate item as a literal text to list the question. It was printed at the back of paper and pencil forms, or could be popped up in the digital form underlying the present study. It was thought that the script may facilitate questioning of sensitive questions (e.g. domestic violence), and decreases error in questions with known intra-professional variation (e.g. miscarriage, living in a deprived neighborhood).

The standard format of question and closed response was derived from the WIC prenatal risk factor score card. Response was dichotomous only. The 'yes' was an indicator for the presence of the risk factor with a known relative risk of adverse perinatal outcomes. The resulting list of candidate items was first piloted for feasibility and reliability.[18]

Connection of risk profile to care pathways

The present study added a connection between risk profile as established through the R4U scorecard and a tailored care pathway. To this purpose, each item was categorized into four groups according to their instrumental use:

1. Single risk: such a risk factor that is directly linked to Big 3 and / or perinatal mortality, and justifies intervention independent from other considerations (e.g. drug use).
2. Additive risk: such a risk factor that is associated with Big 3 and / or perinatal mortality (both medical and non-medical risk factors, irrespective of the avoid ability of the risk factor), and has been reported to contribute to adverse outcome as cumulative risk (e.g. lack of social support or being unemployed).
3. Conditional risk: such a risk factor that is known to be relevant for Big 3 or perinatal mortality, but being a risk factor dependents on more information. E.g. being unemployed is a risk factor if family income depends on maternal employment, but may be of minor importance if a partner provides sufficient income.
4. Instrumental risk: from the Woman, Infants and Children (WIC) prenatal risk factor score card [33] we adopted the inclusion of some risk factors which are not associated with adverse perinatal outcome, but which could strongly affect the provision of perinatal care. Detection of these risk factors creates awareness by the care professional. E.g. Jehovah's Witness (blood transfusion), illiteracy (health promotion and

instruction materials), ethnic background (the use of interpreter services; the taking into account for specific cultural habits and expectations).

Occasionally risk factors belong to more than one category. A single risk of e.g. preterm birth may also act as additive risk for other adverse outcomes.

In the development, we also introduced 'weighing' and the cumulative risk score. To obtain a cumulative risk score from an individual profile of positive risk items, weights have to be assigned to each abnormal 'yes' category. A cumulative risk score above a predefined cut-off point would imply a follow-up action, including multidisciplinary consultation between perinatal professionals and other healthcare professionals, such as paediatricians or social workers. It offers the opportunity to customise antenatal policy to the individual woman's need. Such a cut-off may also be locally adapted to accommodate the availability of facilities. The present weights were obtained from published odds ratios (OR) and relative risks (RR) in large, representative birth cohort studies, meta-analysis, and an occasional case-control study (source data available upon request). We expressed weights in points, depending on the OR/RR of a risk factor: risk factors consistently associated with OR/RR smaller than two were assigned 1 point, higher than two or related to perinatal mortality were assigned 2 points, and for risk factors associated with OR/RR higher than four, 3 points were assigned. For a few items, assignment of a weight was primarily based on expert opinion. Occasionally publication delay underrated current practice: e.g. previous stillbirth or previous small-for-gestational-age (SGA) justified a higher weight than papers so far suggested. These items were expert opinion prevailed, for example in case of a high relapse rate (e.g. preconceptional use of drugs). The remaining items, for which there was currently no evidence available, received 0 points.

The use of both paper and pencil (A4-format) and digital score card was intended. The first version employed a paper and pencil version following the 2 column lay-out of the WIC prenatal risk factor score card.[33] The digital form used an open source software system to present a digital questionnaire to the healthcare professional.

Service responses to the score card

As mentioned previously, responses from the R4U score card (the risk profile) were connected to corresponding care pathways. Care pathways were included to address the management of (non-)medical risk factors.[9] We developed 28 templates of care pathways for all risk factors (single and cumulative) incorporated in the R4U score card.

These care pathways support conventional medical and obstetrical risk factors, but also incorporate unconventional, non-medical risk factors. Each care pathway consists of a defined set of measures a healthcare professional could take to meet the specific need of the pregnant women. Predesigned templates should be adapted to the local settings

to fulfill local needs. The details and service response will be described in detail in the section 'practical experiences'.

Pilot study

The resulting R4U risk score card was piloted in several hospitals and midwifery practices in Rotterdam. Data collection of this pilot study on feasibility and reliability took place from 2010 until 2011.[18]

In the result section below we provided the results of the developmental steps of the R4U score card, including the risk factor selection and categorization, the summary score procedure, and the application-oriented extension from screening to tailored care provision through care pathways. The results include the subsequent modifications derived from the first pilot study. To illustrate the potential service impact of the R4U score card, we provided an illustration of the summary score and the application of a threshold was with the use of real data from a first pilot in practice.

Approval was obtained from the Institutional Review Boards of the Erasmus Medical Center before the study began, and decided that written informed consent was not necessary.

RESULTS

Table 6.1 presents a review of 8 predictive instruments for routine use in antenatal care published from 1990 onwards.[17 33-39] Five out of 8 instruments focused on more than one predictive outcome, for one the predicted outcome is unknown. None of the instruments took congenital anomalies into account. Six instruments can be applied to identify risks at the first antenatal visit, and all except one are used for an unselected group of pregnant women, rather than a specific group. The instruments often specialized on either medical or non-medical factors, rather than a combination; the number of items included ranges from 4 to 45. In 7 instruments a validation test of the claimed predictive power had taken place, among these are only 2 instruments that are externally validated. The positive predictive value was available for 4 instruments, ranging from 1.4% to 33%. As far as we know, 4 instruments were currently in use.

In table 6.2 we show the contents of the R4U score card in terms of domains, items, item relevance, and weighing factors. The final R4U score card included 70 items categorized into 6 domains, namely social status (n=14), ethnicity (n=3), reproductive factors (n=8), lifestyle (n=14), medical history (n=14) and obstetric history (n=17). The assignment of item categories (1-4) in the column 'item relevance' was based on consensus by the project group. Items were grouped according to subject for ease of history taking. In the paper and pencil version, the four non-medical domains are listed on the left

Table 6.1 Predictive instruments for routine use in antenatal care (published from 1990 onwards)

Author	Chard et al. 1992[17], United Kingdom	Knox et al. 1993[34], New Zealand	Mercer et al. 1996[35], USA	Simmons et al. 2001[36], Canada	Gueorguieva et al. 2003[37],USA	Carroll et al. 2005[38], Canada	WIC score card 2007[33], USA	Burstyn et al. 2010[39], Canada
Predicted outcome	Low birth weight (< 2500g); Preterm birth(< 37 weeks); 5 minute Apgar < 6; Perinatal death	Perinatal morbidity (> 5 days in neonatal unit); Perinatal mortality (> 20 weeks of gestation–7 days pp)	Preterm birth (< 37 weeks)	Low birth weight (<2000g) or preterm delivery (<34 weeks)	Very low birth weight (< 1500g)	NA	NA	Low birth weight (< 2500g); Preterm birth (<37 weeks); 5 minute Apgar < 7; Neonatal intensive care; Resuscitation measures
Timing of screening	First visit	First visit + pre-delivery	23 - 24 weeks of gestation	First visit	NA	12 - 30 weeks	First visit	First visit, and eventually at 36 weeks
Population	Population based	Hospital deliveries	Hospital deliveries	Population based	Population based	Population based	Low income women	Population based
Registration	40 items: social, lifestyle, general history, gynaecological history, family history, obstetric history	45 items: demographic, social, lifestyle, general history, obstetric history, current pregnancy.	Maximal 7 items BMI, ethnicity, employment social environment, lung disease, Bishop score, vaginal bleeding;	17 items: demographic, environmental social, lifestyle, care in current pregnancy, general history, obstetric history.	31 items: demographic, environ-mental, social, lifestyle, care in current pregnancy.	15 items: demo-graphic, environ-mental, social, lifestyle, current antenatal care, psychiatric.	36 items: demo-graphic, environmental social, lifestyle, care in current pregnancy, psychiatric.	45 items: lifestyle, general history, obstetrical history, and current pregnancy.
Scoring + threshold	NA	Yes, weighted	NA	Yes, weighted	Yes, weighted	NA	Yes, weighted	Yes, weighted
Dis-advantages	Demo-graphic items except for age not included; Retrospective and model based: feasibility not evaluated.	Gynaecological and family history not included; Not feasible: caregiver has to calculate risk score from a formula with logistic regression coefficients	Depended on physical examination Calculation of risk score from a formula with regression coefficients; Limited time window of applicability	Mainly social and lifestyle related items, few medical items included;	Mainly social and lifestyle related items, few medical items included.	No formal prediction: itemwise detection of non-normals only; no medical items. Open questions referring to caregiver's opinion	Main focus on non-medical risk factors No data on development or effective-ness;	No social, environmental items, or ethnicity items.

Table 6.1 Predictive instruments for routine use in antenatal care (published from 1990 onwards) (continued)

Author	Chard et al. 1992[17], United Kingdom	Knox et al. 1993[34], New Zealand	Mercer et al. 1996[35], USA	Simmons et al. 2001[36], Canada	Gueorguieva et al. 2003[37],USA	Carroll et al. 2005[38], Canada	WIC score card 2007[33], USA	Burstyn et al. 2010[39], Canada
Validation	N = 2029 pregnancies: Primiparous, n = 929, adverse outcome: 14.9%; Multipara, n = 1100, adverse outcome: 12.2%	N = 20985 pregnancies to develop score system. External validation on n = 3120 women of which 7.6% had adverse outcome	N = 2929 singleton pregnancies10,4% adverse outcome. Primiparous: n = 1218, 8.2% adverse outcome, Multi: n = 1711, 11.9% adverse outcome.	N = 76763 singleton pregnancies; 4.0% adverse outcome.	N = 166372 singleton pregnancies, 0.9% adverse outcome. External validation on n = 37250 women, 1.0% adverse outcome	N = 227 pregnancies.	NA	N = 191686 live born singletons 18.8% at least one adverse outcome: low birth weight 4.9%, preterm birth 7.2%, low Apgar 2%, NICU 11.1%, resuscitation 3.4%
Discrimi-nation	NA	PPV 0.16 - 0.42 (booking and onset of labour)	PPV Primiparous: 0.29 Multiparous: 0.33	PPV 0.06* *calculated by the author	PPV 0.014 - 0.030, depending on cut-off point	NA	NA	NA
Current status*	Only original research setting	Only original research setting	Only original research setting	In use	Unknown	In use	In use	In use
Specialties	-	External validation available	Distinction between primiparous and multiparous women	Self-report (15/18 questions); Cut-off point indicates referral to Healthy Start intervention program	External validation available; Explicit assessment of the woman's 'strengths' and positive opportunities	Effectiveness of detection studied in RCT: In intervention group more psycho-social and family violence related concerns	Explicit assessment of woman's 'strengths' and positive opportunities	2 prediction moments: in early and late pregnancy

* To our knowledge, NA: not available, PP = postpartum, PPV = Positive Predicted Value, RCT = Randomized Controlled Trial

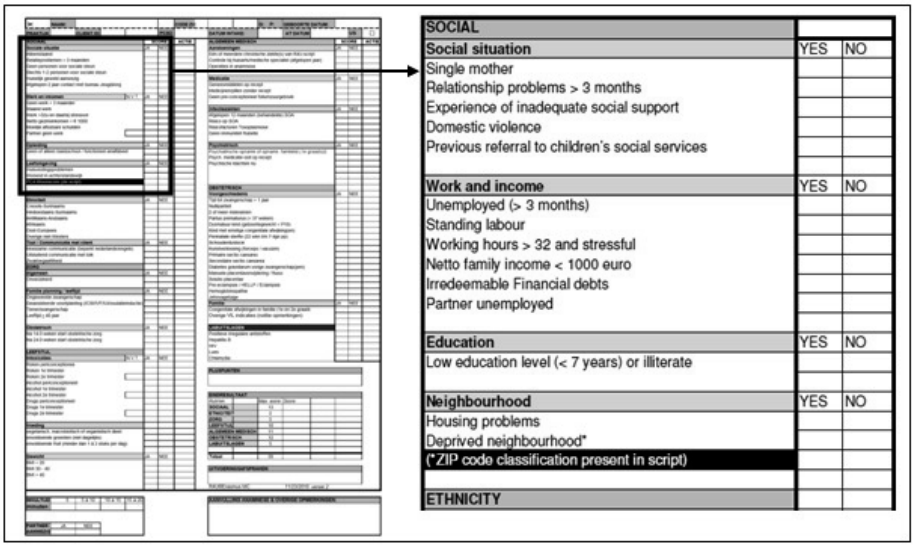
Table 6.2 Domains and items of R4U, according to predictive and clinical management relevance

Domain	Item	Item relevance				Weight
		1	2	3	4	
Social	Single mother		x	x	x	1
	Relationship problems			x	x	0
	Experience of inadequate social support		x	x		1
	Domestic violence	x	x		x	2
	Previous referral to children's social services	x		x		0
	Unemployed (> 3 months)		x	x		1
	Standing labour		x			1
	Working hours > 32		x			2
	Netto family income < 1000 euro		x			2
	Irredeemable financial debts			x	x	0
	Partner unemployed		x	x		1
	Low education level (or illiterate		x		x	2
	Deprived neighbourhood		x		x	2
	Housing problems			x	x	0
Ethnicity	Nonwestern ethnicity*		x		x	2
	Language barrier			x	x	0
	Mentally disabled				x	0
Reproductive factors	Uninsured	x		x		0
	Unwanted pregnancy	x	x			1
	Unplanned, but wanted pregnancy				x	0
	Assisted reproduction		x			2
	Teenage pregnancy (≤18 years)	x	x	x		3
Lifestyle	**No daily** intake of fruit and vegetables				x	0
	Vegetarian, vegan or macrobiotic diet				x	0
	BMI <18 kg/m^2		x	x		1
	BMI 30 -35 kg/m^2				x	0
	BMI > 35 kg/m^2	x	x			2
General	Chronic maternal illness	x	x			2
	Annual consultation physician			x	x	0
	Prescribed medication	x		x		2
	Over-the-counter drugs			x		2
	No preconceptional folic acid use	x	x			2
	Sexually transmitted disease last year	x			x	2
	Promiscuity	x			x	2
	At risk for toxoplasmosis	x	x			1
	At risk for rubella	x	x			1
	Refuses blood transfusion (Jehovah)			x	x	0
	History of psychiatric admission or positive family history (1stdegree relative)	x	x		x	3
	(History of) psychiatric medication			x	x	0
	Current psychiatric problems	x	x		x	3
Obstetric	Nulliparous		x			2
	Recurrent miscarriage (2 or more)		x			1
	Interpregnancy interval < 6 months	x	x			3
	History of preterm birth	x	x			3

Table 6.2 Domains and items of R4U, according to predictive and clinical management relevance (continued)

Domain	Item	Item relevance				Weight	Domain	Item	Item relevance				Weight
	Advanced maternal age (>40 years)		x	x		2		History of asphyxia (Apgar < 7 after 5 min)				x	3
	Start antenatal care 12 - 14 weeks			x	x	0		History of small for gestational age <p5	x	x			3
	Late start antenatal care > 14 weeks	x	x			3		History of major congenital anomalies	x	x			3
Lifestyle	Preconceptional smoking past 6 months			x		1		History of still birth (22 weeks - 7 days pp)	x	x		x	3
	Smoking during pregnancy 1st trimester	x	x			2		History of shoulder dystocia				x	0
	Smoking during pregnancy 2st trimester	x	x			2		History of instrumental delivery				x	0
	Preconceptional alcohol past 6 months				x	0		History of caesarean section				x	0
	Alcohol during pregnancy 1st trimester	x	x			1		History of gestational diabetes	x	x			1
	Alcohol during pregnancy 2st trimester	x				1		History of placental abruption		x	x	x	3
	Preconceptional illicit drug use past 6 months	x		x	x	1		History of manual placental removal or PPH			x	x	0
	Illicit drugs during pregnancy 1st trimester	x	x			3		History of (pre)eclampsia or HELLP	x	x			3
	Illicit drugs during pregnancy 2st trimester	x	x			3		Positive booking bloods	x		x	x	2
								Congenital anomaly in 1st degree relative			x	x	1

BMI, body mass index; pp, postpartum; PPH, postpartum haemorrhage; HELLP, haemolysis elevated liver enzymes and low platelets.



SOCIAL		
Social situation	YES	NO
Single mother		
Relationship problems > 3 months		
Experience of inadequate social support		
Domestic violence		
Previous referral to children's social services		
Work and income	YES	NO
Unemployed (> 3 months)		
Standing labour		
Working hours > 32 and stressful		
Netto family income < 1000 euro		
Irredeemable Financial debts		
Partner unemployed		
Education	YES	NO
Low education level (< 7 years) or illiterate		
Neighbourhood	YES	NO
Housing problems		
Deprived neighbourhood*		
(*ZIP code classification present in script)		
ETHNICITY		

Figure 6.1 Elaborated example of one domain in R4U.

side (n=39 items), and the two medical domains on the right side (n=31 items). The digital version presents the items one by one. As explained previously, for some items the assigned weight was expert opinion based: small for gestational age, previous still birth, short interpregnancy interval, body mass index > 35 kg/m^2, living in a deprived neighborhood, preconceptional smoking, and preconceptional illicit drug use. For other items, risk estimates were dependent on nature of the disease which varies across women: prescribed drugs during pregnancy, type of psychiatric disorder, recurrence rate of congenital anomalies, major congenital anomalies in first degree relative, and positive booking bloods. In case of item category '4' zero points were allocated for the summary score.

Figure 6.1 shows an excerpt of the R4U score card in its original paper and pencil form (social domain). A paper and pencil version cannot apply automated skipping of irrelevant items, nor the automated summation of weights. The whole R4U score card is added as supplementary file (Addendum 'R4U score card').

Three midwifery practices and 2 hospitals used the paper and pencil version R4U score card during their first antenatal visit.[18] The pilot version items were closely related to the current version as items rarely need adaptation. From the first 218 pregnancies, we derived the weighted summary scores as presented in figure 6.2. Pregnancies were sorted on ascending summary scores. The figure illustrates that each domain contributes from the beginning to our summary scores, and at any risk level all domains contribute to the risk load. The cut-off of 16 points indicated an advice for multidisciplinary consultation in 20% of all pregnant women.

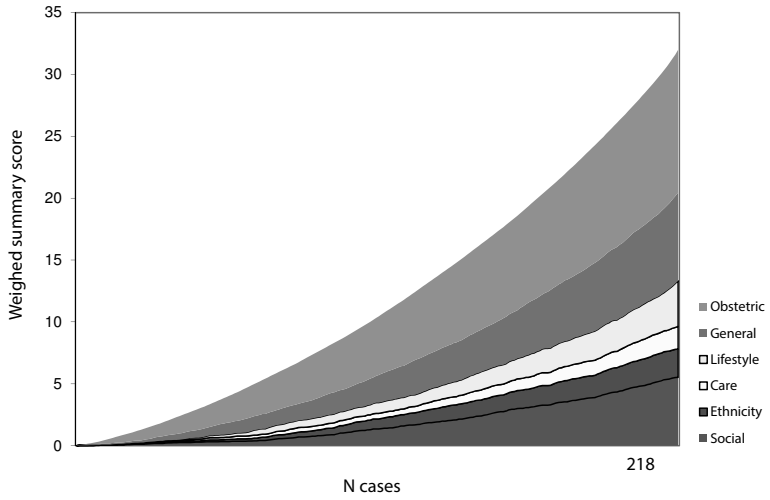


Figure 6.2 Cumulative weighted R4U summary scores for all domains separately for the first 218 cases of the pilot study.

PRACTICAL EXPERIENCE

The R4U score card was proposed to facilitate improved coordination of antenatal care through systematic and uniform risk screening for medical and non-medical risk factors.[18] Via 28 predefined care pathways it contributed to unequivocal division of tasks and responsibilities for non-medical risk factors. While we here have described the use of the R4U as instrument for triage, optimal profit from the risk information arises if care pathways were connected to the individual needs of pregnant woman.[9] Care pathways were used to modify these risk factors, and as these pathways are explicit as to which caregiver will be responsible, the efficiency and accountability are enhanced. Together with local healthcare professionals in perinatal care, municipal services, community health services, and other services, these pathways were projected on the local setting in organized meetings. This means that the availability of local facilities and insurance agreements were taken into consideration.

In addition, a risk score above the predefined cut-off point implied follow-up action. This follow-up action included multidisciplinary consultation between obstetric caregivers and non-obstetric caregivers, prioritization of risk factors, and feedback in subsequent meetings. For the client, an effect of this approach was the prevention of doubling of history taking by different professionals at different stages. The standardized format facilitated risk communication across disciplines.

The introduction of organized meetings to customize care pathways induced a change in the mutual professional relationship. Initially obstetric caregivers and non-medical caregivers functioned strictly separate, each covering their 'own' part of the case. The organized meetings induced mutual respect and much more awareness among both professionals on the impact and effect of non-medical risk factors. It realized the necessity to address these non-medical risk factors to improve perinatal outcome.

Early detection and active involvement of 'non-medical caregivers' through care pathways provided the opportunity to monitor actively from on the onset of pregnancy. This was not the case in the conventional scenario in which non-medical risk factors were passively noticed. Note that this approach might induce a shift in workload to the early antenatal phase, including more registration for monitoring.

The R4U scorecard enables a considerable change in early antenatal healthcare as illustrated in box 2. Here we present the impact on the service response of the comprehensive R4U-based approach versus the conventional approach in a representative case example.

Box 2 Impact on service response of the comprehensive (R4U-based) versus the conventional approach: a representative case example

Random Case (R4U score card pilot data)

Ms. X is a non-western 22 year old G2P1 with no medical history. In the first pregnancy her daughter was born at 40+0 weeks of gestation with a birth weight of 2,800 g (< p10, 10th percentile). After the break up with her former boyfriend, she got pregnant unplanned. The current father is not in the picture. Ms. X is unemployed, receives social welfare payment, and she is struggling to get by. She smokes 2 cigarettes each day 'to relax'.

Service response

1. Conventional antenatal policy

Risk assessment

- Anamnesis focused on medical and obstetrical risk factors (no guideline available)

Antenatal policy

- In response to obstetric history: no specific action
- In response to smoking: passive approach
- In response to social situation: no specific action

Multidisciplinary consultation

- Depending on local commitments; non-medical caregivers (e.g. social services) are usually not involved at this stage

Remark: as none of the individual risk factors are considered as critical, a case like this usually escapes extra surveillance.

2. Comprehensive antenatal policy

Risk assessment

- R4U score – card in first trimester

Result: Score of 16 points (7 in the social domain, 3 in the lifestyle domain, and 6 in the obstetric domain)

Antenatal policy

- In response to obstetric history: care pathway 'growth restriction' à growth ultrasounds as non-medical risk factors (smoking, social situation) add to obstetric risk factors (previous child birth weight below 10th percentile) in this case. The combined risk justifies extra efforts.
- In response to smoking: care pathway 'smoking' à therapeutic options and therapists for active cessation will be offered to her directively. Progress will be discussed every consultation.
- In response to social history: care pathway 'psychosocial' à social services will be involved.

Multidisciplinary consultation

- Antenatal policy will be defined in a multidisciplinary setting in first trimester. Feedback in subsequent meetings.

Remark: this approach defines an explicit monitoring and prevention. The policy can be declined at any stage at the request of clients and caregivers.

DISCUSSION

The resulting R4U score card is proposed as a universal risk screening instrument. It incorporates recent evidence on non-medical risk factors for adverse pregnancy outcomes and could facilitate an integrated antenatal healthcare setting. Unique is the close connection between risk profile and care pathways focusing on non-medical factors. The intended users are obstetric professionals, such as midwives, obstetricians, obstetrical nurses or general practitioners, and it can be applied to all pregnancy populations. An integrated setting (including psychosocial and public health workers) is preferable for optimal use, as the resulting care pathways require medical and non-medical expertise. The R4U score card is a method for integrated risk management, which facilitates coordination of antenatal healthcare through uniform risk screening, and a clear division of tasks when high risk cases are treated through predefined care pathways. The score card enables and supports a shared care provision model.[9]

Through its concept and standardized assessment, it bridges the gap between the clinical working area and the public health domain ('minimal duplication and disruption'). By the inclusion of risk factors that were directly associated with adverse perinatal outcome and uniform definition of risks by all professionals involved, it enhances the ultimate aim to reduce adverse perinatal outcome ('high quality outcomes'). Care pathways add to efficiency and task division in multidisciplinary settings. This all facilitates effective and efficient management of women at risk, without ambiguity who is in charge.[9 10]

Risk scoring in apparently asymptomatic persons for triage purposes is also known from other specialties such as the Framingham Coronary Heart Disease Prediction Scores for predicting risk of clinical coronary heart disease events.[40] In obstetrics, risk scoring is at this moment rarely routinely applied – and if so – only for obstetrical risk factors. We believe that the emerging knowledge on the predictive role of both medical and non-medical risk factors, and risk accumulation justifies the introduction of a formal 'evidence-based' screening tool. Inspired by the Women, Infants, and Children (WIC) antenatal score card, we aimed to develop an extended version, anticipating on multiple risk factors which commonly determine care and support.

We are aware of the fact that the performed search on previous instruments was still an exploration of the rapidly expanding literature. There may still be methods that we have overlooked that could be a valuable addition. In addition, we omitted some instruments without apparent scientific evaluation. However, since we have also checked professional guidelines at the international level, we believe the probability is low that we overlooked a checklist with important application.

Although the current version of the score card covers 70 common items, we are well aware on the potential presence of rare risks. A score card cannot replace professional responsibility for careful history taking, as is also true with the use of for example cardiologic prediction scores and surgical checklists.[41] Over time, items can be added or deleted or adapted to local circumstances.

For the implementation of such a new approach in antenatal risk assessment, a number of conditions need to be fulfilled. Most importantly, professionals from obstetric care, social welfare, psychiatric services, and community health services should agree on the comprehensive risk concept as a base to collaborate. Conflicting financial incentives and existing inter-professional communication barriers may represent a challenge for the implementation of this innovative screening plus intervention method.[9] Healthcare professionals may need training to question and encounter the new non-medical risk factors, and the time schedule of the first antenatal visit may require adaptation. Health insurance reimbursement schemes might need revision in order to enable this. This is also true for the non-medical preventive and curative measures following the care pathways. However, the administration of the R4U score card is not the time consuming part of antenatal health care, rather the professional effort to guide the detected high women being compliant to the proposed care pathways.

Future research is necessary to investigate the performance of the R4U score card under routine conditions and to measure the extent of integrated care it invokes.[10] The feasibility, inter-intra observer variability and predictive value are investigated, and it seems that the R4U risk score card is a feasible and reliable instrument.[18] A nationwide randomized controlled trial recently started to establish the effectiveness of early systematic antenatal risk detection with the R4U on pregnancy outcomes.[42] Over time the

effectiveness and efficiency of this comprehensive risk assessment should be clarified - currently little is known on the cost-effectiveness of routine antenatal screening.

CONCLUSION

The present study describes the development of the R4U score card, a non-invasive, standardized instrument for routine early antenatal risk screening which covers both medical and non-medical risk factors. The R4U score card is designed as a universal, non-invasive risk screening instrument incorporating recent evidence on non-medical risk factors for adverse birth outcomes and their treatment to facilitate integrated antenatal healthcare.

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Chapter 7

Assessment and care for non-medical risk factors in current antenatal healthcare

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ABSTRACT

Objective This study aims to identify current practice in risk assessment, current antenatal policy and referral possibilities for non-medical risk factors (lifestyle and social risk factors), and to explore the satisfaction among obstetric caregivers in their collaboration with non-obstetrical caregivers.

Design Cross-sectional study

Setting Dutch antenatal care system

Participants Community midwives from 139 midwifery practices and gynaecologists, hospital-based midwives, and trainees in obstetrics from 38 hospitals.

Measurements and findings Results were analysed with chi-squared tests and unpaired t-tests. Caregivers universally screened upon lifestyle risk factors (e.g. smoking or drug use), whereas the screening for social risk factors (e.g. social support) was highly variable. As national guidelines are absent, local protocols were reported to be used for screening on non-medical risk factors in more than 40%. Caregivers stated multidisciplinary protocols to be a prerequisite for assessment of non-medical risk factors. Only 22% of the caregivers used predefined criteria to define when patients should be discussed multidisciplinary.

Conclusion Despite their relevance, non-medical risk factors remain an underexposed topic in antenatal risk factor screening in both the community and hospital-based care setting.

Implications for practice Structural antenatal risk assessment for non-medical risk factors with subsequent consultation opportunities is advocated, preferably based on a multidisciplinary guideline.

INTRODUCTION

Poor social and economic circumstances affect health throughout life. Even in the most developed countries, less affluent individuals have substantially shorter life expectancies and higher prevalence of disease.[1] Scientific research has led to a growing understanding of the influence of social environment on health outcomes. Barker et al. showed that the foundation of some adult disease lies in the (pre)conception and early pregnancy periods.[2] Suboptimal circumstances during pregnancy, other than medical risk factors, may lead to impaired fetal development. Such circumstances include maternal stress due to for example lack of social support, nutrient deficiencies, or maternal intoxication.[2] Furthermore, recent evidence from large cohort studies showed that these so-called non-medical risk factors (lifestyle and social risk factors) play an independent, risk-enhancing role in perinatal and maternal outcomes.[3-5] The impact of non-medical risk factors is visible through their prevalence, their independent relative risk or both.[6 7] Moreover, it was shown that an accumulation of these risk factors can further harm the chances of a good pregnancy outcome.[8 9]

Early identification and management of risk factors is therefore seen as a promising intervention to prevent or limit fetal exposure to these risk factors. Several preconception and early antenatal intervention programs showed promising results in reducing risky health behaviors, such as smoking, alcohol consumption, and unhealthy diet.[10 11] However, in most countries preconception care is often – when available – only offered to women with predefined medical risk factors such as chronic diseases[12], and much less frequently offered to women in the general population.[13] The practice of visiting a healthcare professional for preconception care is not common in many countries, including the Netherlands.[14] Therefore, the first antenatal visit is often the first opportunity to identify these risk factors.

In the Dutch obstetric care system, community midwives and gynaecologists work autonomously in a 3-tier system, and generally play a complementary role.[15] The national guideline for referral to a gynaecologist is restricted solely to medical and obstetrical risk factors.[16] Depending on the risk factor, this guideline appoints the midwife or the gynaecologist to be the primary indicated caregiver. Non-medical risk assessment in antenatal healthcare lacks however a comprehensive tool as the available routine antenatal screening instruments focus mainly on medical factors.[17 18]. Practitioners usually do not use a template for the intake consult. Some caregivers use a template which is often offered by the software system they use, however, these are almost always limited to on medical risk factors only.

If non-medical risk factors are not routinely addressed in antenatal healthcare systems, surveillance of these exposed pregnancies is at stake. More specifically, risk factors are likely to be detected too late or at a point at which the pregnancy has already been

negatively affected. This is the case in particular for modifiable risk factors, such as smoking during pregnancy, lack of social support, domestic violence, or inadequate housing. Early identification of pregnancies with a high risk profile can lead to prevention and intervention - not necessarily restricted to that by professionals in the curative sector - which in turn can contribute to the improvement of perinatal outcomes. It was recently demonstrated that timely detection of growth restriction maximizes the potential benefit of clinical management of such cases.[19]

Several community-based projects with a focus on non-medical risk factors in pregnancy reported successful results.[20-22] However, little information is known on the performance of systematic screening for non-medical risk factors in routine antenatal healthcare. Published studies indicate that the number of available instruments for antenatal screening is scarce. Experience with these tools is limited to implementation in research settings, which is essentially different from real time situations.[23-27] Therefore, the present study aims (1) to identify current manners of assessment, current antenatal policy and referral possibilities for non-medical risk factors (lifestyle and social risk factors), and (2) to explore the level of satisfaction of obstetrical caregivers in their collaboration with non-obstetrical caregivers.

MATERIALS AND METHODS

Study design

This cross-sectional study was conducted in 39 municipalities in the Netherlands amongst community midwives working in a primary care setting, and amongst gynaecologists, hospital-based midwives and trainees in obstetrics and gynaecology (O&G) working in a hospital setting

Municipalities were extracted after a municipal selection process which was performed for the Healthy Pregnancy 4 All study.[13] This national project, supported by the Dutch Ministry of Health, Welfare and Sport, aims to improve perinatal health by offering and amending preconception care and providing timely risk assessment for both medical and non-medical risk factors in pregnancy. In a thorough analysis, 50 geographical areas were identified in which adverse perinatal outcomes were high. The list was obtained by combining epidemiological evidence on adverse outcomes from the national perinatal registries of midwives, gynaecologist and paediatricians.[28 29] The Healthy Pregnancy 4 All study takes place in 10 out of the 50 selected geographical areas (14 municipalities) in the Netherlands. For this study, areas showing the highest perinatal morbidity and mortality rates were selected for both interventions.[13] In order to optimally assess the current manner of risk selection in the Netherlands, we did not conduct our study in the areas in which the Healthy Pregnancy 4 All study was implemented. All community

midwives and hospital caregivers in the remaining municipalities were approached. These municipalities do not participate in the Healthy Pregnancy 4 All study, but remain representative of all areas of the Netherlands based on their coverage level (approaching 50% of the country) and population size. One municipality was excluded because it was already participating in a concurrent perinatal municipal program.

Since the working area of midwives can be defined by zip codes, we identified all midwifery practices covering a working area corresponding to the selected zip codes of one of our selected municipalities. Through the website 'www.knov.nl', areas in which midwifery practices were located were identified. Gynaecologists were selected based on hospital location, and all gynaecologists working in a hospital situated in - or adjacent to - one of the 39 municipalities were approached. Contact information for these gynaecologists was found on the websites of the hospitals. Hospital-based midwives and trainees in O&G were also approached to cover the full spectrum of hospital-based obstetric caregivers.

Community midwives' practices were contacted by telephone and during this calls introduction to the study and verification of the working area took place. From all participating midwives, e-mail addresses were obtained in order to send the web-based questionnaire. If the working area did not correspond to the area codes of one of the 39 selected municipalities, practices were excluded. Gynaecologists, hospital-based midwives and trainees in O&G were directly contacted by e-mail. E-mail addresses were obtained from an up-to-date address file. If an e-mail address was not available, administrative staff of the department of O&G distributed the study information and questionnaire.

Development of the questionnaire

The questionnaire was developed as part of the Healthy Pregnancy 4 All program (available upon request).[13 30] The questionnaire was piloted among practices of municipalities that participated in the Healthy Pregnancy 4 All study (n=36). After this, the questionnaire was distributed to individual caregivers (rather than practices) in order to appreciate personal opinions, gain more knowledge on antenatal screening policy, and measure the level of satisfaction among caregivers on collaboration with other caregivers. The questionnaire assessed baseline characteristics of caregivers, current practice in risk screening (e.g. with or without non-medical factors), current antenatal policy for medical and non-medical risk, and collaboration with different (obstetric) caregivers.

Data collection & Statistical analysis

Data was collected between May and August 2013. A distinction was made between community caregivers and hospital caregivers. The questionnaire was sent to 139 community midwife practices and 38 hospitals with obstetrical units. All individual caregiv-

ers of the practices (midwives) and obstetrical units (gynaecologists, hospital-based midwives, and trainees in O&G) were invited to complete the questionnaire. The minimal request was that at least one caregiver of each practice or obstetrical unit complete the questionnaire. Caregivers who did not respond within two weeks were sent a reminder via e-mail. Another four weeks later non-responders were reminded by telephone.

Conventional comparative statistics were used (differences between group frequencies: chi-square test; differences between number: unpaired t-test or Mann-Whitney U test). Statistical analysis was performed using SPSS 20.0 for Windows software (SPSS Inc, Chicago, IL).

RESULTS

We received completed questionnaires from 74 of the contacted community midwife practices (53%) and 33 of the contacted hospitals (87%). We excluded 34 incomplete questionnaires (empty or sparsely completed (less than 10%)). Table 1 shows the baseline and practice characteristics of included caregivers. In total 118 community midwives

Table 7.1 Characteristics of study participants on the practice and caregiver level

Practice level	Community practices (N = 74)	Hospitals (N = 33)
Type of practice, N(%)	Solo 6 (8.1)	Academic 3 (9.2)
	Duo 7 (9.5)	Peripheral teaching 18 (54.4)
	Group 60 (81.1)	Peripheral non-teaching 12 (36.4)
	Unknown 1 (1.3)	
Practice assistant available, N(%)	39 (68.4)	NA
Minutes per intake consult	45 (10-80)	Gynaecologist 20 (5-30)
		Hospital-based midwife 30 (10-45)
		Trainee O&G 30 (10-45)
Number of consults in 1st trimester	2 (1-5)	2 (1-5)
Number of consults in total	13 (1-18)	11 (7-16)
Caregiver level	**Community midwives (N = 118)**	**Hospital based caregivers (N = 154)**
Age in years	34 (21-65)	39 (23-62)
Gender, N(%)		
Male	2 (1.7)	32 (20.5)
Female	116 (98.3)	122 (78.2)
Job position, N(%)	Self-employed 96 (82.1)	Gynaecologist 68 (44.2)
	Wage service 21 (17.9)	Hospital-based midwife 48 (31.8)
		Trainee O&G 37 (24.0)

Data presented as median +/- range. unless otherwise specified
NA: not applicable. O&G: obstetrics and gynaecology

(21%), 68 gynaecologists (19%), 49 hospital-based midwives, and 37 trainees in O&G completed the questionnaire. Only the median scheduled time for an intake at booking differed among community midwives and hospital caregivers.

Risk screening

Table 2 presents the assessment of non-medical risk factors, subdivided into lifestyle risk factors (e.g. smoking and drug use) and social risk factors (e.g. social support and domestic violence) at the individual caregiver level. From the 118 community midwives and 154 hospital caregivers that responded to our questionnaire, 101 community midwives and 124 hospital caregivers completed this section. Lifestyle risk factors were universally screened, whereas the extent of screening for social risk factors varied amongst respondents. Community caregivers were found to screen significantly more for all risk factors asked for, except household income. This was especially the case for domestic violence, work-related stress, and intake of fruit and vegetables ($p < 0.001$). Self-reported reasons why caregivers did not screen for non-medical risk factors were: 1. it compromised the privacy of the patient [this was applicable for the risk factors: income (49%), relational problems (52%), debts (48%) and domestic violence (42%)], 2. a lack of time [applicable to risk factors related to social support (32%) and intake of vegetables and fruits (45%)], and 3. a perceived lack of relevance [applicable to questions about work-related stress (36%)]. Note that not all respondents completed this part of the questionnaire (respec-

Table 7.2 Self-reported risk identification of non-medical risk factors (lifestyle and social risk factors) among community midwives and in-hospital caregivers during first antenatal visit

Risk factor	Community midwives	Hospital caregivers	p
Lifestyle risk factors			
Smoking	100 (99.0%)	124 (100%)	0.45**
Alcohol	101 (100.0%)	124 (100%)	NA
Drugs	101 (100.0%)	124 (100%)	NA
Use of medication	100 (99.0%)	124 (100%)	0.45**
Intake of sufficient amount of vegetables and fruits	76 (75.2%)	37 (29.8%)	<0.001*
Social risk factors			
Low income	14 (13.9%)	9 (7.3%)	0.11*
Relation problems	30 (29.7%)	21 (16.9%)	0.023*
Domestic violence	92 (91.1%)	24 (19.4%)	<0.001*
Work related stress	51 (50.5%)	32 (25.8%)	<0.001*
Financial debts	11 (10.9%)	2 (1.6%)	0.004**
Lack of social support	53 (53%)	48 (39%)	0.037*

*Chi-square test **Fisher exact test
NA: test not applicable

Table 7.3 Practice and professional factors associated with the number of assessed non-medical risk factors (lifestyle and social risk factors) by community midwives

	Number of non-medical risk factors		
Factor	0-3	4-7	p
Case manager present	31 (51.7%)	29 (48.3%)	0.327
Deprived area benefits*	18 (46.2%)	21 (53.8%)	0.184
Scheduled meetings with non-obstetricians**	27 (50.1%)	26 (49.1%)	0.959
Sufficient referral possibilities for psychosocial problems	42 (53.2%)	37 (46.8%)	0.644
Years of working experience			
<10 years	30 (55.6%)	24 (44.4%)	0.471
10-20 years	11 (42.3%)	15 (57.7%)	
>20 years	11 (57.9%)	8 (42.1%)	
Workload***			
<300 units	13 (41.9%)	18 (58.1%)	0.040
300-400 units	14 (48.3%)	15 (51.7%)	
>400 units	18 (75.0%)	6 (25.0%)	
Satisfied with duration of the intake	41 (51.9%)	38 (48.1%)	0.804

The non-medical risk factors included income, relational problems, domestic violence, work-related stress, financial debts, social support and intake of a sufficient amount of vegetables and fruits
*Additional rate for community midwives working in deprived areas
Defined as: social services, youth and family centers, municipal health services, and youth care * Presented as units of care: Since a considerably part of women will be referred to a hospital during pregnancy or during labour, the definition 'unit of care' has been introduced. This composite measure represents the total number of pregnancies a community midwife has responsibility for in the primary level of care.

tively 18 midwives and 30 hospital based caregivers), because they indicated not to be involved in the intake of pregnant women.

Table 3 shows the relation between the assessment of non-medical risk factors and specific in-practice circumstances amongst community midwives. Hospital caregivers were not displayed since only 10 of them assessed more than 4 non-medical risk factors. Only workload (number of clients) was associated with the assessment of non-medical risk factors: in smaller practices non-medical risks were screened more often (p = 0,040).

The perceived prevalence of non-medical problems differed considerably between community and hospital caregivers (p<0,001). More than half of all hospital caregivers indicated that they deal with non-medical problems on a weekly (40%) or daily basis (16%). This is in contrast to the frequency at which community midwives report dealing with non-medical problems (23% on weekly basis and 8% on daily basis). However, systematic screening for non-medical risk factors was more common amongst community caregivers (figure 1). Both the community midwives and the hospital caregivers

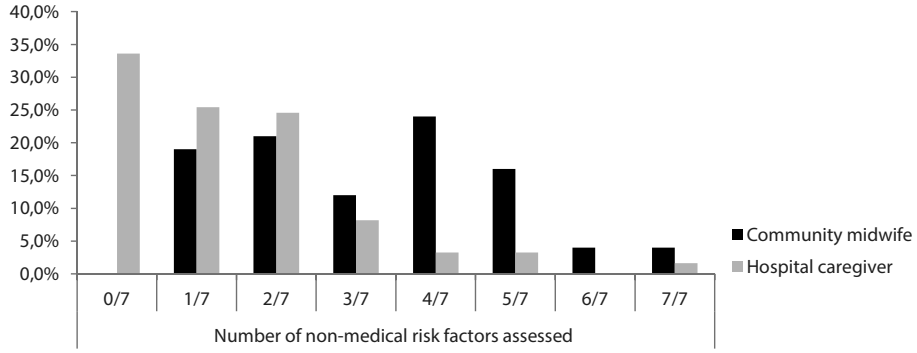

Figure 7.1 Systematic screening for non-medical risk factors assessed by community midwives and in-hospital caregivers.
Non-medical risk factors are defined as: income, relational problems, domestic violence, work-related stress, financial debts, social support and intake of fruits and vegetables. 0/7 means that none of the questioned non-medical risk factors were assessed during intake;
7/7 means that all questioned non-medical risk factors were assessed during intake.

appointed the community midwife as the most appropriate care provider for dealing with non-medical problems, followed by a combination of caregivers. The general practitioner was barely mentioned as the most appropriate care provider for non-medical problems.

Antenatal policy

The current antenatal policy for medical risk screening was mainly based on national guidelines or local protocols (>90%). In case of non-medical risk factors, the most common policy was consulting other caregivers. In absence of national guidelines, local protocols were used for non-medical risk screening if present (41% of the respondents in the community-based setting, 45% in hospital-based setting). In 18% and 23% of the respondents respectively, decisions were based on personal judgment.

Community midwives worked with case managers more often than hospital caregivers (70% vs. 46% resp.). They designated their own profession as being the most appropriate for the role of case-manager in case of non-medical problems (89%), followed by the general practitioner (31%) and Youth and family centers (17%). Gynaecologists and hospital-based midwives were least likely appointed to be suitable care managers in such cases. This corresponded with the responses given by hospital caregivers, who appointed the community midwife as the most appropriate case manager (72%), followed by the gynaecologist (70%), the hospital-based midwife (65%), and the social services (25%).

Differences in reported antenatal policy were also reported with respect to the continuity of care. Hospital caregivers reported that antenatal visits were performed

by the same caregiver, more often than the community midwives. In community care, consultations were mostly reported to be performed by the caregiver that happened to be scheduled to do the antenatal check-ups at that moment.

Collaboration and satisfaction

Only 22% of respondents reported using predefined criteria to discuss patients during interdisciplinary consultations. Interdisciplinary consultation was mainly reported between gynaecologists and community midwives. Table 4 indicates the level of collaboration with other caregivers in the current situation. A higher case load of non-medical problems (more than weekly) resulted in more consultation with social services. In case of more consultations, caregivers showed more professional satisfaction. Lack of satisfaction was mostly due to a lack of insight in the referral possibilities that applied to a patient and the limited availability of non-obstetric caregivers who were available for referral.

Table 7.4 Contact moments and referral possibilities with other caregivers

Contact moments	Community midwives	Hospital caregiver	p*	Satisfaction	Community midwives	Hospital caregiver
Social services	14 (12.7)	45 (35.2)	<0.001	Less needed	1 (1.0)	0 (0.0)
				More needed	40 (38.5)	50 (37.6)
				Satisfied	63 (60.6)	83 (62.4)
Youth and family center	42 (43.3)	14 (9.9)	<0.001	Less needed	0 (0.0)	0 (0.0)
				More needed	39 (37.1)	48 (39.3)
				Satisfied	66 (62.9)	74 (60.7)
Maternity care assistent	63 (71.6)	21 (15.2)	<0.001	Less needed	0 (0.0)	0 (0.0)
				More needed	8 (7.5)	41 (33.9)
				Satisfied	98 (92.5)	80 (66.1)
General practitioner	25 (22.9)	12 (8.3)	0.001	Less needed	0 (0.0)	0 (0.0)
				More needed	58 (55.2)	54 (43.2)
				Satisfied	47 (44.8)	71 (56.8)
Municipal health services	14 (12.5)	10 (7.0)	0.140	Less needed	0 (0.0)	0 (0.0)
				More needed	33 (32.0)	44 (37.0)
				Satisfied	70 (68.0)	75 (63.0)
Youth care	9 (8.1)	28 (20.4)	0.008	Less needed	0 (0.0)	0 (0.0)
				More needed	45 (43.3)	50 (39.7)
				Satisfied	59 (56.7)	76 (60.3)

*Chi-square test
Data are presented as N(%)

DISCUSSION

Main findings

In this study we focused on the current practices regarding assessment and care of non-medical risk factors in antenatal healthcare. Performance of systematic screening for non-medical risk factors was rare and approaches were highly variable between community midwife practices and hospitals. In the majority of cases, lifestyle risk factors were screened during pregnancy, whereas the frequency of screening for social risk factors was highly variable. It is remarkable that while caregivers indicate that they deal with non-medical risk factors frequently, national guidelines or protocols and supportive tools to deal them are lacking. Therefore, systematic structured screening is not part of routine antenatal healthcare and preventive intervention strategies rely on local resources.

In the absence of national guidelines and protocols, local protocols were used for non-medical risk screening. Structural multidisciplinary meetings with non-obstetric caregivers (e.g. social services) were uncommon. In case of a higher case load of social problems (more than a weekly confrontation with social problems), caregivers had more consultations with social services and experienced more professional satisfaction due to their collaboration with these non-obstetric caregivers. Nevertheless, structured prescheduled meetings were uncommon.

Research about systematic assessment of non-medical risk factors is a relatively new phenomenon in antenatal healthcare.[5 13 30 31] We found it to be limited to a few studies. These however all focused on the assessment of perinatal mental health by midwives.[32 33] Their conclusions were consistent with our findings: there are many opportunities for improvement in (mental health) services during the antenatal period.

We also tried to identify factors that might explain the underexposure of non-medical risk factors in current antenatal risk assessment. Therefore, we explored differences at both the caregiver and practice level. The assessment of non-medical risk factors seems to be influenced by the workload of the midwifery practice. Midwives working in smaller practices screen for non-medical risk factors more frequently than their colleagues in larger (group) midwifery practices. These findings are also in line with prior findings, where caseload midwifery - in which midwives work in one-to-one partnerships with a woman during pregnancy and childbirth - showed much higher levels of continuity of care compared to conventional team midwifery care.[34 35]

This study was conducted within the unique Dutch obstetric care system. However, non-medical problems are a universal and increasingly important issue within antenatal healthcare. Inequalities in perinatal and maternal outcomes persist, especially in women who of specific ethnicities, who have lower socioeconomic status, and who live in deprived areas.[5] Social disparities, often reflected in non-medical risk factors, have

lifelong consequences and are therefore an important challenge for both obstetric and non-obstetric health care professionals, and policy makers.[2 5]

Strengths and limitations

A major strength of this study was the contribution of both community midwives and hospital caregivers, representing all tiers of care. Moreover, we selected municipalities in different parts of the Netherlands to provide substantial coverage and reflect regional spreading.

The uniqueness and complexity of the Dutch antenatal care system, in which several healthcare providers and tiers of care are involved, provided us with the opportunity to investigate aspects of inter-professional collaboration which are less applicable to other (antenatal) healthcare systems.

Our study also has some limitations. First of all, the response rate in community practices was lower than the response rate in our hospital based setting. The addition of an extra questionnaire (13 questions from a different study) to our questionnaire might have contributed to a lower response rate. These questionnaires were merged in order to limit the number of questionnaires that community midwives were asked to fill in. The extended questionnaire may have influenced the number of respondents that completed the whole questionnaire.

Secondly, we cannot exclude the presence of a selection bias. Even though we received responses from nearly all selected municipalities, not all midwife practices and hospitals located within a municipality responded to the questionnaire. The same holds for the number of caregivers working at a particular practice or hospital that completed the questionnaire. We had 100% non-response in three municipalities, and there were two municipalities in which only midwife practices responded to the questionnaire.

Lastly, sample sizes were too small to explain the differences in assessment of type of non-medical risk factors. Small sample sizes meant that we could not detect differences between working areas at the neighbourhood level, and between urban and rural working areas. Previous studies showed an independent or added effect of neighborhood.[9 36] Also an urban-rural gradient in perinatal health disparities was demonstrated, in which both urban and isolated rural residents exhibit poor perinatal outcomes.[37] This might have influenced our interpretations.

Practical implications

In the present study we focused attention on the importance of structural assessment and care of especially non-medical risk factors in antenatal healthcare and policy. We have learned from previous studies that these risk factors contribute to adverse pregnancy outcomes and have a risk-enhancing role in perinatal and maternal outcomes.[3-5] However, we observed now that these risk factors remain relatively underexposed in

antenatal risk assessment. Given the scarce number of available instruments for antenatal screening that are employed beyond our research setting, we hypothesize that this insufficiency in antenatal risk assessment is not limited to the Netherlands. [23-27] A systematic approach to preconceptional and antenatal risk selection for both medical and non-medical risk factors with subsequent continuity of care might support early detection of potentially high-risk women. This means that increased attention for non-medical risk factors needs to be embedded in routine practice first. We also noticed a discrepancy between the actual performance of non-medical risk screening, the reported confrontation of non-medical problems and the consultation and collaboration with other caregivers such as social services. This might indicate that awareness and needs are dependent on each other. In other words, to provide non-medical risk screening, a number of prerequisites need to be met.

First, structural antenatal risk assessment for non-medical risk factors with subsequent consultation opportunities is advocated.[38] Early detection (preferably at the intake) may contribute to the improvement of perinatal outcomes either by increasing awareness or allowing for risk modification. An implementation program could increase awareness for non-medical risk factors amongst caregivers. A multidisciplinary guideline supporting the standardized screening of these risk factors would benefit the implementation of non-medical risk screening in the current antenatal healthcare system. Regardless of the methods of antenatal risk assessment, developing care pathways tailored to the individual needs of each pregnant woman could optimize the benefits from risk screening. By providing standardized information on both medical and non-medical risk factors, collaboration between both obstetric caregivers and non-obstetric caregivers, such as social welfare, psychiatric services, and community health services, can be optimized.[38]

Lastly, it would be insightful to understand why caregivers do (or do not) perform non-medical risk screening. This could identify explanatory factors (promoting or impeding factors) which could be utilized to promote implementation of risk factor screening approaches. In addition, research should reveal the effectiveness of standardized and broadened risk screening (including screening on non-medical risk factors) on the improvement of pregnancy outcomes in order to convince caregivers and policy makers to assess these risk factors.

CONCLUSION

Despite their relevance, non-medical risk factors remain underexposed in both the community and hospital-based care setting. Structural antenatal risk assessment for non-medical risk factors with subsequent consultation opportunities is advocated, preferably based on a multidisciplinary guideline.

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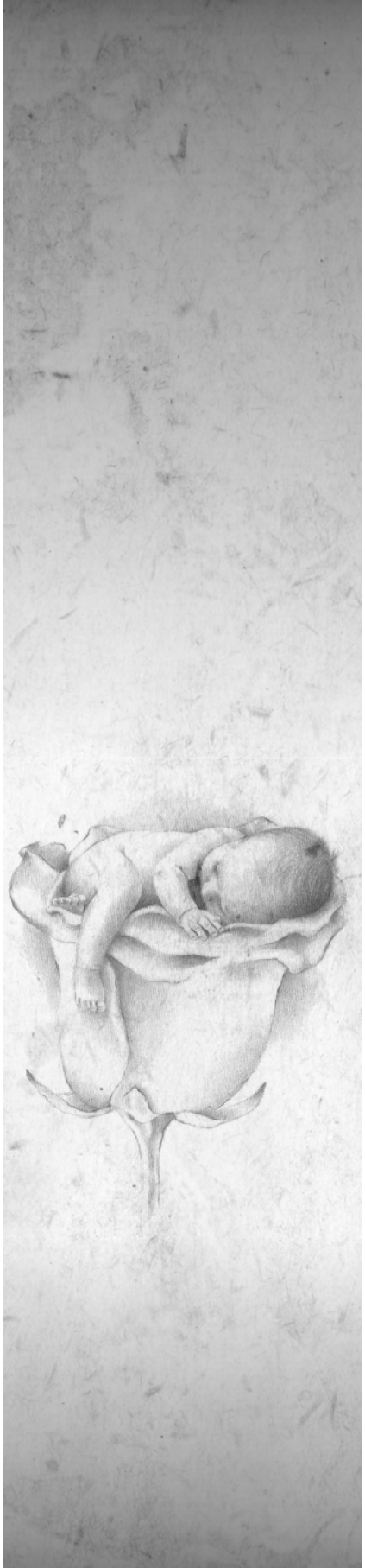

Chapter 8

Non-medical risk factors and risk accumulation in relation to perinatal outcomes (the Healthy Pregnancy 4 All study)

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Submitted

ABSTRACT

Objective We aimed to study in women grouped to socio-economic status (SES) and ethnicity: 1) the prevalence differences of specific non-medical risk factors; and 2) the assumption that risk accumulation of non-medical factors played an independent role for the presence of a set of major adverse perinatal outcomes.

Design Cross-sectional study nested in a cohort study

Setting Dutch antenatal care system

Participants Pregnant women living in a deprived neighbourhood in 14 Dutch municipalities selected for high prevalence of deprivation.

Measurements and findings Primary outcome was previous adverse perinatal outcome (any presence of congenital abnormalities, small-for-gestational-age, preterm birth, or low Apgar). Observed risk profiles were related to SES and ethnicity. In multiparous women, previous obstetrical outcome was related to the observed risk profile. In total data from 3214 women were analysed. More non-medical risk factors were present in women in the lowest SES category and in women of non-western descent ($p<0.05$). Of the multiparous women, 24.7% had any adverse perinatal outcome in the obstetric history. In these women, the absence of non-medical risks was associated with less adverse outcomes (OR 0.63; 95%-CI 0.50-0.80). So-called risk accumulation resulted in a threefold risk in case of 3 risk factors (OR 2.70, 95%-CI 1.27-5.7).

Conclusion Women in the lowest SES category and women of non-western descent were at a substantially increased risk for adverse pregnancy outcomes through the increased level of non-medical risk factors. Our results might be explained by the accumulation of individual risk factors.

Implications for practice Risk targeted antenatal healthcare could be delivered in order to reduce the gap in adverse perinatal outcomes due to SES and ethnicity.

INTRODUCTION

Neighbourhood deprivation is associated with adverse perinatal outcome. The highest rates of perinatal morbidity and mortality are observed in the most deprived areas.[1 2] Social deprivation and belonging to an ethnic minority group are generally accepted as adverse etiologic factors.[3-5] Numerous studies have shown the independent role of so-called non-medical risk factors such as single partnership, family income, or low education level for the occurrence of adverse perinatal outcomes as small-for-gestational age, preterm birth and subsequent perinatal mortality.[6-9]. Structural and genetic congenital anomalies are partly related to neighbourhood deprivation, for example due to the non-use of folic acid, obesity, or the influence of epigenetic effects. [4]

However, these studies were performed retrospectively or were registry-based. Such designs are subject to limitations like heterogeneity of definitions, limited amount of detailed clinical information (e.g. admission data, intervention data, risk and indication data), lack of measurement precision (e.g. only crude health outcome categories), and lack of clinical validity of the registration process (e.g. in case of registration for insurance purposes). In particular non-medical risk factors such as low household income and low education level are under-reported despite their agreed prognostic value.[10]

Timmermans et al. suggested that the excess risk for adverse outcomes could be attributed to the accumulation of socio-demographic, lifestyle, and obstetric risk factors.[11] They defined risk accumulation as the combined contribution of a number of seemingly less important risk factors on the occurrence of adverse outcomes. Risk accumulation appeared to be more common in deprived neighbourhoods, and its effect may rest on factors being effective through several pathways.[11]

The national Healthy Pregnancy 4 All (HP4All) study - was designed to improve perinatal health in especially deprived areas.[12] The study combines a public health approach of antenatal care innovation with epidemiologic research. Two perinatal interventions before (preconception care) and during pregnancy (antenatal risk assessment) were actively introduced in deprived neighborhoods of 14 municipalities across the Netherlands. The local caregivers participating in this study provided care to predominantly deprived pregnant women. As the interventions were practiced as routine care for all participating pregnant women, the collected data allow for analysis of the risk contributing role of non-medical risk factors.[12]

The first aim of this study was to investigate the association between specific non-medical risk factors and socio-economic status and ethnicity. Next we explored in a nested retrospective analysis whether so-called risk accumulation of these non-medical factors could be demonstrated as independent contributor to major adverse perinatal outcomes.

METHODS

Study design

This cohort study was part of the Risk Assessment (RA) study within the HP4All study. The RA study is a cluster randomized controlled trial in 14 municipalities of which the design, methods, and data collection have been described in detail.[13] In summary, midwifery practices in participating municipalities were randomly assigned to either 'intervention municipalities' including the use of a scorecard-based antenatal risk assessment, care pathways and multidisciplinary consultation or 'control municipalities' in which conventional risk assessment was measured.

Participants of the present study were pregnant women living in selected neighbourhoods of 14 municipalities that enrolled from August 2012 until June 2014. Municipalities were selected on the base of an above average perinatal mortality rate. Subsequently, within these municipalities a set of disadvantaged areas was defined using pre-existing neighbourhood borders. Among these neighbourhoods cases were selected if high adverse perinatal outcome rates were present. Both municipality and neighbourhood selection were based on complete national perinatal registry data. The selection process of the municipalities and neighbourhoods has been described elsewhere.[12]

Community midwives and gynaecologists providing care to women living in these zip codes were invited to participate in the RA sub-study. All pregnant women that visited a participating midwifery practice or hospital were eligible to participate in the RA sub-study. The caregiver decided on the enrollment format: either all patients or a selection based on zip-code. This choice was part of the design of the trial which accommodated the most acceptable implementation of this new approach of risk assessment at the individual practice level. Exclusion criteria were kept to a minimum, and included an obstetric situation during the booking visit requiring instantaneous intervention (e.g. ectopic pregnancy), and already being in labour during this initial visit.

This study has been approved by the ethics committee of the Erasmus Medical Center Rotterdam (Ref. No. MEC-2012-322), and by the Executive Board of all participating hospitals.

Data collection

Obstetric history

Eligible women received participant information and were asked for written consent prior to their inclusion in the study to collect data on their general and obstetric history pregnancy outcomes by the participating caregivers. Caregivers registered all participating women anonymously by a study number in a web-based database. They registered the 4-digit zip code, date of birth, gestational age at booking visit, gravidity and parity,

and the obstetric history (date of birth, gestational age at delivery, birth weight, gender, single or multiple pregnancy, congenital anomaly, Apgar score < 7, previous caesarean section, and any previous miscarriages, termination of pregnancy, or ectopic pregnancy. Missing data were as many sought out in patient records by the project team or research midwives.

Individual perinatal risk factors

Baseline characteristics were prospectively assessed by a survey early in pregnancy. This self-reported survey was completed preferably in the waiting room after the first antenatal visit. Otherwise a return envelope was handed, or an online version of questionnaire was offered, all according to the women's' wish. In all scenarios, the answers were sent directly to the project team. We also asked caregivers to bring up the questionnaire during the next visit. Study information for counselling and the questionnaire were available in the 6 most commonly spoken languages (Dutch, English, Spanish, Arabic, Turkish, and Polish).

The baseline characteristics included marital status, household composition and family household income, maternal occupation, education level, ethnicity (country of birth pregnant woman and her parents), lifestyle (smoking, alcohol, soft and hard drugs use), use of folic acid, medical history, and use of medication. Net household income was classified as less than 1000 euro, 1000-1499 euro, 1500-1999 euro, 2000-2499 or more than 3000 euro. Having a paid job was asked dichotomously, and further assessed in weekly working hours. The following information on the lifestyle risk factors smoking, alcohol and drug use was assessed: preconceptional use, current use, history, quantity per day or week (if applicable), and quit date (not applicable, before pregnancy, positive testing, first trimester, other).

Primary outcome

The primary outcome measure was previous perinatal morbidity. Primary classifiers were socio-economic status (SES), ethnicity, and zip code based relative deprivation level of the neighbourhood with the municipality as reference. Previous perinatal morbidity, so-called Big 4 morbidities, were defined as the presence (single or combined) of small for gestational age (SGA) (birth weight < 10th percentile for gestational age) [14], preterm birth (PTB) (birth < 37 weeks of gestation), congenital disorders (list defined), and / or suboptimal start at birth (Apgar score < 7 after 5 minutes). SES was classified as low SES (< p20), middle SES (p20 – p80), and high SES (>p80). Data on socio-economic status was available from The Netherlands Institute for Social Research (open access) on zip code level and linked to the birth record database. SES status scores were composed of 4 indicators: the average household income, the proportion of residents receiving a low family income, the proportion of poorly educated residents, and the proportion of

unemployed residents in a particular post code[16] (SCP 2010). Allocation of ethnicity was established by guidelines of national Central Bureau for Statistics (open access), taking into account the country of birth of the pregnant women herself, her mother and her father [17]. A pregnant woman was classified as 'immigrant' (non-indigenous) - if one of her parents was born outside the Netherlands - or non-immigrant. A further distinction was made between immigrants from western descent (Europe (excluding Turkey), North America, Oceania, Indonesia or Japan) and non-western immigrants (remainder). Neighbourhoods were classified on zip code level according to perinatal morbidity rates relative to the local level: 'below municipal level', 'on municipal level' or 'above municipal level'. It was assumed that the included determinants such as SES, ethnicity, household income and educational level (often set before the age of 20) were almost invariable for an individual and that these determinants were present before the first pregnancy.

Data analysis

Only cases of which we received the registration form completed by the caregiver and the self-reported survey were eligible in this study. Since the RA sub-study was a randomized controlled trial that aimed to improve pregnancy outcomes in the intervention group, the risk associations were based on the previous obstetric outcome (rather than the current outcome) as proxy outcome measure, assuming risk relations in our context remain similar across parity. We assumed that the static nature of non-medical determinants allowed for the estimation of such a retrospective association. Thereby pregnancy outcomes were not contaminated with the study intervention and we were able to include the results of the 'control' group as well. Consequently, the analyses based on pregnancy outcomes were confined to the multiparous women.

Differences in baseline characteristics and prevalences of individual risk factors based on SES, ethnicity, 'selected neighbourhood' and pregnancy outcomes were compared with conventional statistical methods (chi-square test). Accordingly, we estimated the odds ratios (ORs) and 95%-confidence intervals (95%-CI) for the 'risk group' compared to the 'reference' group (e.g. low SES compared to high SES, Big 4 compared to no Big 4, non-western compared to western, etc.). Subsequently, we graphically compared the amount of risk factors in relation to adverse pregnancy outcome to visualize the potential effect of risk accumulation.

Missing values in the survey were (<5%) excluded from the analysis. Missing values with respect to the obstetric history (<5%) were set to the most favorable values, e.g. all missing birth weights were set to 'no SGA' and included in the analysis. The assumption was that these severe risk factors - if present - rarely will be left unrecorded. Risk estimates will thus not be exaggerated. Above described statistical analyses were performed using Statistical Package of Social Sciences versions 20.0 for Windows (SPSS Inc, Chicago, IL, USA).

RESULTS

In total 36 of the 39 eligible community midwife practices (92%) and 15 of the 16 hospitals (94%) participated in the HP4All study. Of the 4636 pregnant women enrolled in the study between August 2012 and July 2014, 3214 fulfilled the inclusion criteria and were analysed for this study (figure 8.1).

Baseline characteristics of the included women are shown in table 8.1. Overall, 58.5% lived in the lowest SES category, 13.2% was low educated, 8.0% had a household income of less than €1000, and 22.9% was of non-western ethnicity. Of the multiparous women, 24.7% had any Big 4 event in the obstetric history. These characteristics differ among primiparous and multiparous women. More multiparous women lived in the lowest SES category (60.5 vs 56.5%), were low educated (15.1% vs. 11.2%), or from non-western descent (28.0% vs 17.7%), but slightly less women reported a low household income (7.2% vs. 8.8%).This was statistically confirmed by Chi^2-tests for trend ($p < 0.001$).

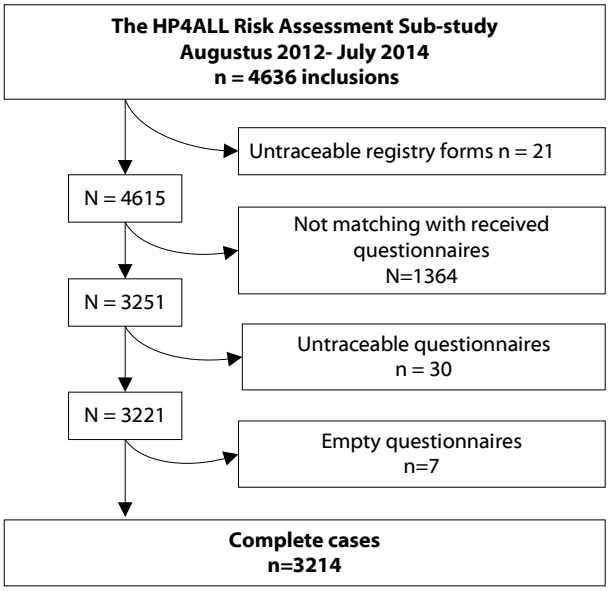

Figure 8.1 Flowchart of the study population

Table 8.1 Baseline characteristics

	Overall N = 3214	Primiparous N=1599 (49.8)	Multiparous N=1615 (50.2)
Maternal age (median, range)	30 (15-47)	29 (15-47)	31 (18-46)
Ethnicity			
Dutch	2150 (66.9)	1148 (71.8)	1002 (62)
Other western	311 (9.7)	159 (9.9)	152 (9.4)
Non-western	736 (22.9)	283 (17.7)	456 (28)
unknown	17 (0.5)	9 (0.6)	8 (0.5)
SES			
<p20	1180 (58.5)	903 (56.5)	977 (60.5)
p20-80	936 (29.1)	498 (31.1)	438 (27.1)
>p80	335 (10.4)	10 (10)	175 (10.8)
unknown	63 (2)	38 (2.4)	25 (1.3)
Education level			
low	423 (13.2)	179 (11.2)	244 (15.1)
middle	1233 (38.4)	601 (37.6)	632 (39.1)
high	1507 (46.9)	797 (49.8)	710 (44.0)
unknown	51 (1.6)	22 (1.1)	29 (1.8)
Household income			
<1000	258 (8)	141 (8.8)	117 (7.2)
1000-1999	837 (26.1)	375 (23.2)	462 (28.6)
2000-2999	933 (29)	457 (28.6)	476 (29.5)
>3000	1058 (32.9)	564 (35.3)	494 (30.6)
unknown	128 (4)	62 (3.9)	66 (4.1)
Obstetric history			
Any miscarriage	718(22.3)	257 (16.1)	461 (28.5)
Any TOP	235 (7.3)	96 (6.0)	139 (8.6)
Any SGA < p10	NA	NA	189 (11.7)
Any SGA < p5	NA	NA	101 (6.3)
Any preterm birth	NA	NA	138 (8.5)
Any Big 4	NA	NA	399 (24.7)

Top = termination of pregnancy; NA = not applicable.
SES = socio-economic status; SGA = small for gestational age
Data are presented as N(%) unless otherwise specified

Prevalence of non-medical risk factors

The prevalence of lifestyle and social risk factors in relation to socio-economic status and ethnicity are described in table 8.2. The risk factors 'single parentship' 2.65 (1.65-4.23), 'low family income' 1.90 (1.43-2.52), 'low education level' 1.61 (1.29-2.01), 'no preconceptional folic acid use' 1.40 (1.20-1.63) all were significantly more present among women in the

Table 8.2 The prevalence of lifestyle and social risk factors in relation to socio-economic status and ethnicity

	SES				Ethnicity		
	low N = 1880 (58.5)	middle N = 936 (29.1)	high N = 335 (10.4)	OR low SES vs rest	non-Western N = 733 (23)	Western N= 2458 (77)	OR Non-western vs Western
Single parentship	84 (4.5)	19 (2.0)	3 (0.9)	2.65 (1.65-4.23)	71 (9.7)	39 (1.6)	6.65 (4.46-9.92)
Low familiy income (<1000)	184 (10.3)	46 (5.1)	24 (7.4)	1.90 (1.43-2.52)	129 (19.0)	127 (5.3)	4.19 (3.22-5.44)
Low education level	288 (15.5)	102 (11)	27 (8.1)	1.61 (1.29-2.01)	160 (22.2)	262 (10.7)	2.37 (1.91-2.94)
Age < 20 years	34 (1.8)	15 (1.6)	3 (0.9)	1.28 (0.72-2.28)	19 (2.6)	32 (1.3)	2.01 (1.13-3.57)
Age > 35 years	314 (16.7)	128 (13.7)	66 (19.7)	1.11 (0.92-1.35)	149 (20.2)	365 (14.8)	1.46 (1.18-1.80)
Maternal employment	1355 (72.8)	733 (82.4)	297 (88.9)	0.51 (0.41-0.61)	387 (53.3)	2075 (84.7)	0.21 (0.17-0.25)
Work hours > 36 hours	417 (22.2)	254 (27.1)	115 (34.3)	0.84 (0.71-0.99)	138 (18.8)	665 (27.0)	1.21 (0.96-1.52)
No preconceptional folic acid	738 (47.5)	345 (40.5)	105 (35.8)	1.40 (1.20-1.63)	348 (66)	862 (38.9)	3.06 (2.51-3.73)
Preconceptional smoking (<6 months)	279 (14.8)	177 (18.9)	54 (16.1)	1.04 (0.81-1.33)	109 (14.8)	404 (16.4)	0.37 (0.25-0.54)
Smoking in first trimester	213 (11.4)	100 (10.8)	14 (4.3)	1.30 (1.02-1.65)	67 (9.2)	261 (10.7)	0.85 (0.64-1.13)
Passive smoking	550 (29.3)	238 (25.4)	58 (17.3)	1.36 (1.15-1.60)	197 (26.8)	657 (26.7)	0.98 (0.81-1.18)
Preconceptional alcohol use	1162 (61.8)	690 (73.7)	271 (80.9)	0.52 (0.44-0.61)	270 (36.7)	1884 (76.6)	0.18 (0.15-0.21)
Preconceptional drugs use	87 (4.8)	46 (5.1)	12 (3.7)	1.01 (0.72-1.42)	35 (5.0)	114 (4.8)	1.05 (0.71-1.55)

OR = odds ratio, SES = socio-economic status

low SES category and among non-western women. Such an association was absent in non-western women for the risk factors 'smoking in first trimester' 0.85 (0.64-1.13) and 'passive' smoking' 0.98 (0.81-1.18).

In total, 1751 women (55%) lived in one of the selected zip codes. Above associations were also observed among women that were assigned as 'potentially at risk' (i.e. living in one of the selected zip codes). The risk factors single parentship (OR 2.64; CI 1.59-4.39), low family income (OR 1.81; CI 1.34-2.44), low education level (OR 1.62; CI 1.28-2.05), no preconceptional folic acid use (OR 1.32; CI 1.12-1.56), smoking in first trimester (OR 1.41; CI 1.08-1.83), and passive smoking (OR 1.24; CI 1.04-1.48) were more prevalent in these areas when compared to zip codes with perinatal morbidity rates below municipal level (N = 444 women) (data not shown).

The above risk factors were clearly related to perinatal outcomes, e.g. we observed a significant association between the outcome Big 4-morbidities and the risk factors: long working hours (OR 1.65; CI 1.18-2.30), low family income (OR 1.58; CI 1.06-2.36), and low education level (OR 1.65; CI 1.23-2.21) respectively (data not shown). Figure 8.2 displays

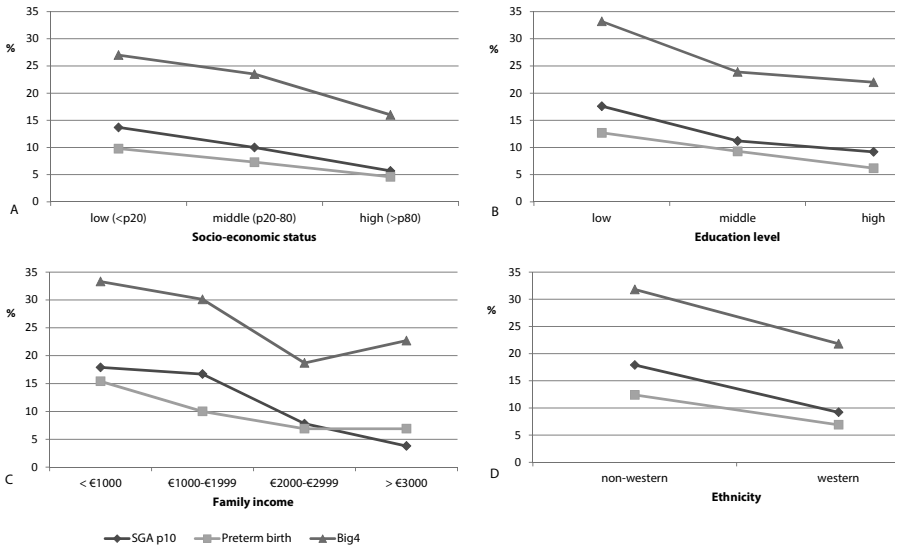

Figure 8.2 The association between risk factor categories and the adverse perinatal outcomes small for gestational age (SGA), preterm birth, and Big 4 morbidities.

Big 4 morbidities are defined as the presence of either SGA, preterm birth, congenital anomalies and/or Apgar score < 7

A. Socio-economic status below 20th percentile, between 20-80th percentile and above the 80th percentile.

B. Education level: low (primary school or preparatory middle-level vocational education), high (high-level vocational education, pre-university education, (post)-university), middle (remainder).

C. Family income

D. Ethnicity

the association between risk factor categories and adverse perinatal outcomes. It shows a gradual decrease in the likelihood of an adverse perinatal outcome going from unfavourable tot more favourable categories (e.g. from low to high educated). These trends were statistically confirmed by Chi^2-tests ($p<0.05$). We observed a threshold for the protective effect of 'family income' beyond an income level of € 2000. The associations between adverse perinatal outcome and socio-economic status and non-western ethnicity were both significantly associated with the shown adverse perinatal outcomes ($p<0.05$). However, with respect to figure 8.2, stratified analysis suggests that both variables follow identical pathways. If we adjusted the effect of socio-economic status on adverse perinatal outcome (any previous SGA or any previous Big 4) for non-western ethnicity, the effect of SES became non-significant, while, reversely, the effect of non-western ethnicity remained highly significant after SES adjustment ($p<0.001$).

Risk accumulation

Table 8.3 depicts the influence of risk accumulation of non-medical risk factors on pregnancy outcomes among multiparous women. Generally the risk for all perinatal outcomes gradually increased with the number of risk factors. In women with no non-medical risk factor, the risk for all adverse outcomes was below average (Big4 (OR 0.63; CI 0.50-0.80), SGA (OR 0.51; CI 0.37-0.69) or PTB (OR 0.67; CI 0.47-0.96). In women with 1 or more risk factors, we observed an increase in the presence of risk accumulation for Big 4 morbidities and SGA, resulting in a threefold risk for Big 4 (OR 2.70; CI 1.27-5.7) and SGA (OR 2.57; CI 1.08-6.14) in case of 3 risk factors.

Table 8.3 Risk accumulation of non-medical risk factors and pregnancy outcomes

	Obstetric history		
	Any Big 4	Any SGA (<p10)	Any Preterm birth
0 risk factor	0.63 (0.50-0.80)	0.51 (0.37-0.69)	0.67 (0.47-0.96)
1 risk factor	1.31 (1.01-1.71)	1.50 (1.06-2.12)	1.31 (0.87-1.96)
2 risk factors	1.65 (1.11-2.46)	2.09 (1.29-3.36)	1.37 (0.75-2.51)
3 risk factors	2.70 (1.27-5.7)	2.57 (1.08-6.14)	2.38 (0.89-6.35)

Risk factors: single parentship, work hours > 36 hours, smoking in first trimester, low family income, low education level

Big 4: small for gestational age, preterm birth, congenital anomaly, and/or Apgar score < 7

SGA = small for gestational age

DISCUSSION

Main findings

Our results confirm findings from studies reporting that women in the lowest SES category and women of non-western descent are at a substantially increased risk for adverse pregnancy outcomes, through the mechanism of accumulation of non-medical risk factors. We observed a gradual increase in prevalence of adverse perinatal outcome (overall perinatal morbidity and SGA and PTB separately) regarding the severity of a risk factor category, going from the least to the more favourable category of the risk factor. Apparently risk accumulation explains perinatal inequalities between groups. The risk impact on non-medical risk factors on adverse perinatal outcome was proportionally related to the number of non-medical risk factors up to a three-fold increased risk in case of 3 factors.

Possible explanations

This proportional relation between non-medical risk factors and adverse perinatal outcome was previously reported [5 7 11], and most likely reflects a general mechanism of health inequalities, in this case emerging in the offspring of pregnant women. [18 19] Multiple pathways are in place, acting on different aggregation levels (individual, family, neighbourhood), but low income and low education seem pivotal.[6]. Low income is associated with poor housing, nutrition, and health care access, and low education is associated with low health literacy adding to the effects of decreased health care access.[4] Decreased wealth and living conditions also increase physiological stress.[20] Beside individual risk factors, neighbourhood deprivation at a higher aggregation level plays also an independent role in adverse perinatal outcome.[2] It is known that lifestyle and social risk factors (non-medical risk factors) are much more common in these deprived areas, while their prevention and modification is also more demanding.[4 21]

We found that both SES and non-western ethnicity were both significantly related to adverse perinatal outcomes. However, when we adjusted the effect of SES on adverse perinatal outcome for non-western ethnicity, the effect of SES became non-significant. This suggests that there might be an independent effect of ethnicity. This independent effect was previously described by others. [5 22] It was also shown that social deprivation plays a different role among Western and non-Western women. Possible causative explanations were increased density of migrant groups in particular neighbourhoods [23], the influence of social capital in these particular neighbourhoods [24], differences in lifestyle behaviours (e.g. smoking behaviour) [25], and for example epigenetic effects.[5 26] Unfortunately, the design of our study did not allow to investigate whether the effect of SES and non-western ethnicity were truly independent or in some way interrelated, neither did our sample size permitted for specific ethnic subgroup analysis.

Beside differences between socio-economic status and ethnicity, we also observed outcome specific differences in the impact of non-medical risk factors. As previously noted, these relationships are stronger for SGA than for preterm birth.[7] This difference could be explained by its etiology. The presence of preterm birth is in part a iatrogenic factor (in clinical entities without non-medical risk profile) is namely absent for SGA.

The overall prevalence of non-medical risk factors was higher in non-western women. This may be of importance as recent evidence demonstrated social deprivation to play a different role in western and non-western women, with much strong contrasts in the non-western group [5 22 27 28] In our study, numbers were unfortunately too small to further investigate this interaction effect.

In accordance with Timmermans et al, we found that risk accumulation may prepossess the apparently moderately sized individual effects of heterogeneous risks. The individual contribution of non-medical risk factors may be small, but the risk accumulating general effect of a deprived social background may rise an often accompanied by several medical and non-medical risk factors, may lead to a relevant high risk case.[11]

Strengths and limitations

A strength in the current study was the availability of prospectively collected data in selected geographical areas of potentially high risk populations exposed to routine antenatal healthcare. This approach created a suitable population with enough 'risk load' to study the prevalence of non-medical risk factors according to socio-economic status, and ethnicity. Eventually, more than half of our study population lived in one of the selected zip codes. The use of individually, prospectively collected determinants rather than the dependence on area based aggregates adds to its strength.

Some limitations are present as well. First of all, this study was embedded in a cluster randomized controlled trial.[12] In this trial, an intervention to improve antenatal healthcare for especially non-medical risk factors was implemented in half of the municipalities involved. Consequently, we were dependent on the obstetric history of the women included since perinatal outcomes from the present pregnancy might be contaminated as we hypothesized improvement through this intervention. This resulted in the rather unusual postdiction association in which we predicted adverse outcomes based on determinants that were measured in a subsequent pregnancy. We assumed that the static nature of non-medical determinants allowed for the estimation of such a retrospective association. This also implied that we could use only half the database for the analysis regarding perinatal outcomes since the obstetric history is nonexistent primiparous women. Thereby we cannot rule out a selection bias, because observed a difference in baseline characteristics between primiparous and multiparous women. With the use of obstetric history, an information bias should also be noted through its retrospective nature. Although obstetric history was recorded by healthcare professionals self and

retrievable for the investigators, some information was unavailable (for example 5% missing birth weights). We addressed this by analyzing the data conservatively by setting all missing to the most favourable setting, but it might have influenced our results.

A second limitation is related to the questionnaire we have used. All risk factors were self-reported, so under-reporting cannot be excluded. Also misclassification through language proficiency should always be considered, although all questionnaires were available in 6 languages.

Thirdly, we cannot rule out a selection bias due to selective participation. Selective participation would limit the potential to study risk accumulation as a less deprived population decreases the risk factor prevalence, in particular from non-medical domains, which in turn decreases the number of patients with multiple exposure categories.[11 29]

Despite our targeted study design, we observed a relatively well-educated, western population. It was shown that the level of area deprivation was associated with selective participation, with participation rates almost 10 percent lower in the most deprived areas.[30] We were not able to verify the non-response the questionnaires in relation to socio-demographic characteristics, but both selective participation and selective non-response might have biased our results.[29]

Lastly, risk accumulation was now based on the measurement of only five socio-demographic risk factors, as feasibility limits the length of our instrument. In a larger practice-based study, we expect the influence of the cumulative presence of non-medical risk factors could be studied in more depth.

Practical implications

Taking the evidence from the present study and previous studies on non-medical risk factors and risk accumulation into account, it makes sense to organize tailor-made antenatal healthcare responsive to women's needs, preferably with the involvement of local initiatives and engagement of Public Health services to approach these risk factors.[12 31] Early detection (preferably at the intake) may contribute to the improvement of perinatal outcomes either by increased awareness or the ability of risk modification.[32] In the view of already increased risk of medical risk factors in these women[11], non-medical risk factors require active screening and active intervention.[33] We believe that the emerging knowledge on the predictive role of both medical and non-medical risk factors, and risk accumulation justifies the implementation of structural risk assessment in antenatal healthcare.[32]

Future research could focus the effectiveness of such approach on pregnancy outcomes, could reveal the predictive value of non-medical risk factors on pregnancy outcomes and time of assessment (preconceptional, early antenatal, repetitive or post-

natal), could investigate the pathway behind risk accumulation, and could further reveal risk patterns in specific ethnic subgroups related to deprivation.

CONCLUSION

Women in the lowest SES category and women of non-western descent are at a substantially increased risk for adverse pregnancy outcomes through the increased level of non-medical risk factors. Our results might be explained by the accumulation of individual risk factors. Our findings show in accordance with other studies the importance of maternal non-medical risk factors (especially educational level and income) and neighbourhood of living, which are both strong predictors for the observed inequalities. Targeted antenatal healthcare could be delivered in order to reduce this gap.

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Part III

PERINATAL OUTCOMES ON NEIGHBOURHOOD LEVEL

Chapter 9

Differences in perinatal morbidity and mortality on the neighbourhood level in Dutch municipalities: a population based cohort study

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ABSTRACT

Background In a national perinatal health programme, we observed striking heterogeneity in the explanation of the most prominent risks across municipalities. Therefore we explored the separate contribution of several socio-demographic risks on perinatal health inequalities between municipalities and neighbourhoods. The study aims to identify perinatal health inequalities on the neighbourhood level across the selected municipalities, and to objectify the contribution of socio-demographic risk factors on pregnancy outcomes in each municipality by the application of the population attributable risk concept.

Methods Population based cohort study (2000-2008). Perinatal outcomes of 352,407 single pregnancies from 15 municipalities were analysed. Odds ratios and population attributable risks were calculated. Main outcomes were combined perinatal morbidity (small-for-gestational age, preterm birth, congenital anomalies, and low Apgar score), and perinatal mortality.

Results Perinatal health inequalities existed on both the municipal and the neighbourhood level. In municipalities, combined perinatal morbidity ranged from 17.3% to 23.6%, and perinatal mortality ranges from 10.1‰ to 15.4‰. Considerable differences in low socio-economic status between municipalities were apparent, with prevalences ranging from 14.4% to 82.5%. In 7 municipalities, significant differences between neighbourhoods existed for perinatal morbidity (adjusted OR ranging from 1.33-2.38) and for perinatal mortality (adjusted OR ranging from 2.06-5.59). For some municipalities, socio-demographic risk factors were s a strong predictor for the observed inequalities, but in other municipalities these factors were very weak predictors. If all socio-demographic determinants were set to the most favourable value in a predictive model, combined perinatal morbidity would decrease with 15% to 39% in these municipalities.

Conclusions Substantial differences in perinatal morbidity and mortality between municipalities and neighbourhoods exist. Different patterns of inequality suggest differences in etiology. Policy makers and healthcare professionals need to be informed about their local perinatal health profiles in order to introduce antenatal healthcare tailored to the individual and neighbourhood environment.

BACKGROUND

It is becoming increasingly clear that health inequalities in western countries are also expressed in adverse perinatal outcomes, such as preterm birth, growth restriction, and perinatal mortality. These adverse perinatal outcomes are especially observed in deprived districts and are often associated with socio-economic and ethnicity related risk factors such as low education, low-income and poor integration into society. Socio-economic status and neighbourhood deprivation are most consistently related to these adverse outcomes.[1-4] Socio-economic status can induce adverse perinatal outcome though multiple pathways, but most importantly through low education and low income levels.[5] However, it is still unclear to what extent the effect of neighbourhood deprivation goes beyond the effect of poor level of socio-economic status at the individual level.[6]

Two consecutive reports on perinatal health revealed a relatively unfavourable position of the Netherlands regarding perinatal mortality.[7, 8] Subsequent nationwide cohort studies revealed an equally high impact on perinatal outcomes of non-medical risk factors (e.g. social or lifestyle) compared to medical and obstetrical risk factors.[9-11] In order to gain more insight into these causes and their impact, the concept of 'Big 4 morbidities' was introduced.[12] This study showed that four specific defined conditions precede perinatal mortality in 85% of all cases of perinatal mortality, namely small for gestational age (birth weight < 10th percentile for gestational age)[13], preterm birth (birth < 37 weeks of gestation), congenital disorders, and / or low Apgar score (< 7 after 5 minutes).

Taking this prior knowledge into account, the Healthy Pregnancy 4 All (HP4All) study was initiated to improve perinatal health and to generate effective strategies in disadvantaged areas in the Netherlands.[14] This national study was supported by the Dutch Ministry of Health, Welfare and Sport and combines epidemiologic and health services research to evaluate the effectiveness of two obstetric interventions in preconception care and antenatal healthcare. Municipalities were selected to participate according to socio-demographic data (high risk load) and perinatal outcome data (high adverse outcome prevalence).[14]

Part of the initial fieldwork included consultation with local stakeholders (e.g. caregivers, policy makers) to identify reasons for deprivation. We observed a striking heterogeneity in the explanation of the most prominent risks across municipalities. Unlike the hypothesised homogeneity in deprived areas as known from findings described above, the differences in relative weight of socio-economic and ethnicity related risk factors were much more divergent according to these local stakeholders.

We therefore explored the separate contributions of several socio-demographic risks in neighbourhood perinatal health inequalities in more detail. This study aims (1) to identify perinatal health inequalities on the neighbourhood level across the selected

municipalities, and (2) to objectify the contribution of socio-demographic risk factors on pregnancy outcomes in each municipality by the application of the population attributable risk (PAR) concept.

METHODS

Study population

The selection of the 15 municipalities took place within the Healthy Pregnancy 4 All study. In a thorough preparatory analysis, 50 geographical areas (municipalities) were identified in which adverse perinatal outcomes were high. The list was obtained by combining epidemiological evidence on adverse outcomes from the national perinatal registries of midwives, obstetricians and paediatricians.[15, 16, 14] The 15 municipalities showing the highest perinatal morbidity and mortality rates were selected. All selected municipalities have an above average perinatal mortality rate and have numerous disadvantaged neighbourhoods. Data of pregnant women from these 15 selected Dutch municipalities were analysed in this study. The detailed selection process of these municipalities was described elsewhere.[14]

Study context

The study was conducted in the Dutch antenatal healthcare system. The organisation of the Dutch perinatal care system is unique as, in contrast to most other western countries, midwifery and obstetric care is delivered by primary, secondary and tertiary healthcare providers who function autonomously. At the primary level of care, community midwives provide care to pregnant women with an assumed or estimated low risk for complications during pregnancy and childbirth. Women allocated by the midwife to this low-risk status can opt for a home birth or for an out-patient hospital birth under supervision of their own community midwife. Around 80% of all pregnant women start their antenatal health care in the primary level of care. If complications threaten to occur during pregnancy or during delivery, women are referred to an obstetrician in a secondary or tertiary hospital.[17]

Data sources

Data from all singleton pregnancies in 15 selected municipalities over the period 2000-2008 were obtained from the Dutch Perinatal Registry (PRN). The PRN committee gave ethical approval for this study (amendment on application 11.36). As the database protects the anonymity of the included pregnant women and data were analysed anonymously, their written consent was not needed.

This registry contains detailed population-based information on pregnancies, deliveries, and neonatal (re)admissions until 28 days postpartum, recorded at the level of the child. Source data were obtained by validated linkage of three independent registries: the midwife registry (routinely collected by 94% of the midwives), obstetrics registry (collected by 99% of the obstetricians), and pediatric registry (68% of the paediatricians including 100% of the Neonatal Intensive Care Unit (NICU) paediatricians).[15, 16] Registration of midwifery and obstetric data starts at the first antenatal visit, and complete perinatal data is available from 20 weeks of gestation. The neonatal registry only contains data on hospital admissions of neonates following delivery. Overall, the PRN contains data of > 97% of all pregnancies in the Netherlands.

For determination of neighbourhood boundaries, we used both four-digit post codes and municipal neighbourhood boundaries, as established by the national Central Bureau for Statistics (CBS) in 2012 (open access). This last institute is responsible by law for the subdivision of all municipalities in the Netherlands into districts and neighbourhoods amongst others for statistical purposes. This subdivision is based on existing municipal boundaries which occasionally do not coincide with four-digit post code boundaries. As our primary data were post code based, in those instances the post code was assigned to the neighbourhood with the largest share in that particular post code. An exception was made for 'The Hague'. Historically, this municipality has a different post code classification system resulting in 44 neighbourhoods with many overlapping post codes. We therefore combined several adjacent neighbourhoods and reduced the number to 24 neighbourhoods which allowed for adequate projection of post codes to neighbourhoods. Neighbourhoods containing industrial areas were generally excluded because these areas are non-residential.

Primary outcomes and determinants

Primary outcomes were perinatal morbidity (Big 4) and perinatal mortality. Big 4 was defined as the presence (single or combined) of small for gestational age (SGA) (birth weight < 10th percentile for gestational age)[13], preterm birth (PTB) (birth < 37 weeks of gestation), congenital disorders (list defined), and / or suboptimal start at birth (Apgar score < 7 after 5 minutes). Perinatal mortality rate was defined as death in the period from 22 weeks gestational age until 7 days postpartum per 1000 births.

Socio-demographic risk factors included socio-economic status (SES), ethnicity (western, non-western), parity (nulliparous, multiparous) and maternal age. Data on socio-economic status was made available by The Netherlands Institute for Social Research (open access) and provided as status scores on post code level. The SES status scores were composed of 4 indicators: the average household income per particular post code, the proportion of residents with a low family income, the proportion of poorly educated residents and the proportion of unemployed residents in a particular post

code. We divided these status scores into tertiles: below the 20th percentile, between the 20th and 80th percentile, or above the 80th percentile. The post code comprises of socio-economically rather homogeneous small areas with about 25-50 newborn per year. This data was individually linked to the birth record database.[19] Ethnicity was assigned by the caregiver according to the classification of the PRN. The PRN defines 'ethnicity' along seven categories in line with the formal guidelines of the CBS: Western Dutch, Western other (including women from other European countries, Australia, and the United States), and non-Western: Mediterranean, (East) Asian, African, South Asian, or other non-Western. The classification of ethnicity recorded in the PRN was made by the health care professional and is typically based on a woman's appearance, name, and information provided in the context of history taking (at least until January 2015). Note that there is a distinction in the execution of classification between the PRN database and the formal, governmental CBS guidelines where classification was more nationality based on the basis of the information provided by the person (country of birth and parents' country of birth).

Statistical analysis

The prevalence of perinatal morbidity and mortality was analysed on the municipal level, and specifically within the selected municipalities.[14] We used data from the years 2000–2008, with the total number of singleton births as denominator. We restricted our data to all singleton pregnancies in the 15 selected municipalities.

Logistic regression was used to study the relation between perinatal morbidity and mortality, and the neighbourhood of residence. The neighbourhood that had the lowest prevalence of adverse perinatal morbidity was chosen as the reference category. These analyses were adjusted for individual factors such as SES, maternal age, parity, ethnicity, and calendar year. In all analyses, municipalities were analysed separately with a significance level set at 0.05. All variables were tested for interaction, and included when statistically significant. Above described statistical analyses were performed using Statistical Package of Social Sciences versions 20.0 for Windows (SPSS Inc, Chicago, IL, USA).

Population attributable risks

In order to visualise the contribution of socio-demographic risk factors on perinatal morbidity in each municipality, we calculated the population-attributable risk (PAR) percentages. The PAR of a risk factor is the proportion of disease (i.e. pregnancy outcomes) that can be attributed to a specific risk factor only among individuals with the risk factor. [20] In the standard formula, PAR estimations are subject to limitations because the formula is not additive if multiple risk factors interact.[11] Therefore, we followed the staged

approach as described by Poeran and colleagues to estimate perinatal morbidity in case selected risk factors were hypothetically absent.[11]

The aim of this analysis is to estimate the PAR of socio-demographic risk factors. Therefore, we calculated the PAR for two scenarios. In the first scenario, risk factors were set to 'the most favourable values' in terms of outcome whereby all women were 'assigned' to the highest SES category (>p80), multiparous, western ethnicity, and 25-29 years old. In the second scenario, risk factors were set to 'more reasonable values'. Only the women in extreme categories were reassigned: women in the low SES category were assigned to middle SES category (p20-p80) and women aged < 18 years or > 35 years were assigned to the reference category '25-29 years'. The values in the original dataset remained unchanged.

To estimate perinatal morbidity (Big 4), we created a duplicate dataset in which the outcome variables were set to 'missing values'. We fitted a multivariate logistic regression model on the original dataset to calculate predicted values. The predicted values obtained from the fitted model were used to predict the number of Big 4 cases for both scenarios, the 'most favourable values' and 'more reasonable values'. For example, the expected number of Big 4 cases in the 'most favourable scenario' was estimated by applying the predicted values from the fitted multivariate logistic regression model to the duplicate dataset in which all women were hypothetically reassigned to above listed scenario (e.g. highest SES category).

Finally, the observed Big 4 cases in the original dataset were compared to the predicted cases of Big 4 for both duplicate datasets. PARs were estimated as the proportional change of the predicted and observed cases. For this analysis, we used the GLIMMIX procedure in SAS version 9.2 to calculate the predicted values of perinatal morbidity (SAS Institute Inc., Cary, NC).

RESULTS

A total of 352,407 singleton pregnancies were analysed. The number of pregnancies per neighbourhood ranged from 105 to 16,614 (mean of 2,908 pregnancies per neighbourhood).

As a total of 1,584,800 births occurred in the Netherlands during 2000-2008, our study represents 22% of all births. Considerable differences in prevalences of low SES (prevalences ranging from 14.4% – 82.5%) and non-Western ethnicity (prevalences ranging from 8.8% - 47.8%) were apparent across municipalities (table 9.1).

SGA (ranging from 6.9% - 10.3%) and PTB (ranging from 5.6% - 7.8%) determined the largest part in Big 4 outcomes (17.3% - 23.6%). In the years 2000-2008, the average

Table 9.1 Characteristics of 15 studied Dutch municipalities in 2000-2008

Municipality	Number of residents*	Number of births 2000-2008	Number of neighbour-hoods	Number of births in low SES (<p20)**, N (%)	Number of births in non-western women, N (%)
Almere	193163	19302	5	2789 (14.4)	5996 (31.1)
Amsterdam	790110	90535	8	58944 (65.1)	41897 (46.3)
The Hague	502055	53712	24	27125 (50.5)	22856 (42.6)
Enschede	158 048	15312	10	8103 (52.9)	3006 (19.6)
4 villages in the province Groningen	309244	5850	4	3282 (56.1)	515 (8.8)
Groningen city	193127	17372	10	7689 (44.3)	2499 (14.4)
Heerlen	89016	6864	12	5663 (82.5)	1008 (14.7)
Nijmegen	165 182	15519	10	7254 (46.7)	2529 (16.3)
Rotterdam	616260	64353	15	46218 (71.8)	30755 (47.8)
Schiedam	76244	5715	7	3350 (58.6)	2312 (40.5)
Tilburg	207580	20354	10	9548 (46.9)	4528 (22.2)
Utrecht	316275	37519	10	1289 (34.4)	10110 (26.9)
The Netherlands	16730348	1584800	NA	399999 (25.2)	257383 (16.2)

NA = not applicable, SES = socio-economic status
*In 2012
**Defined as status score below the 20th percentile

Table 9.2 Perinatal morbidity and mortality rates of the 15 studied Dutch municipalities in 2000-2008

Municipality	SGA (<p10), n(%)	Preterm birth	Congenital anomaly, n(%)	Low apgar score	Perinatal morbidity, n(%)	Perinatal mortality (‰)
Almere	1544 (8.0)	1300 (6.7)	532 (2.8)	222 (1.2)	3788 (19.6)	198 (10.3)
Amsterdam	7397 (8.2)	5677 (6.3)	1763 (1.9)	1307 (1.4)	16707 (18.5)	963 (10.6)
Den Haag	4747 (8.8)	3474 (6.5)	1812 (3.4)	701 (1.3)	11075 (20.6)	590 (11.0)
Enschede	1214 (7.9)	1005 (6.6)	370 (2.4)	226 (1.5)	2290 (19.5)	170 (11.1)
Nijmegen	1274 (8.2)	1048 (6.8)	350 (2.3)	254 (1.6)	2997 (19.3)	191 (12.3)
Groningen city	1226 (7.1)	1073 (6.2)	334 (1.9)	311 (1.8)	3005 (17.3)	175 (10.1)
4 villages in the province Groningen	462 (7.9)	455 (7.8)	126 (2.2)	65 (1.1)	1140 (19.5)	90 (15.4)
Heerlen	709 (10.3)	515 (7.5)	261 (3.8)	90 (1.3)	1618 (23.6)	69 (10.1)
Schiedam	535 (9.4)	448 (7.8)	158 (2.8)	88 (1.5)	1255 (22.0)	75 (13.1)
Rotterdam	5892 (9.2)	4490 (7.0)	1670 (2.6)	973 (1.5)	13668 (21.2)	730 (11.3)
Utrecht	2582 (6.9)	2087 (5.6)	1912 (5.1)	410 (1.1)	6962 (18.6)	415 (11.1)
Tilburg	1850 (9.1)	1384 (6.8)	461 (2.3)	223 (1.1)	4142 (20.3)	212 (10.4)
The Netherlands	111712 (7.0)	97353 (6.1)	44868 (2.8)	18211 (1.1)	281863 (17.8)	15093 (9.5)

Perinatal morbidity is defined as a combined measure of small for gestational age (SGA), preterm birth, congenital anomaly, and / or low Apgar score.

Table 9.3 Difference between neighbourhoods with lowest and highest prevalence of perinatal morbidity and perinatal mortality, expressed as crude and adjusted odds ratios within 15 studied Dutch municipalities

	Perinatal morbidity in neighbourhoods				Perinatal mortality in neighbourhoods			
Municipality	Lowest prevalence n/N, (%)	Highest prevalence n/N, (%)	Crude OR (95% CI)	Adjusted OR (95% CI)*	Lowest prevalence n/N, (‰)	Highest prevalence n/N, (‰)	Crude OR (95% CI)	Adjusted OR (95% CI)*
Almere	16/105 (15.2)	2268/11248 (20.2)	1.40 (0.82 - 2.40)	1.32 (0.77- 2.27)	56/6009 (9.5)	123/11248(10.9)	1.18 (0.86 - 1.62)	1.11 (0.80 - 1.54)
Amsterdam	2317/14801 (15.7)	2871/10677 (26.9)	2.00 (1.88 - 2.13)	1.59 (1.48 - 1.70)	104/14801 (7.0)	102/9675 (10.5)	3.03 (2.39 - 3.84)	2.06 (1.57 - 2.71)
Den Haag	312 / 2181 (14.3)	693 / 2624 (26.4)	2.15 (1.85 - 2.49)	1.59 (1.33 - 1.90)	6/2181 (2.8)	43/2624 (16.4)	6.14 (2.56-14.74)	5.36 (2.07-13.87)
Enschede	63/483 (13.0)	764/3654 (20.9)	1.76 (1.34 - 2.32)	1.48 (1.11 - 1.97)	2/483 (4.1)	15/1401 (10.7)	4.19 (0.95 - 18.40)	4.78 (1.01 - 22.59)
4 villages in the province Groningen	210/1144 (18.4)	486/2422 (20.1)	1.12 (0.93 - 1.34)	1.16 (0.96 - 1.40)	15/1127 (13.3)	38/2422 (15.7)	1.18 (0.65-2.16)	1.79 (0.91-3.52)
Groningen city	82/737 (11.1)	226/1084 (20.8)	2.10 (1.60 - 2.76)	1.58 (1.17 - 2.14)	9/1593 (8.1)	14/1084 (12.9)	2.62 (1.23 - 5.56)	2.94 (1.32 - 6.55)
Heerlen	72/396 (18.2)	94/346 (27.2)	1.68 (1.19 - 2.38)	NA	3/755 (4.0)	7/323 (21.7)	5.56 (1.43-21.61)	5.59 (1.43-21.79)
Nijmegen	90/680 (13.2)	441/1633 (27.0)	2.43 (1.89 - 3.11)	2.38 (1.84 - 3.07)	5/923 (5.4)	75/1633 (45.9)	8.84 (3.56-21.93)	3.06 (0.66-14.25)
Rotterdam	779/4721 (16.5)	168/638 (26.3)	1.81 (1.49 - 2.19)	1.33 (1.17 - 1.51)	2/522 (3.8)	7/397 (17.6)	4.67 (0.96-22.59)	5.24 (1.08-25.47)
Schiedam	321/1675 (19.2)	353/1390 (25.4)	1.44 (1.21 - 1.70)	1.14 (0.90 - 1.44)	9/1000 (9.0)	26/1390 (18.7)	2.10 (0.98 - 4.50)	1.92 (0.89-4.17)
Tilburg	185/1116 (16.6)	583/2513 (23.2)	1.52 (1.27 - 1.83)	1.06 (0.84 - 1.33)	3/791 (3.8)	32/2513 (12.7)	4.32 (1.33-14.0)	4.22 (1.25-14.25)
Utrecht	657/4053 (13.9)	1080/4791 (22.5)	1.80 (1.61 - 2.00)	1.72 (1.48 - 1.99)	33/3570 (9.2)	51/4791 (10.6)	1.53 (0.99-2.38)	1.10 (0.67-1.79)

Perinatal morbidity is defined as dichotomous measure, where presence of morbidity means the presence of any of the following either single or combined: small-for-gestational age, preterm birth, congenital anomaly, and / or low Apgar score.
*model 1.Adjusted for maternal age, parity, ethnicity socio-economic status (SES), and year effect
OR = odds ratio, NA = not applicable

perinatal mortality rate in the Netherlands was 9.5‰. In all municipalities, perinatal mortality rates were higher than the national average (10.1‰ - 15.4‰) (table 9.2).

Neighbourhood inequalities

Almost all 15 municipalities showed significant differences between neighbourhoods for both perinatal morbidity and mortality rates. Differences were especially large for perinatal mortality, in which the adjusted odds ratios between the lowest and highest prevalence was 4 to 5 (table 3). Analyses were adjusted for maternal age, parity, ethnicity, SES, and calendar year effect. The multivariate analysis for the municipality 'Heerlen' was not applicable. In this particular municipality, there were only low SES areas. Since neighbourhood and SES are strongly correlated if not identical, it was not possible to make a proper comparison between highest and lowest categories. Interactions between all variables were found to be non-significant. Overall, missing values were less than 1%. Missing values were set to the most favourable values, e.g. all missing birth weights were set to 'no SGA' and included in the analysis (table 9.3).

Socio-demographic factors

In figure 9.1 we displayed the observed Big 4 outcome of pregnant women in each municipality (from the original dataset), and the predicted Big 4 outcomes from the duplicate dataset in case of 'the most favourable' and 'most reasonable' values with the

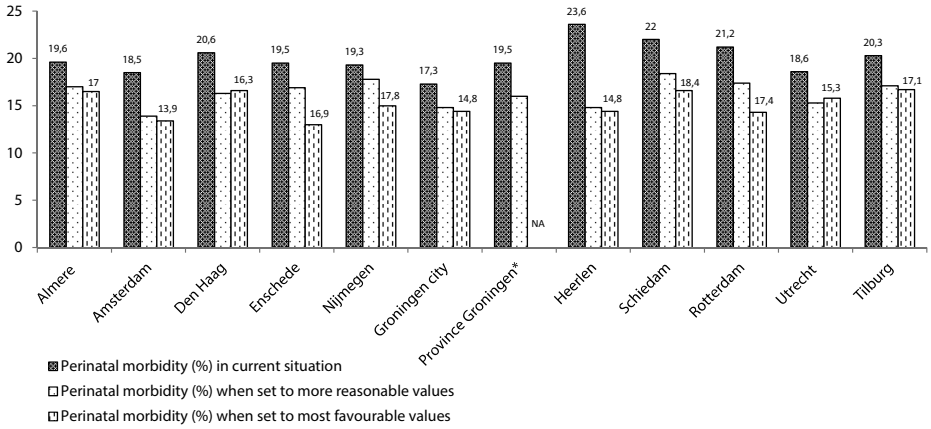

Figure 9.1 Observed and predicted perinatal morbidity in the 15 selected municipalities.
The selected risk factors were set to 'the more reasonable values' and to 'most favourable values'. In the first scenario, only the women in extreme categories were reassigned: women in the low SES category were assigned to middle SES category (p20-p80) and women aged < 18 years or > 35 years were assigned to the reference category '25-29 years'. In the second scenario, all women were 'assigned' to the most favourable values: highest SES category (>p80), multiparous, western ethnicity, and 25-29 years old. NA = not applicable (no cases in highest SES category), *4 villages in the province Groningen

corresponding PARs. In both scenarios, the predicted Big 4 decreased in all municipalities if socio-demographic risk factors were hypothetically 'absent'.

With this figure we illustrated that the contribution of socio-demographic risk factors to Big 4 outcomes differed considerably among municipalities. If – hypothetically - all women would be multiparous, 25-29 years old, of western ethnicity and correspond to the highest SES category (above the 80th percentile), perinatal morbidity would be reduced by 39% in Rotterdam and 15% in Utrecht. In other words, the contribution of socio-economic risk factors was nearly one third for some municipalities such as Enschede (33%), Heerlen (39%), and Rotterdam (33%), but appeared to be much lower for others such as the municipalities Almere (16%) and Utrecht (15%) (data not shown).

DISCUSSION

In this study we showed that patterns in perinatal health inequalities differ on both the municipal and neighbourhood level: some municipalities show overall high rates of adverse perinatal outcomes, while others show large differences between neighbourhoods. These neighbourhood differences were particularly pronounced for perinatal mortality. After adjustment for socio-demographic risk factors, such as SES, maternal age, parity, and ethnicity, these differences remained largely present.

These findings are in line with previous studies in which area-level socio-economic variables, such as neighbourhood income or poverty, remained significant after adjustment of individual variables.[10, 21, 22] A previously conducted study in the Netherlands also observed regional differences within the Netherlands, but focused more on care related factors such as travel time.[23]

With the use of PARs, we tried to further explore these differences across municipalities by calculating the attribution of socio-demographic risk factors on adverse outcomes. In some municipalities these risk factors are a strong predictor for the observed inequalities by explaining almost a third of the observed differences, while in others their contribution seem less prominent. Behind the general observation that perinatal morbidity and mortality rates are high in these municipalities, different mechanisms are apparently involved. This might be attributed to other explanatory factors, not included in this analysis, such as travel time to a hospital, place of birth, child factors, organisational factors and / or caregiver related factors which are all associated with adverse pregnancy outcomes.[24-26, 11] Two other studies conducted in the Netherlands also calculated PARs by using the same data, but both focused on perinatal mortality and were therefore not entirely comparable.[27, 11] Poeran and colleagues used the same PAR method as we did in our analysis. They estimated the PAR for (the combined effect of) maternal, child and organisational factors. They found a large reduction (over 94%) in perinatal mortality

when all factors were set to the most favourable value.[11] However, this was a nationwide study without focus on area-based differences.

Strengths and limitations

A major strength of this study was the usage of a validated national perinatal dataset with an almost complete coverage of all pregnancies in the Netherlands over a long period (2000-2008). This dataset includes many variables on both risk and healthcare factors which allowed for detailed analyses. Although the included municipalities had higher rates of perinatal morbidity and mortality than average, they represent one fifth of all pregnancies in the Netherlands. Previous studies were often municipality-based but not nationwide.[3] By including 15 different municipalities, we revealed major differences between areas in a relatively small country and high standards of health care.

This study also has some limitations. Area based measures such as socio-economic status may not correspond to the individual pregnant women, and do not reflect heterogeneity among individuals, healthcare professionals or other characteristic factors within a particular neighbourhood. We dealt with three levels of data (individuals that were clustered in a neighbourhood setting which were in turn nested in cities), so one can consider the use of multilevel type of analysis. Multilevel models address the hierarchical nature of data. Clustering primarily violates the independence of error assumption of most other regression designs.[28] The net effect of multilevel models is a widening of confidence intervals of individual effects, while careful comparison of differences between random slope and random intercept models give an impression on the degree to what level effects actually are present. In the case of the selected 15 countries, we judged that the use of multilevel-modelling was not beneficial. Foremost, this is a comparison of selected cities and neighbourhoods. This aimed a straightforward contrast, rather than a complete neighbourhood study where we felt that multi-level modelling would be more appropriate. We phrased the findings in a non-exaggerating way, which circumvents over optimism with the estimated (individual) intervals.

A limitation was the use of neighbourhood level SES instead of a single individual variable which was unavailable. It has been shown that without adequate control of individual socio-economic factors, neighbourhood effects might act as proxy for unmeasured aspects of unmeasured individual factors.[29] The post code size was small (on average 50 deliveries per year) and post codes were therefore also used as pseudo-individual SES indicator in for example compensation payments to caregivers for the assumed added services in deprivation areas. It has been suggested that the choice of using neighbourhood level variables may be less critical since this captures the unmeasured individual level variation in outcomes and that misspecification of the neighbourhood effect is less likely to occur.[30] However, the invincible use of post code boundaries in our study did

not always reflect the actual neighbourhood boundary, which may be a limitation of this study if adjacent neighbourhoods were contrasting.[30, 31]

The two greatest advantages of using the PRN database were the large amount of data from pregnancies in the Netherlands that became available over time (over 1 million records) and the high rate of complete cases (more than 97%). However, by using the PRN database we also faced some limitations. Firstly, the medical registry mainly captures data on specific processes in the healthcare process such as admissions or pregnancy complications. Data on medical, social and pregnancy related risk factors as well as the performance and outcome on prenatal screening are lacking. Using this data for research purposes, other requirements such as the amount and quality of information also become important. One of the disadvantages we faced in our study was the participation of only 70% of all pediatric wards in the Netherlands (and 100% of the NICU facilities). This means that partial and selective participation challenges the completeness of short term neonatal outcome. The outcomes reported here, however, are complete as these primarily are recorded by midwife and obstetrician. Secondly, the lack of data of some important maternal risk factors for perinatal morbidity and mortality, such as level of education, smoking during pregnancy, maternal body mass index and folic acid intake was another important limitation of using this database. Smoking is registered in the Perinatal Registry, but this information was not used because of underreporting (prevalence 0.5%). Thirdly, we faced some limitations in the approach of dichotomous grouping of Western and non-Western women. By dichotomising diverse ethnic groups, socio-demographic characteristics may resemble but groups may differ with respect to patterns of social status, health behavior, biological set up, and consequently birth outcomes. As mentioned in our second limitation, we were unable to study specific risk factor patterns among various ethnic groups, if they should exist. In addition, this approach might result in an oversimplification as this dichotomy might lead to the perception that all non-Western ethnic groups are 'the same', reflecting a uniform problem.[32] As we were primarily interested in examining perinatal health inequalities on the neighbourhood level across the selected municipalities, and to objectify the contribution of socio-demographic risk factors on adverse pregnancy outcomes in each municipality by the application of the population attributable risk concept, we opted for this dichotomous classification of Western versus non-Western women. By using two simplified two categories, we tried to evade a potential misclassification due to the allocation of ethnicity on basis of a woman's appearance in the PRN database. This dichotomous approach was also used in previous studies.[32, 33]

Practical implications and future research

In this study, we observed marked differences in perinatal outcomes across municipalities. We observed different patterns in these disparities: some showed high rates of

perinatal morbidity and / or mortality, while others showed large differences between neighbourhoods, or both. Remarkably, socio-demographic risk factors were not always associated with the observed inequalities.

With this study we also emphasise the importance of tailor-made antenatal healthcare, which seems necessary to encounter potential high risk pregnancies. We advise policy makers and health care professionals to develop additional local policy to define their high risk population, e.g. by means of customised preconception care and systemic risk assessment tailored to the individual and social environment of both the woman and the working area of a caregiver. This implicates that more research is necessary to explore etiologic factors associated with perinatal morbidity and mortality on regional level. In 2012 in the Netherlands regional so-called research consortia were constituted to enhance local collaboration which could anticipate to our findings. In addition, more research is necessary to develop specific recruitment strategies to timely reach high risk populations.

CONCLUSION

In conclusion, substantial differences in perinatal morbidity and mortality between municipalities and neighbourhoods exist. Socio-demographic risk factors in municipalities are not always a strong predictor for the observed inequalities, implicating that different mechanisms are involved. Our findings suggest that the identification of perinatal morbidity and mortality rates, organisational features of care and etiologic factors on regional level are a valuable first step to customise antenatal healthcare.

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Chapter 10

Deprived neighbourhoods and adverse pregnancy outcomes: a systematic review and meta-analysis

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ABSTRACT

Objective This study aims to summarize evidence on the relation between neighbourhood deprivation and the risks for preterm birth, small for gestational age (SGA), and stillbirth.

Design Systematic review and meta-analysis.

Methods Study selection was based on a search of Medline, Embase and Web of Science for articles published up to April 2012, reference list screening, and email contact with authors. We included studies that directly compared the risk of living in the most deprived neighbourhood quintile with least deprived quintile for at least one perinatal outcome of interest (prematurity, SGA, and stillbirth). Data on study characteristics, outcome measures, and quality were extracted by two independent investigators. Random-effects meta-analysis was performed to estimate unadjusted and adjusted summary odds ratios (ORs) with the associated 95% confidence intervals.

Results We identified 2863 articles of which 24 were included in a systematic review. A meta-analysis (N = 7 studies, including 2 579 032 pregnancies) assessed the risk of adverse perinatal outcomes by comparing the most deprived neighbourhood quintile with the least deprived quintile. Compared to the least deprived quintile, ORs for adverse perinatal outcomes in the most deprived neighbourhood quintile were significantly increased for prematurity (OR 1.23, 95%-CI 1.18-1.28), SGA (OR 1.31, 95%-CI 1.28-1.34), and stillbirth (OR 1.33, 95%-CI 1.21-1.45).

Conclusion Living in a deprived neighbourhood is associated with preterm birth, SGA and stillbirth.

INTRODUCTION

The association between socio-economic status and health has been recognized for a long time.[1] Socio-economic inequalities are associated with a decrease in life expectancy up to 10 years in developed countries.[2]

Perinatal mortality is a key indicator for population socio-economic inequalities.[3] Results from large cohort studies have shown that lifestyle risk factors (e.g. smoking) and social deprivation (e.g. household income, education level, or poverty) are strongly related to adverse perinatal outcomes such as preterm birth, low birth weight (LBW) and fetal growth restriction.[4-6] Over 75 percent of all causes of perinatal mortality are preceded by premature delivery and fetal growth restriction, which are conditions with different prevalences in different socio-economic groups.[7-9] Preterm birth and fetal growth restriction usually are the result of the concurrence of a large number of individual risk factors, known as risk accumulation.[10 11] Risk accumulation comprises the large influence of a number of smaller, seemingly less important risk factors, on the risk of adverse outcomes.[10-12] Such accumulation of risk factors is more common in deprived neighbourhoods, which generally show poor perinatal outcomes.[11]

The term 'neighbourhood deprivation' does not have a standard definition in literature. Rajaratnam et al. examined which neighbourhood characteristics are routinely addressed in perinatal health studies. This study found twelve broad categories of factors used to characterize neighbourhoods (e.g. education, employment, occupation, income).[13] Deprivation is often characterized by indexes with cut-off points to categorize the level of deprivation. The most common used indexes are the Carstairs-Morris score, Index of Multiple deprivation, Townsend deprivation index, and the Jarman score. The Carstairs-Morris score measures domestic overcrowding, male employment, car ownership and social class distribution.[14] The Index of Multiple Deprivation combines income, employment status, health and disability, education, housing problems and crime.[15] The Townsend Deprivation Index converts zip codes in deprivation scores by taking into account local unemployment, car ownership, overcrowding, and housing.[16] The Jarman score is a continuous measure which combines unemployment, overcrowding, lone parents, under-fives, elderly living alone, ethnicity, low social class and residential mobility.[17] However, often other self-composed indices are used.

To date it is unknown to what extent the effect of deprivation goes beyond the effect of poor individual level of socio-economic status of citizens in deprived neighbourhoods.[18 19] An additional effect of neighbourhood has been demonstrated in diseases in adulthood [20], and was suggested to occur in adverse perinatal outcomes.[3 21 22] For instance, a recent meta-analysis demonstrated such an additional role in the occurrence of LBW, which combines both growth restriction and premature cases.[23]

The newest systematic review takes the heterogeneous evidence into account by including studies with neutral, possible, and positive associations of deprivation with perinatal outcomes.[24] Here we present a systematic review and meta-analysis complementary to the existing LBW analysis, for other perinatal outcomes: preterm birth and fetal growth restriction separately, and stillbirth. It seems timely to show the broader evidence on the association of neighbourhood deprivation with other perinatal outcomes than LBW.

MATERIALS AND METHODS

Sources

We performed an electronic search on May 1st 2012 in Medline, Embase and Web of Science from inception to May 2012 for meta-analysis, randomized controlled trials, cohort studies, longitudinal studies and case-control studies. A search strategy was developed and adapted for each database. It included search terms regarding adverse perinatal outcome (e.g. "stillbirth" "fetal death*", "fetal mortalit*", "adverse pregnancy outcome*", "small for gestational age*", "low birth weight*", "dysmatur*", "intrauterine growth restrict*", "preterm deliver*", "preterm birth*", "prematur*"), and search terms regarding deprivation (e.g. "neighborhood*", "neighbourhood*", "urban*", "city", "town*", "disadvantag*", "deprived", "pover*", indigen*", "disadvantaged communit*", "residential segregation"). The search terms regarding adverse perinatal outcome were restricted to 'prematurity', 'small-for-gestational-age' or 'intra-uterine growth retardation' or 'fetal growth retardation' 'stillbirth' and 'perinatal mortality.' Because the search term 'congenital anomaly' resulted in too much heterogeneity in the results (for both underlying cause as well as type of congenital anomaly), this search term was not used in the present study. Reference lists from main articles and relevant reviews were hand searched for additional eligible studies. The search was restricted to studies in humans. No language restrictions were applied. Ethical approval was not required in the Netherlands.

Study selection

For inclusion the studies had to meet the following criteria. They had to (1) be a randomized controlled trial, cohort (including longitudinal), cross-sectional or case-control study; (2) report how deprived neighbourhood or neighbourhood index was defined; (3) report data of perinatal outcomes on the whole neighbourhood population; (4) report any of the main outcome measures preterm birth, LBW, small for gestational age (SGA), stillbirth, and / or perinatal mortality; (5) report either prevalences, odds ratios, or relative risks; (6) be conducted in a developed country, defined as all countries listed by the World Bank.[25]

Two reviewers (AV, AP) independently examined titles, abstracts and full-text articles for eligibility. They independently extracted all relevant data into a preformatted spreadsheet. In case of discrepancies or uncertainties regarding the data extraction, the two reviewers aimed to achieve consensus together or by approaching a third party (the senior investigator (SD)). In case of missing tabular data in studies deemed eligible for meta-analysis, we contacted authors of the respective study.[26 27] We followed the procedures in accordance to the PRISMA statement.[28]

Two reviewers (AV, AP) assessed the quality of each included study independently by using the Newcastle-Ottawa scale.[29] Since no randomized controlled trials were retrieved from the search, we used a quality assessment scale suitable for observational studies. The Newcastle Ottawa scale was developed to assess the quality of non-randomized studies with regard to its design, content and ease of use directed to the task of incorporating the quality assessments in the interpretation of meta-analytic results. The scale was scientifically evaluated and is regarded suitable to use for quality assessment of observational studies.[30] We defined study quality as 'high' if the study was appointed the maximum of nine stars on this scale, 'medium' in case of seven or eight stars and 'low' in case of seven or less stars. Discrepancy in quality assessment was resolved by the two reviewers.

As LBW could not be distinguished in low birth weight related to preterm birth and low birth weight babies at term, we decided only to analyse results from studies when growth restriction was explicitly defined as SGA. Studies that met the inclusion criteria but in which the reported determinant or outcome measure was not eligible for meta-analysis (e.g. not using quintiles as cut-off point or LBW), remained eligible for the systematic review but were not incorporated in the meta-analysis. Statistical analysis was performed with Biostat Comprehensive Meta-Analysis (CMA) version 2. Higgins I^2 (with a significance level at $P < 0.05$) and tau^2 were calculated to assess statistical heterogeneity across studies. We used random-effects meta-analysis to estimate unadjusted and adjusted summary odds ratios (ORs) with the associated 95% confidence intervals. Adjusted ORs were obtained from fully adjusted models as presented in the original papers. If the risk estimate of interest was not explicitly stated, ORs were calculated with CMA. Because different indices were used to determine deprivation, a subgroup moderator analysis was performed to explore the effect of these different neighbourhood indices on the outcome of interest.

Assessment of deprivation

Apparently different cut-off points were used across studies in the categorizing of neighbourhood deprivation. We opted for categorization into quintiles (with the lowest quintile representing the least deprived neighbourhoods) because of three reasons. The most important reason was that the majority of studies applied a division into quintiles,

assuming the extreme categories to be large enough to be relevant and small enough to demonstrate contrasts if present. Other reasons were that we considered quintiles valuable for the cross-study comparability. We assume that the relative socio-economic position within a country is much more important as determinant than absolute measures. Thirdly, the key indicators of interest are summary risk estimates which themselves are relative indicators as well because baseline risk is set to one or zero. We asked 21 authors of papers with other than quintile divisions to re-categorize their determinants in quintiles accordingly, and to subsequently re-analyse their study data. One author was willing and able to do so.[27] In the meta-analysis, we evaluated the contrast between least and most deprived neighbourhood quintiles in preterm birth (birth before 37th week of gestation, SGA (birth weight below the 10th percentile for gestational age), and stillbirth (≥ 20 weeks).

RESULTS

The initial search identified 2 863 articles, which were potentially relevant based on title / abstract screening. All studies were in English except for one study, which was in Dutch. After exclusion of studies that did not meet our inclusion criteria, 108 articles remained of which the full texts were evaluated. We identified another 4 studies from reference list tracking, of which 2 met inclusion criteria. In total, 24 studies met the inclusion criteria for the systematic review and 7 studies were included in the meta-analysis (figure 10.1).

Table 10.1 [11 21 22 26 27 31-49] summarizes the characteristics of the studies included in respectively the systematic review (n=17) and meta-analysis (n=7). Many articles presented results for multiple outcomes. The included studies were conducted in either the United Kingdom (n = 10), Canada (n = 5), The Netherlands (n=4), United States (n=2), Spain (n=1), Sweden (n=1), and Australia (n=1), with data collected from 1985 up to 2008. Four of the included studies performed a multilevel analysis [21 27 31 41], of which one study was included in the meta-analysis.[27] The remaining 20 studies assessed neighbourhood-level exposure.

Deprivation indicators varied across studies. One study used the Carstairs-Morris score, 5 studies used the Index of Multiple Deprivation, another 5 studies used the Townsend Deprivation Index, 1 study used the Jarman score, and 5 studies used neighbourhood income as a proxy for deprivation at the neighbourhood level.

Table 10.2 shows the prevalences and risk estimates of the included studies for respectively preterm birth, SGA and stillbirth. Twenty-one of the 24 included studies showed positive associations between adverse perinatal outcomes and neighbourhood deprivation. The prevalence of preterm birth ranged from 3.8% to 6.7% in the least deprived quintile and 5.6% to 11.9% for the most deprived quintile. For SGA this was respectively

Table 10.1 Design, characteristics and quality assessment of included studies ordered by publication year (n = 24)

Spencer et al, 1999 (38)	Retrospective cohort study, 1991-1993, West Midlands, United Kingdom, N = 194081	Townsend deprivation index – deciles; Register Generals social class index – quintiles	LBW, VLBW	Medium
Smeeton et al, 2004 (44)	Case control study,1996-1998, London, United Kingdom, N = 2735	Jarman score – continuous	Still birth, early neonatal death	Medium
Luo et al. 2004 (49)	Birth cohort study, 1985-2000, British Colombia, Canada, N = 697477	Neighbourhood income – quintiles	PTB, SGA, still birth	High
Manning et al, 2005[x] (35)	Retrospective review of neonatal unit admission records, 1990-2002, place, United Kingdom, N = 47614	Townsend deprivation index – quartiles	Admission at neonatal unit	Low
Dibben et al, 2006 (32)	Retrospective birth cohort study,1996-2000, United Kingdom, N = 306067	Index of multiple deprivation – quintiles	LBW, VLBW	High
Delpisheh et al, 2006 (42)	Retrospective analysis, 1993, 1998 and 2001, United Kingdom, N = 4637	Townsend deprivation index – [-6–12]	Smoking, birthweight	Low
Janghorbani et al, 2006[x] (34)	Prospective case-record study, Plymouth United Kingdom, 1996-1997 N= 3834	Townsend deprivation index – tertiles	PTB	High
Collingwood Bakeo, 2006 (40)	Retrospective cohort study, 1991-2000, England and Wales, United Kingdom, N = 116261	Carstairs – quintiles	LBW	High
Luo et al. 2006 (47)	Birth cohort study, 1991-2000, Quebec, Canada, N = 825349	Neighbourhood income – quintiles	PTB, SGA, still birth	High
Cubbin et al, 2007 (41)	Case record study, 1997-1998, Washington and Florida, United States, N = 8359	Townsend deprivation index – tertiles	LBW	High
Urquia et al. 2007 (48)	Retrospective cohort study, 1996-2001, Toronto, Canada. N = 143030	Neighbourhood income – quintiles	PTB	High

Table 10.1 Design, characteristics and quality assessment of included studies ordered by publication year (n = 24) (continued)

Spencer et al, 1999 (38)	Retrospective cohort study, 1991-1993, West Midlands, United Kingdom, N = 194081	Townsend deprivation index – deciles; Register Generals social class index – quintiles	LBW, VLBW	Medium
De Graaf et al, 2008¥ (22)	Retrospective birth cohort study, 2002 – 2006, the Netherlands, N = 877816	Dutch deprivation score – binary	PM	Medium
Gray et al. 2008 (45)	Retrospective cohort study, 2000-2003, United Kingdom, N = 149690	Carstairs-Morris scores – quintiles	PTB	Medium
Beard et al, 2009 (31)	Retrospective cohort study, 1994-2004, Australia, N = 877951	Index of relative socio-economic disadvantage – quartile	SGA < p3	High
Agyemang et al, 2009¥ (21)	Prospective cohort study, 2003-2004, Amsterdam, The Netherlands, N = 7883	Neighbourhood income – quartile	PTB, SGA	Medium
Smith et al, 2009 (37)	Prospective cohort study,1998-2007, United Kingdom, N = 7402	Composite neighbourhood index – quintiles	Very preterm birth (<33 weeks)	Medium
Janevic et al, 2010 (43)	Case record study, 1998-2002, New York, United States, N = 517994	Messer neighbourhood deprivation index c quartile	Term LBW, PTB	High
Liu et al. 2010 (46)	Retrospective birth cohort study, 2004-2006, Canada, N = 334231	Neighbourhood income Prevalences and risk estimates of the included studies ordered by publication year (n = 24) quintiles	PTB, SGA, still birth	High
Timmermans et al, 2011¥ (11)	Retrospective birth cohort study, 2002-2006, Rotterdam The Netherlands, N = 8668	Dutch deprivation score – binary	PTB, SGA	Medium
Poeran et al, 2011¥ (36)	Retrospective birth cohort study, 2000 – 2006, Rotterdam, The Netherlands, N = 50000	Dutch deprivation score – top 5 highest deprived neighbourhoods compared to top 5 lowest	PTB, SGA, PM	Medium
Sundquist et al, 2011 (39)	Prospective cohort study, 1992-2004, Sweden, N = 720357	Composite neighbourhood index – tertiles	SGA < p2,5	High
Garcia Subirats et al, 2011 (33)	Retrospective cohort study,2000-2005, Barcelona, Spain, N =61676	Contextual socioeconomic variables (e.g. unemployment) –quintiles	PTB, LBW, SGA < p3	High

Table 10.1 Design, characteristics and quality assessment of included studies ordered by publication year (n = 24) (continued)

Spencer et al, 1999 (38)	Retrospective cohort study, 1991-1993, West Midlands, United Kingdom, N = 194081	Townsend deprivation index – deciles; Register Generals social class index – quintiles	LBW, VLBW	Medium
Taylor-Robinson et al. 2011 (26)	Retrospective cohort study 2002-2008, United Kingdom, N = 31785	Index of multiple deprivation – quintiles	PTB	Medium
Urquia et al. 2011 (27)	Birth cohort study, Ontario, 2000-2007, Canada, N = 397470	Neighbourhood income – quintiles	PTB	High

LBW = low birth weight (< 2500 gram); PTB = preterm birth < 37 weeks unless otherwise specified, SGA = small for gestational age (birth weight < p10) unless otherwise specified; VLBW = very low birth weight (< 1500 gram); ¥ exclusion based on index subdivision (not in quintiles).

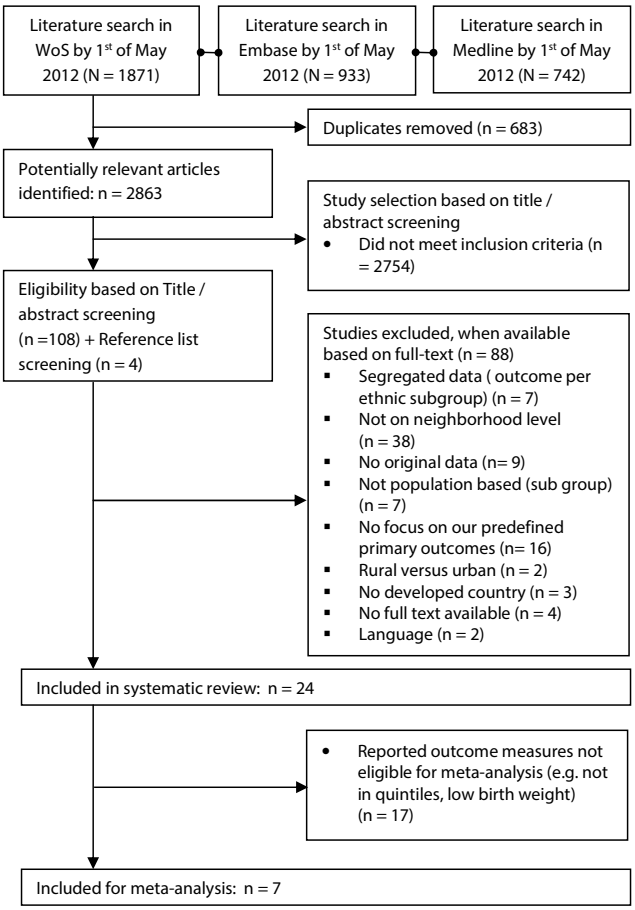

Figure 10.1 Flow diagram of included studies in the systematic review and meta-analysis.

4.8% - 10.4% versus 6.2% - 14.5%. Still birth rates ranged from 3.2 to 6.3 per 1 000 births in the least deprived quintiles and from 4.6 to 7.0 per 1 000 births in the most deprived quintile. All studies included in the meta-analysis used a wide variety of variables to adjust for potential confounders. One study did not report crude odds ratios, but we calculated these with CMA.[46]

Table 10.2 Prevalences and risk estimates of the included studies ordered by publication year

Study	Prevalence of the outcome of interest	Risk estimates (95% CI) for most deprived compared to least deprived neighbourhood	Covariates in fully adjusted model
Spencer et al, 1999 (38)	LBW TDI MD: n=3578 (9,8%), LD: n=888 (5.1%) RGSC: MD: n=128 (11.3%), LD: n=63 (5.5%), VLBW TDI MD: n=329 (0.9%), LD: n=103 (0.6%); RGSC: NA	LWB TDI: RR 1.99 (1.85 - 2.18) RGSC: RR 2.04 (1.53 - 2.73) VLBW TDI: RR 2.11 (1.73-2.57) RGSC: NA	NA
Smeeton et al, 2004 (44)	Still birth Overall: n = 351; Early neonatal death Overall: n = 198	Still birth not significant (results not reported) Neonatal death OR 0.947 (0.849, 0.997, p = 0.038)	NA
Luo et al. 2004 (49)	PTB MD: n = 10163 (7.4%), LD: n = 5855 (6.3%); SGA LD: n=4461 (4.8%), MD: n=8515 (6.2%); Still birth LD: n=585 (0.63%), MD: n=961 (0.70%);	PTB OR 1.16 (1.09 - 1.23), aOR 1.26 (1.17 - 1.35) SGA OR 1.41 (1.33-1.49), aOR 1.50 (1.40-1.60) Stillbirth OR 1.17 (0.95-1.43), aOR 1.30 (1.04 - 1.63)	Infant sex, parity, plurality, ethnicity, maternal age, marital status, abortion history, mode of delivery, maternal illness, community size, and distance to the nearest hospital with obstetricians.
Manning et al, 2005[¥] (35)	PTB MD: n = 334 (8.2%), LD: n = 156 (3.8%)	NA	NA
Dibben et al, 2006 (32)	LBW Overall: 6.0%, MD: n=25005 (8.2%), LD: n=12946 (4.2%); VLBW Overall: 0.9%, MD: n=3672 (1.2%), LD: n=2020 (0.7%);	LWB OR: NA, aOR 1.03 (0.99 - 1.07) VLBW OR: NA, aOR 1.14 (1.12 - 1.16)	Age, social class of household, registration status, estimated household income, age–household income interaction, area income deprivation (AID), age–AID interaction.
Delpisheh et al, 2006 (42)	PTB MD: 14%, LD: 9% Term LBW MD: 2%, LD: 0%; LBW MD: 8% LD: 2%	PTB NA Term LBW OR: NA, aOR 2.9 (0.9–9.6) LBW NA	Maternal smoking, household smoking, parents in paid employment, father's employment, maternal employment, unemployed parents; Townsend score
Janghorbani et al, 2006[¥] (34)	PTB Overall: n=202 (5.3%), MD: n=92 (6.1%), LD: n=49 (4.7%);	PTB RR 1.31 (95%-CI 0.94 - 1.84)	Townsend score, age, gender
Collingwood Bakeo, 2006 (40)	LBW Overall: n=3390 (5.8%) MD: n=297 (7.2%), LD: n=1388 (4.2%);	LBW OR: NA, aOR 1.78 (1.54-2.05)	Economic activity, number of people in the household, number of rooms in the household, household access to a car, housing tenure, region of usual residence carstairs deprivation quintile, ethnicity, limiting long term illness status.
Luo et al. 2006 (47)	PTB MD n=14917 (8.2%), LD n=9939 (6.7%); SGA MD: n = 22376 (12.3%), LD: n=13500 (9.1%); Still birth MD: n = 836 (0.46%), LD: n=474 (0.32%);	PTB OR 1.23 (1.2-1.26), aOR 1.14 (1.10-1.17) SGA OR 1.40 (1.37-1.43), aOR 1.18 (1.15-1.21) Stillbirth OR 1.44 (1.29– 1.62), aOR 1.30 (1.13-1.48)	Infant sex, parity, plurality, maternal age, education, ethnicity, marital status, and neighbourhood income quintile.
Cubbin et al, 2007 (41)	LBW Washington: Overall n= 171(4.4%) MD: n= 198(5.1%), LD n=151 (3.9%); LWB Florida: Overall n=290 (6.5%) MD: n=353 (7.9%), LD n=219 (4.9%);	LBW Washington OR 1.21 (0.61-2.40), aOR 1.21 (0.61 - 2.40) LBW Florida OR 1.34 (1.17-1.54), aOR 0.99 (0.85 -1.17)	Neighbourhood-level deprivation, income, education, paternal education, race/ethnicity, marital status, age, parity

Table 10.2 Prevalences and risk estimates of the included studies ordered by publication year (continued)

Study	Prevalence of the outcome of interest	Risk estimates (95% CI) for most deprived compared to least deprived neighbourhood	Covariates in fully adjusted model
Urquia et al. 2007 (48)	PTB Overall: n = 7580 (5.3%) MD: n = 1605 (5.6%), LD: n = 1340 (4.7%);	PTB OR 1.19 (1.11-1.28); aOR 1.25 (1.15-1.37)	Infant sex, maternal age group, neighbourhood income quintile, and recent immigrant status
De Graaf et al, 2008[¥] (22)	PM MD: 13,5‰, LD: 9,3‰	NA	NA
Gray et al. 2008 (45)	PTB Overall: n = 8394 (5.6%) MD: NA, LD: NA	PTB OR 1.15 (1.13-1.18); aOR 1.07(1.04-1.10)	Deprivation, age, height, parity, sex, smoking, and obstetric intervention
Beard et al, 2009 (31)	SGA(<p3) Overall n=26592 (3.4%) MD: n=9879 (4.5%), LD: n=4171(2.4%);	SGA OR 1.88 (1.22-1.34), aOR 1.45(1.37-1.53)	Quartile of disadvantage, baby's gender, maternal smoking , mother's age , aboriginality , pre-existing diabetes, pre-existing hypertension , gestational hypertension, gestational diabetes, previous pregnancy, year of birth, onset antenatal care, ethnicity, season of birth
Agyemang et al, 2009[¥] (21)	PTB MD: n=138 (6.8%), LD: n=96 (5.4%); SGA MD: n=339 (16.6%), LD: n=150 (8.4%).	PTB OR NA, aOR 1.03 (0.76 - 1.40) SGA OR NA, aOR1.62 (1.25 - 2.08)	Age, parity, educational level, ethnicity, smoking and obesity
Smith et al, 2009 (37)	VPTB Overall: n=103 (1.4%), MD: n=35 (1.8%), LD: n=10 (1.0%);	VPTB RR 1.91 (1.77 - 2.06)	
Janevic et al, 2010 (43)	NA	LBW OR 1.99 (1.80-2.19), aOR 1.19 (1.11-1.27) PTB 32-36 weeks: OR 13.7 (1.30-1.44), aOR 1.06 (1.01-1.11) PTB <32 weeks: OR 1.55 (1.45-1.65), aOR 1.24 (1.13-1.36)	Age, education level, parity, ethnicity, nativity, and smoking.
Liu et al. 2010 (46)	PTB MD: n=5026 (7.5%), LD: n = 4192 (6.3%); SGA MD: n = 7719 (11.6%), LD: n = 5046 (7.6%); Stillbirth MD: n = 434 (0.65%), LD: n = 300 (0.45%);	PTB OR 1.21 (1.16–1.26), aOR 1.17 (1.12 - 1.23) SGA OR 1.60 (1,54-1.66), aOR 1.51 (1.46–1.57) Stillbirth OR 1.45 (1.25–1.68), aOR 1.39 (1.19-1.62)	Maternal age, parity, smoking during pregnancy, maternal health problems, initiation prenatal care in 1st trimester
Timmermans et al, 2011[¥] (11)	PTB: MD: n=163 (5.9%), LD: n=219 (4.8%); SGA: MD: n=402 (14.5%), LD: n=476 (10.4%);	PTB aOR 1.22 (1.00–1.48) SGA aOR 1.41 (1.24 - 1.59)	Indicators for adverse perinatal outcome was related to all individual risk factors and the deprivation indicator
Poeran et al, 2011[¥] (36)	PTB Overall: n=3865 (7.7%), MD: n=204 (11.9%), LD: n=84 (4.7%) SGA Overall: n=4704 (9.4%), MD: n=378 (11,8%), LD: n=92 (4.7%) PM Overall: n=600 (1.2%), MD: n=53 (2.3%), LD: n=2 (0.2%)	NA	NA
Sundquist et al, 2011 (39)	SGA (<p2.5) Overall n=20487 (2.8%) MD: n=4696 (3.5%), LD: n=3942 (2.5%);	SGA OR 1.38 (1.32-1.44), aOR 1.28 (1.22 - 1.34)	Age, marital status, family income, educational level, urban/ rural status, employment, mobility

Table 10.2 Prevalences and risk estimates of the included studies ordered by publication year (continued)

Study	Prevalence of the outcome of interest	Risk estimates (95% CI) for most deprived compared to least deprived neighbourhood	Covariates in fully adjusted model
Garcia Subirats et al, 2011 (33)	PTB Overall: 3395 (5.6%), MD: n=382 (7.1%), LD: n=197 (3.5%); LBW Overall: n=3931 (5.6%), MD: n=372 (6.9%), LD: n=708 (4.5%); SGA(<p3) Overall: n=1741 (2.3%), MD: n=197 (3.5%), LD: n=358 (2.2%);	PTB aOR 1.51 (1.27–1.79) LBW aOR 1.56 (1.37–1.78) SGA aOR 1.66 (1.29–1.12)	Maternal age, country of origin, parity, sex of newborn
Taylor-Robinson et al. 2011 (26)	PTB Overall: n = 1612 (5.1%), MD: n = 1146 (5.6%), LD: n = 27 (4.1%);	PTB OR 1.55 (1.36 - 1.76), aOR 1.32 (1.12 - 1.55)	Maternal age, parity, smoking status, BMI, ethnicity
Urquia et al. 2011 (27)	PTB Overall: n = 24623 (6.2%), MD: n = 5594 (7.0%), LD: n = 4559 (5.7%);	PTB OR 1.25 (1.20 - 1.30), aOR 1.26 (1.21 - 1.31)	Maternal age, parity and immigrant status

aOR = adjusted Odds Ratio, CI-95% = 95% confidence interval; LBW = low birth weight (< 2500 gram); LD = least deprived; MD = most deprived; NA = not available; OR = Odds Ratio; PM = perinatal mortality PTB = preterm birth < 37 weeks unless otherwise specified; SGA = small for gestational age (birth weight < p10) unless otherwise specified; VLBW = very low birth weight (< 1500 gram); VPTB = very preterm birth (<33 weeks)
*studies included in the meta-analyses. ¥ exclusion based on index subdivision (not in quintiles).

Meta-analysis

The two most common reasons for exclusion in our meta-analysis were lack of results at neighbourhood level (e.g. results were provided for whole villages, counties or states, n = 38) or outcome measures were defined that were not eligible for our meta-analyses (e.g. LBW, data not reported in quintiles, n = 17). The meta-analysis eventually included cohort studies on adverse perinatal outcomes associated with neighbourhood deprivation. If outcomes for several years were reported, the most recent results were used for the meta-analysis. Assessment of study quality showed that five studies were of high quality [27 46-49] and two of medium quality.[26 45]

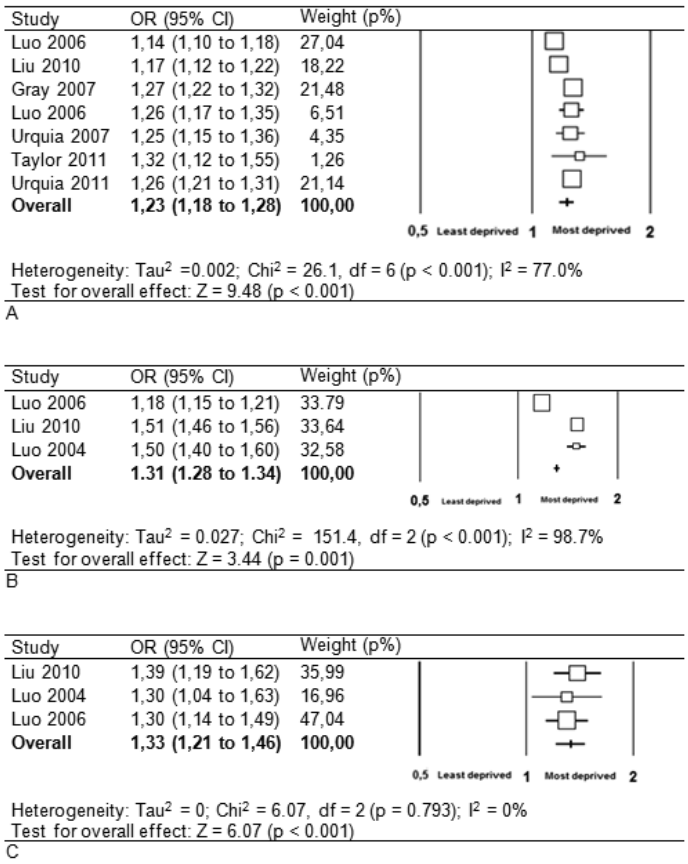

Figure 10.2 Forest plot of pooled random effects adjusted odds ratio (aOR) and 95% confidence intervals (CIs) of adverse perinatal outcome comparing the most deprived neighbourhood quintile with the least deprived neighbourhood quintile.
White squares indicate the aOR in each study, with square sizes inversely proportional to the standard error of the OR. Horizontal lines represent 95% CIs. P values represent P for heterogeneity. A. Pooled effects for preterm birth. B. Pooled effects for small for gestational age. C. Pooled effects for stillbirth.

Figure 10.2 summarises the comparison of the least and most deprived neighbourhoods for preterm birth, SGA and stillbirth. None of the included studies reported data on perinatal mortality, but all reported stillbirth (> 20 weeks of gestation). The random effects model comprising all 7 studies suggests a positive association for preterm birth (crude OR 1.28 (95% confidence interval 1.20 to 1.37), adjusted OR 1.23 (95% CI 1.18 to 1.28). Heterogeneity was noted among the individual study effects (I^2 (crude) 94% (P< 0.001), I^2 (adjusted) 77% (P< 0.001)). Countries included in the meta-analysis have comparable preterm birth rates.[50] For the outcomes SGA and stillbirth, only studies that indicate deprivation by means of the index neighbourhood income remained after the selection process. Similar positive associations between least and most deprived neighbourhood quintiles were found. The OR from crude results for SGA was 1.47 (95% CI 1.34 to 1.60), I^2 95 %, P<0.001, adjusted OR 1.31 (95% CI 1.28 to 1.34), I^2 99%, P<0.001. For stillbirth, the crude OR was 1.38 (95% CI 1.23 to 1.54), and adjusted OR was 1.33 (95% CI 1.21 to 1.45) without marked heterogeneity (I^2 (crude) 41 %, P = 0.185, I^2 (adjusted) 0%, P = 0.793). The studies in our meta-analysis showed a consistent association between living in a deprived neighbourhood and adverse perinatal outcomes.

Subgroup analysis

In a subgroup analysis comprising 5 studies that used neighbourhood income as measure of deprivation, we also found a positive association between the least and most deprived neighbourhood quintiles (crude OR 1.22 (95% CI 1.19 to 1.25), I^2 24%, P = 0.261), adjusted OR 1.21 (95% CI 1.15 to 1.27), I^2 78%, P = 0.001).

Since 6 studies were excluded based on how they categorized their neighbourhood index (e.g. cut-off point other than quintiles), we performed a univariate meta-regression analysis with neighbourhood cut-off point as moderator to assess the empirical relationship between neighbourhood cut-off point and the log of the observed OR. Crude ORs from 4 out of these six studies were available for this analysis in preterm birth [11 21 34 35], and crude ORs from 2 studies were available for SGA. [11 21] This figure indicates that we found no empirical relationship for the cut-off point in this analysis (figure 10.3).

A sensitivity analysis was performed for all outcomes to evaluate the stability of the results. We performed a subgroup moderator analysis to compare the mean odds ratio for five studies using income as measure of deprivation and two other studies using another index in preterm birth: OR_{income} 1.25 (95% CI 1.15 to 1.37) and OR_{other} 1.38 (95% CI 1.25 to 1.70). These studies were also the studies rated as high quality. This difference was not statistically significant (Q = 0.70, p = 0.404).

Although no asymmetry was seen on the funnel plot (not shown), the largest analysis included only 7 studies. This number of studies is too small to perform an adequate assessment of publication bias.[51] We tried to minimize risks of publication bias with our search strategy. Firstly by including Web of Science as one of the search engines,

because of its provision of conference abstracts. Secondly, we reviewed reference lists of all 108 studies which were eligible based on title or abstract, and of one meta-analysis and several reviews within this topic.

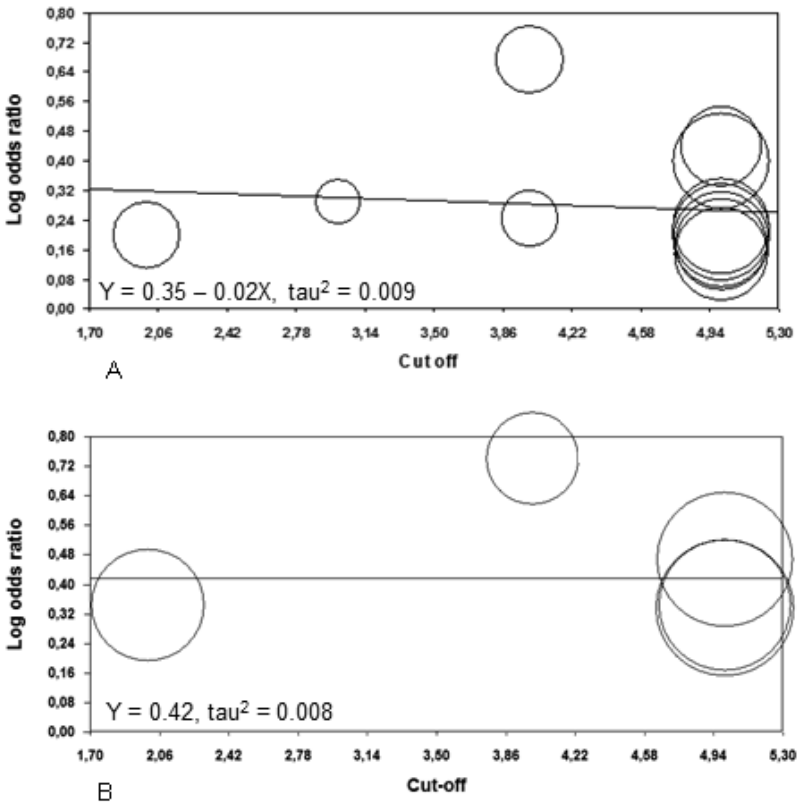

Figure 10.3 Scatter plot representing the meta-regression analysis to test the association between the cut-off point for neighbourhood index and the log adjusted odds ratio (aOR) of preterm birth and small for gestational age (SGA) respectively.
The area of each circle is inversely proportional to the variance of the log relative risk estimate. A. Preterm birth. B. SGA.

DISCUSSION

This systematic review and meta-analysis indicates that neighbourhood deprivation is associated with preterm birth, SGA and stillbirth. Compared to the least deprived neighbourhood quintile, ORs of adverse perinatal outcomes in the most deprived neighbourhood quintile were significantly increased for preterm birth (OR 1.23, 95%-CI 1.18-1.28), SGA (OR 1.31, 95%-CI 1.28-1.34), and stillbirth (OR 1.33, 95%-CI 1.21-1.45). This is the first meta-analysis in which preterm birth and SGA are analysed separately. While the previous analysis on LBW showed an excess prevalence due to deprivation effect of 11%.[23], our meta-analysis - in which we analysed SGA and preterm birth separately - provided a prevalence of 31% and 23% respectively. Our findings suggest that these two disease entities only share part of the deprivation pathway, because the stratified ORs for SGA and preterm birth are higher individually than LBW in which preterm birth and SGA are combined. Stratification seems to distinguish both the risk pathways of preterm birth and SGA more than LBW alone. The etiology of both outcomes is not always related to each other (preterm birth could be induced by infectious diseases whereas placenta insufficiency primarily induces SGA). Furthermore, preterm birth often has a strong care effect (iatrogenic preterm birth), which is absent in SGA. Stratification may therefore clarify the neighbourhood effect. Although such excess risks may seem small, it suggests the high attributable risk impact of deprivation through the high prevalence of deprivation.

The association between many adverse perinatal outcomes and low socio-economic status is known. This is thought to be induced though multiple pathways, most importantly low education and low income levels.[52] Although the present analysis did not focus on etiologic factors that could explain the relationship between non-medical risk factors and adverse perinatal outcomes, it is known from previous studies that decreased wealth and living conditions increase physiological stress[53], and low income levels and deprivation are associated with poor housing, nutrition, and health care access.[3] If we assume that adverse perinatal outcomes are the result of the interrelationship between individual, environmental, and care-related factors[3 11], deprived areas could contribute to adverse outcomes in several ways. In deprived areas, so-called non-medical risk factors (e.g. lifestyle- and social risk factors) are much more common, especially in urban areas.[3 23 54]

Within patient care perspective it is important to acknowledge that risk accumulation not only includes the commonly measured standard risks, but also many unmeasured disadvantage or risk factors, which often escape standard epidemiologic research. Also the physiological (air pollution, noise) and psychological environment (safety) are part of the usually unmeasured risk burden in deprived neighbourhoods.[55]

The greatest challenge in the meta-analysis was to overcome heterogeneity. We believe this is mostly due to the variable cut-offs used in forming neighbourhood quintiles. In our meta-analysis, the results for preterm birth in our primary analysis did not differ from our subgroup analysis for income level. We approached all authors from potentially eligible studies to cooperate in our meta-analysis in order to pool pregnancy outcomes on individual level, so that we could investigate the comparability of the different indices (n = 11). Unfortunately, most authors did not respond so we were unable to perform analysis. Another reason for this heterogeneity might be the variety of used definitions to indicate neighbourhood deprivation. Some of these indices were compared in previous studies, and the use of area based deprivation indices is an accepted method for measuring social inequality in neighbourhoods.[18] Moreover, income seems to be a good proxy for area based deprivation related to health.[19] However, it is still unclear whether area based measures reflect the cumulated impact of individual socio-economic status, or represent the crude neighbourhood effect or a combination of both.[19 49] Despite the high heterogeneity, we believe that pooling of the available data provides valuable information about neighbourhood deprivation and the risk of unfavourable pregnancy outcomes, and used random-effect models to calculate pooled risk estimates.

Strengths and limitations

A major strength of this study is that we performed the first a meta-analysis in which preterm birth, SGA, and stillbirth were analysed separately. In addition, we included all study types in the initial search to be able to identify the (cluster) randomized controlled trials. This did not result in inclusion of randomized controlled trials. However this effort is strength because if we had ignored this study type, we could have overlooked studies investigating the effect of deprivation on for example neighbourhood level.

Our analysis has some limitations. First of all, we were unable to answer our research question with only multilevel studies as in the previous meta-analysis we referred to.[23] Some effect of clustering may be present if data was retrieved from true cluster designs in which clusters involve for example schools, hospitals or communities, and ignoring this effect – if present – might lead to some overestimation of the precision and statistical significance. However, in our study neighbourhoods are overall large and defined by different principles and therefore unequally sized. We assume that under these conditions no additional measures are needed to account for the study effect beyond the per study multilevel term.

Secondly, as we decided to use data presented in quintiles for prior mentioned reasons, we had to exclude 6 studies from meta-analysis because they did not report neighbourhood deprivation in quintiles. Risk estimates from these studies were mostly within the range of the risk estimates of studies pooled in the meta-analysis. In a meta-regression analysis we did not found an empirical relationship for cut-off point. Another limitation

was that the definition of fetal growth restriction as 'low birth weight'. This was a reason for exclusion because we were unable to categorize findings into the LBW related to preterm birth outcome or the outcome of LBW babies at term (> 37 weeks of gestation). We only included results from studies when growth restriction was defined as 'small for gestational age below the 10th percentile.' We advocate separation of SGA and preterm birth, because both etiology and long term consequences differ considerably between these outcomes.[56-58] For the association between neighbourhood deprivation and LBW (as a broad category) we refer to the meta-analysis by Metcalfe et al.[23]

Thirdly, we were not able to rank the included countries according to perinatal outcomes. The Euro-Peristat committee was able to make such an over country comparison. In their most recent published report, they compared perinatal outcomes of 29 European countries.[59] They reported marked differences between countries. However, such a report was not available for the non-European countries included in our study. Due to the absence of this information, we were not able to make an 'over country comparison' and relate our findings to the ranking of countries.

Lastly, we were not able to stratify for ethnicity. Although the included studies were adjusted for ethnicity, we missed information of other ethnic groups living in these neighbourhoods which were not included in their analysis. So these outcomes were not representative for the whole neighbourhood population. Confounding by ethnic differences is therefore unavoidable in this study. This is important because neighbourhood effects might not be consistent across ethnic groups.[24] Deprivation could have a stronger negative effect on Western women compared to non-Western women.[60] It seems that simple aggregation of particular individual effects does not explain our findings at neighbourhood level. It seems that other partly unknown underlying mechanisms influence both perinatal risk factors and outcomes at neighbourhood level.

Implications

Since poor maternal circumstances during pregnancy have both short and long term consequences, it makes sense to organize tailor-made antenatal healthcare responsive to women's needs by taking into account deprivation notions, preferably in combination with preconception care. In particular in large cities, this implies involvement of local initiatives and engagement of Public Health services.[61] A systematic approach in antenatal risk selection for both medical and non-medical risk factors with subsequent continuity of care might support early detection of potential high risk. More awareness regarding the medical impact of the non-medical domain should be advocated in healthcare professionals, but also in public health workers and policy makers. It may seem challenging in practice to reach women in deprived neighbourhoods for specific intervention programs, but research has shown that specific recruitment strategies can be used to achieve participation in these women.[62]

CONCLUSION

In summary, this systematic review and meta-analysis suggest that neighbourhood deprivation is associated with SGA, preterm birth, and stillbirth.

However, more methodological research is necessary to determine the comparability of several neighbourhood deprivation indices in relation to these perinatal outcomes. The included studies were not designed to explore mechanisms, so more etiological studies on a neighbourhood and an individual level are necessary to gain understanding of the effect of 'neighbourhood deprivation' on adverse perinatal outcomes. In the meantime this should not withhold us from designing new policies and programs for women living in deprived neighbourhoods where both social and medical risk factors are highly present.

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Chapter 11

General discussion

AIMS OF THIS THESIS

The aims of this thesis were (1) to evaluate the policy process that led to the Healthy Pregnancy 4 All study, (2) to investigate the contribution and the assessment of non-medical risk factors, and (3) to investigate the influence of neighbourhood deprivation on perinatal outcomes. This chapter discusses the principal findings of the conducted studies, methodological considerations, and offers recommendations and implications for clinical field and policy.

PRINCIPAL FINDINGS

Part I: Initiatives to improve perinatal health

Why and how did the perinatal mortality problem make its way into the national political agenda?

The relatively high perinatal mortality and morbidity rates in the Netherlands resulted in a policy process followed by policy changes regarding the organization of Dutch perinatal healthcare system (chapter 2). Between 2004 and 2010 it became a high priority for many stakeholders in the field to reduce perinatal mortality. Several factors promoted the agenda setting. Firstly, the perinatal mortality problem had been quantified by PERISTAT and additional research had provided new information. Secondly, the nature of the subject and the fact that perinatal mortality concerned a relatively large group of people in society engaged more professionals than only those working in the curative field. Whilst contents of perinatal health care were mostly in hands of the curative setting, the perinatal mortality debate engaged several members of the House of Representatives, policy makers, and public healthcare professionals. Thirdly, parliamentary inquiries and the media were eager to be an intermediary and fueled the debate.

Prior to this debate, the organization of perinatal health had not been systematically evaluated before. To propose solid actions and measures, a Steering Group (the Advisory Committee on Pregnancy and Childbirth) was instituted in 2008. The Steering Group proved to be the vehicle to achieve collaboration amongst the whole field and it coordinated the translation of insights in science into measures for practice. Parliamentary inquiries required rapid answering by the ministry of Health, Welfare and Sports. In response a new network, the Baby club, was formed which essentially determined the contents of measures. This interdepartmental network provided a platform to discuss the perinatal mortality problems with policy makers from different departments of the ministry. In this network ties were made between the policy makers from the curative department (traditionally involved in formulation of policy) and policy makers from the

preventive department, which enabled them to answer the parliamentary questions with a multidisciplinary view.

Perinatal health was an underserved aspect in our health policy system. Collaboration between the curative and the preventive system, and their policy makers on national level (the department of curative and public health) with respect to organization of perinatal health care was relatively scarce. The department of public health gained interest and power in the perinatal mortality debate. The department of public health had formulated that more attention should go out to socioeconomic determinants of health (such as non-medical risk factors) and that local municipalities should be involved in effectuation of these measures to achieve optimally tailored and preferably community based care. The perinatal health issue proved to be the suitable topic to effectuate this vision. The academic field was approached to select and effectuate interventions. Amongst other initiatives, budget and effectuators were sought for what came to be the beginning of the Healthy Pregnancy 4 All study.

To what extent is it possible to implement a new method of antenatal risk assessment?
In the risk assessment (RA) sub-study, implementation of the Rotterdam Reproductive Risk Reduction (R4U) scorecard, corresponding care pathways and multidisciplinary consultation was evaluated (chapter 4).

In total, 6 of the 11 municipalities (54%) met our criteria for successful implementation of the entire risk assessment program. These include four 'intervention' and two 'control' municipalities. Three municipalities (27%) were indicated as 'high implementers' as they met the criteria for all parts separately. These were all 'intervention' municipalities. Three municipalities were classified as 'medium implementers' (27%) and the remainder (46%) did not meet the criteria for implementation.

This observed variability in implementation rates was similar to findings of comparable implementation studies.[1 2] Factors that attributed to variation in implementation were contextual factors such as organizational characteristics (e.g. autonomously working healthcare professionals or integrated care setting), availability of resources (e.g. financial or human resources), the complexity of the setting (e.g. pre-existing partnerships among healthcare professionals, competing interests) and time required for organizational uptake of our new approach in antenatal healthcare.[1 3] Additionally, the Dutch antenatal health care system provides some specific contextual challenges, because community midwives in the primary level of care and gynaecologists in secondary and tertiary care are autonomous professionals operating in their own tiers of care in the antenatal system. This was explained by others as different perspectives on antenatal health and suboptimal inter-professional communication.[4] The implementation of our new approach in risk assessment and collaboration primarily required a mind shift amongst all stakeholders, regarding conventional antenatal risk assessment.

The awareness that change in risk assessment approaches was needed proved to be an important success factor for implementation.[5] We therefore might have benefitted from the fact that we conducted our study in a period of time in which perinatal health received high priority by both the field and policy makers.

Part II: Non-medical risk factors in pregnancy

How are non-medical risk factors currently assessed during routine antenatal healthcare?
An instrument for routine screening of non-medical risk factors was lacking in current antenatal healthcare (chapters 6 and 7). We also observed that midwives and gynaecologists rarely screen for non-medical risk factors in the Netherlands and that risk assessment approaches were highly variable between community midwife practices and hospitals. Respondents were used to screen upon lifestyle risks, whereas whether respondents screened for social risk factors or not was highly variable. It was remarkable that while caregivers indicated to deal with non-medical risk factors frequently, national guidelines or protocols and supportive tools to deal them were lacking. Systematic structured screening was not part of routine antenatal healthcare and preventive intervention strategies relied on local resources (chapter 7).

In response, we developed a non-invasive, standardized scorecard for routine use in antenatal health care: the Rotterdam Reproductive Risk Reduction Scorecard (R4U) scorecard. Improvement of current antenatal risk assessment with the R4U scorecard included the combined assessment of medical and non-medical risk factors. Through its standardized assessment, the score card promoted uniform definition of risks by all professionals involved. As it included non-medical risk factors, the scorecard bridges the gap between the clinical working area and the public health domain. It showed to be a promising tool for early antenatal detection of risk factors and tailored prevention in an integrated care setting (chapter 6).

What is the contribution of non-medical risk factors to perinatal outcomes and how is this related to risk accumulation?
We found that women in the lowest SES category and women of non-western descent have a substantial greater risk for adverse perinatal outcomes through the mechanism of accumulation of non-medical risk factors (chapter 8). It was also shown that social deprivation plays a different role among Western and non-Western women. Possible causal explanations were increased density of migrant groups in particular neighbourhoods[6], the influence of social capital in these particular neighbourhoods [7], differences in lifestyle behaviours (e.g. smoking behaviour)[8], and epigenetic effects.[9 10]

We also observed a higher prevalence of adverse perinatal outcome (overall perinatal morbidity and small for gestational age and preterm birth separately) regarding the

severity of a risk factor category, going from the least to the more favourable category of the risk factor. Apparently risk accumulation explains perinatal inequalities between groups. The risk impact on non-medical risk factors on adverse perinatal outcome was proportionally related to the number of non-medical risk factors up to a three-fold increased risk in case of 3 factors. This proportional relation between non-medical risk factors and adverse perinatal outcome has also been reported in prior literature. [10-12] Previous studies revealed multiple pathways, acting on different aggregation levels (individual, family, neighbourhood), but low income and low education seem to play a pivotal role.[13]

Part III: Perinatal outcomes on neighbourhood level

What is the contribution of neighbourhood deprivation to perinatal outcomes and are there any differences between municipalities?

We demonstrated that patterns in perinatal health inequalities differ on both the municipal and neighbourhood level in the Netherlands: some municipalities showed overall high rates of adverse perinatal outcomes, and some also showed large differences between neighbourhoods (chapter 9). These neighbourhood differences were particularly pronounced for perinatal mortality. After adjustment for socio-demographic risk factors, such as SES, maternal age, parity, and ethnicity, these differences persisted.

In some municipalities socio-demographic risk factors appeared to be a strong predictor for the observed inequalities. The risk factors explained almost a third of the observed differences. However in other municipalities, their contribution seems less prominent. This could indicate that different mechanisms may be involved in the extent to which risk factors lead to adverse pregnancy outcomes. Examples of these are travel time to a hospital, place of birth (home or hospital), factors related to the neonate, organizational factors and / or caregiver related factors which are all known to be associated with adverse pregnancy outcomes.[14-17] These factors were not included in our analysis.

These findings were also confirmed by a meta-analysis of observational studies (chapter 10). We demonstrated that neighbourhood deprivation was significantly associated with preterm birth, SGA and stillbirth. Although it was beyond the scope of this thesis to reveal etiologic factors beyond neighbourhood effects that could explain the relationship between non-medical risk factors and adverse perinatal outcomes, it was known from previous studies that decreased wealth and living conditions increase physiological stress[18], and that low income levels and deprivation are associated with poor housing, nutrition, and less health care access.[19] If we assume that adverse perinatal outcomes are the result of the interrelationships between individual, environmental, and care-related factors[19 17], deprived areas could contribute to adverse outcomes in several ways. However, to date it is unknown to what extent the effect of deprivation

goes beyond the effect of poor individual level of socio-economic status of citizens in deprived neighbourhoods.[20 21]

The principal findings related to this thesis were summarized in figure 11.1.

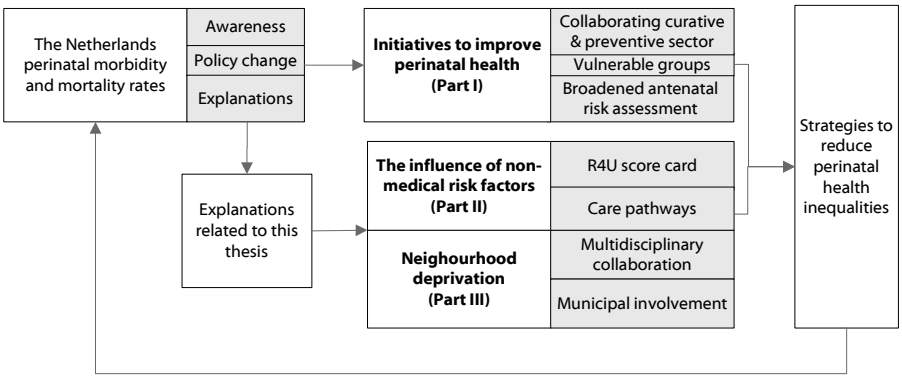

Figure 11.1 Principal findings related to this thesis.

METHODOLOGICAL CONSIDERATIONS

There were some overall methodological considerations in this thesis.

Study population

Participants of the risk-assessment (RA) sub-study were pregnant women residing in the selected neighbourhoods of the 14 municipalities that enrolled from August 2012 until June 2014 (chapter 5 and 8). These neighbourhoods were selected on the basis of zip codes (chapter 3). Due to the selection of geographical areas, the study focused on potentially high risk populations. Community midwives and gynaecologists providing care to women living in these selected areas were invited to participate in the RA sub-study. All pregnant women that visited a participating community midwife or hospital were eligible to participate in the RA sub-study. Regarding the study population, methodological limitations might concern selective enrollment and selective participation and medical ethical requirements.

Regarding enrollment, most practices and hospitals simply enrolled all of their clients for practical reasons, rather than strictly enrolling women that belonged to the targeted population (women residing in the selected zip codes). Consequently, our study population was not strictly confined to the zip codes with high prevalences of Big 4 outcomes, as was intended in the beginning. However, the fact that practices were allowed this

type of inclusion allowed the program to have a larger outreach and actually seemed to promote implementation as no time was lost in selecting participants and routine in the use of the R4U scorecard could easily be acquired.

Selective participation is also an issue that needs to be addressed in this study. It was challenging to reach women living in the selected zip codes (half of the included women were living in one of the selected neighbourhoods), because these women often refused to participate. Furthermore, participation was associated with education levels: higher educated women were more likely to participate more than lower educated women (chapter 8). In general, neighbourhood deprivation has been known to be associated with selective participation.[22] We were not able to verify the non-response to the questionnaires in relation to socio-demographic characteristics, but we cannot rule out that selective participation and selective non-response might have biased the associations.[23]

Medical-ethical requirements to inform participants such as information letters with predefined content and documenting informed consent were mentioned as barriers by healthcare professionals to either ask women (e.g. in case of low literacy) or for women to participate when asked. Thus, medical ethical requirements might have induced selective enrollment and participation.

Context

We conducted our study in a period of time in which antenatal healthcare was a high priority file for policy makers (chapter 2). The current system and collaboration between community midwives and gynecologists was under scrutiny when it became clear that the country had high perinatal mortality rates.[24] The perinatal mortality debate led to discussions about organizational changes and initiation of studies to reveal underlying causes and best practices. The speed and intensity of the debate was overwhelming for some health care professionals that were approached for participation in the Healthy Pregnancy 4 All study. This brought some of them to postpone implementation of the R4U. The competition with other innovation processes was an important impeding factor in achieving maximal implementation.

In the implementation process, inter-professional collaboration between midwives and gynaecologists proved to be challenging sometimes. Bases for these challenges were the autonomy of the different professionals and the fact that they work in different fragments of the perinatal health care system, with different contextual factors.[4] Preexisting inter-professional communication barriers represented a challenge in some municipalities which could not always be bridged by the project team or local project coordinators (chapter 5). The proposed collaboration required a mind shift amongst participating midwives and hospital caregivers, namely to have a shared responsibility. In addition, the study required this mind switch amongst policy makers and the public health sector. Prior to the program delivery of obstetric care was seen as the main re-

sponsibility of healthcare professionals in the curative setting, whereas involvement of the preventive sector (public health) was restricted to lifestyle promotion and provision of information (chapter 2).

These contextual factors had an impact on the rollout of our cluster randomized controlled trial (chapter 5). As the sample size needed to answer the effectiveness question was not reached yet, and remains therefore unanswered in this thesis. It will be evaluated during the subsequent Healthy Pregnancy for All 2 project.

Instruments

In order to implement a new approach in antenatal risk assessment, a number of conditions need to be fulfilled. Most important, professionals from obstetric care, social welfare, psychiatric services, and community health services should agree on the comprehensive risk concept as a base to collaborate. The number of developed care pathways and the establishment of multidisciplinary consultations on municipal level display the great potential of our risk assessment approach to achieve collaboration, which can only contribute to the quality of delivered care. Successful implementation also requires adherence to protocols. We were unable to investigate this performance (i.e. appropriate use of care pathways or risk screening in all situations) in great detail, however we observed that the process of systematic screening, indication, assessment, referral, and treatment is still not functioning optimally in the Netherlands.[25]

The selection of risk factors and design of the R4U scorecard was a multi-phased and systematic process. To obtain the cumulative risk score, weights were obtained from published risk estimates from representative birth cohort studies, meta-analysis, and a few case-control studies. When the pregnancy outcomes of participants of the Healthy Pregnancy 4 All population become available, we can report on the external validity of these weights and make the corresponding adjustments.

Study design

We faced an important limitation due to the design of our study. In order to investigate the effectiveness of our approach, a cluster randomized controlled trial was methodologically the most appropriate study design (chapter 4). Thus, we randomized municipalities to an 'intervention' or a 'control' status. In the 'intervention' municipalities, the risk assessment intervention was started as of inception of the study. In control municipalities, regular antenatal healthcare was measured and none of the interventions were implemented. Evaluation of conventional risk assessment required extra time and effort from caregivers and from local stakeholders assisting with implementation of the project, whilst they were not intervening with regards to the perinatal mortality rates in their neighborhoods. This felt as a contradiction, as the project had made them aware of the mortality rates and the disadvantaged position in comparison to the rest of the

country and the national average. In a context where a lot was expected from healthcare professionals and a lot of new (regional) initiatives were implemented, this might have influenced the commitment to our study over time. This was also reflected in the implementation rate of 'control' municipalities that was considerably lower compared to municipalities that started from the beginning (chapter 5).

Big 4 morbidities

The risk assessment sub-study builds on the results from the Signalement study in which the concept of Big 4 morbidities was introduced.[26] These morbidities include small for gestational age (SGA), preterm birth, congenital anomalies, and/or a low Apgar score. The presence of a so-called 'Big 4' morbidity precedes perinatal mortality in 85% of cases.[26] The presence of one or more Big 4 morbidities was therefore used as a proxy measure of a 'high risk pregnancy'. Although one can debate about the preventability of all of these morbidities, we cannot ignore the importance of timely detection of SGA to maximise the potential benefit of clinical management in order to prevent perinatal mortality.[27] Whilst other obstetric diagnostic procedures and interventions (e.g. progesterone to prevent preterm birth or the widely available 20-week ultrasound) are emerging, the need and benefits of timely risk assessment are increasing.[28 29]

Perinatal registry

The Dutch Perinatal Registry (PRN) was used to identify geographical areas (chapter 3), differences in perinatal outcomes between municipalities (chapter 8) and the contribution of socio-demographic risk factors on perinatal outcomes (chapter 9).[30 31] The two greatest advantages of using the PRN database are the large amount of data from pregnancies in the Netherlands that became available over time (over 1 million records) and the high rate of complete cases (more than 97%). However, by using the PRN database we also faced some limitations. The perinatal registry mainly collects data about specific actions in the healthcare process such as admissions or pregnancy complications. Given our aim to collect data regarding non-medical risks, we perceived some shortcomings. Limitations were present because the information regarding some risk factors (e.g. smoking and onset of antenatal care and population characteristics such as education level or income level) were incorrect or lacking. This was especially unfortunate given the fact that education and income level are thought to be the most important pathway in the relation between social inequalities and adverse perinatal outcomes.[13]

RECOMMENDATIONS AND IMPLICATIONS

From this the following recommendations and implications for the clinical field and policy can be given.

Representation of the curative care and public health echelon in antenatal healthcare policy

Health is not solely influenced by biological factors, but by social and environmental factors as well. Participating in the HP4All study, and especially the development of care pathways, gave professionals from different echelons an opportunity and a motive to get familiar with other professionals than that they are used to work with and with each other's potential roles in antenatal risk assessment and intervention. This led to an integrated care setting (caregivers and public health workers) which was preferable for optimal use for the proposed way of risk assessment and collaboration in antenatal healthcare, because the R4U scorecard and corresponding care pathways require medical and non-medical expertise. In addition, we demonstrated that a tangible concept (a risk assessment tool) such as implemented by us can bridge gaps between the curative setting and the public health.

We advise policy makers and health care professionals to collaborate and to develop additional local policies to define their high risk populations. Ingredients for a successful approach are 1) defining the degree of the problem (numbers are essential) to achieve agenda setting; and 2) placing the problem in a broader multidisciplinary context for the identification of new solutions. The investment in understanding each other's positions may well be rewarded with better collaboration in the selection and effectuation of interventions.

Early and systematic detection of medical and non-medical risk factors in antenatal healthcare

A systematic approach to antenatal risk selection for both medical and non-medical risk factors with subsequent continuity of care supports early detection of women which are potentially at risk for adverse pregnancy outcomes. Early detection (preferably at booking in early pregnancy) contributes to the improvement of perinatal outcomes either by increasing awareness or allowing for risk modification. A risk score above the predefined cut-off point should imply follow-up action. This follow-up action should include multidisciplinary consultation between obstetric caregivers and non-obstetric caregivers, prioritization of risk factors, and feedback in subsequent meetings.

Both medical and non-medical risk factors contribute to adverse pregnancy outcomes and have a risk-enhancing role in perinatal and maternal outcomes. Multiple risk factors are likely to be present amongst women in in deprived neighbourhoods. First of

all, identification of these neighbourhoods on municipal level is necessary. Municipal health services and the Dutch Perinatal Registry (PRN) need to collaborate to identify areas (and thereby women) at risk for adverse pregnancy outcomes. Secondly, (municipal) services outside the healthcare sector (e.g. financial support services, facilities for teenagers) should have a more active role in the care for pregnant women in deprived neighbourhoods. Thirdly, perinatal health should be part of a municipal policy cycle with periodic monitoring on a neighbourhood level.

Collaboration between the curative care and public health echelon to develop care pathways

Regardless of how antenatal risk assessment is performed, without actions from caregivers upon detected risk factors, the value of risk assessment is marginal. Care pathways, which can be tailored to the individual needs, can assist caregivers with acting upon risk factors in a standardized, tailored way. They can be of great practical value as they can be explicit regarding which caregiver will be responsible, and regarding practical concerns such as the names and contact information of institutions with expertise regarding the detected risk factor. This enhances the efficiency and accountability of interventions after risk assessment. Care pathways also contribute to unequivocal division of tasks and responsibilities for medical and non-medical risk factors. The availability of local facilities and insurance agreements should be taken into consideration.

By providing standardized information on both medical and non-medical risk factors, collaboration between both obstetric caregivers (curative care) and non-obstetric caregivers (public health) can be optimized. The introduction of organized meetings to customize care pathways induced a change in the mutual professional relationship. The organized meetings also induced mutual respect and much more awareness among both professionals on the impact and effect of non-medical risk factors.

General recommendations

Several practical considerations should be addressed before a new approach to antenatal risk assessment is implemented in routine practice. Healthcare professionals may need training to assess and encounter non-medical risk factors. Time schedule of the first antenatal visit and extra time for multidisciplinary consultations may require adaptation. Health insurance reimbursement schemes might need revision in order to enable this.

Professionals from obstetric and non-obstetric care should also agree about the comprehensive risk concept as a base to collaborate. A national, multidisciplinary guideline supporting the standardized screening of these risk factors would facilitate implementation of non-medical risk screening in the current antenatal healthcare system. Conflicting financial incentives and existing inter-professional communication

barriers may represent a challenge for the implementation of new approached to risk assessment. Pre-existing barriers and context factors should be identified.

A complex structural intervention such as the HP4All study depends on the participation of local stakeholders. Differences in context and setting make implementation monitoring essential. Further evaluation is recommended to monitor and document the program implementation and to get a better understanding of the associations between specific program elements and outcomes.

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Chapter 12

English and Dutch summary

SUMMARY

Promotion of healthy pregnancies has gained high priority in the Netherlands because of the relatively unfavorable perinatal outcomes compared to surrounding countries which was confirmed by two consecutive European reports on perinatal health. Additionally, large inequalities were observed within the Netherlands. Poor perinatal outcomes seemed to be more prevalent in deprived areas and were often associated with socio-economic and ethnic minority related risk factors such as low-income or less integration into society. Research revealed that in 85% of all cases mortality was preceded by perinatal morbidity (e.g. preterm birth, small-for-gestational age, suboptimal start or congenital anomalies), also known as Big 4 morbidities. In addition, it was demonstrated that non-medical risk factors (social and lifestyle risk factors) had an equally high impact of perinatal outcomes when compared to medical and obstetrical risk factors, and that the accumulation of these risk factors could even further harm the chances of a good pregnancy outcome. Non-medical risk factors and risk accumulation were especially observed in deprived areas. This information made perinatal mortality an important political and social issue, which led to many national and local initiatives in the Dutch antenatal healthcare field.

In this thesis, the aim was threefold: 1) to evaluate initiatives that were implemented to improve perinatal morbidity and mortality rates in the Netherlands, 2) to investigate the influence of neighbourhood deprivation on perinatal outcomes, and 3) to investigate the contribution of (the assessment of) non-medical risk factors. Our results were therefore presented and summarized in three parts.

Part I: Initiatives to improve perinatal health

In **chapter 2** we describe the policy process followed by policy changes in response to the relatively unfavorable position of the Netherlands. We aimed to identify actors, context and process factors that promoted or impeded agenda setting and formulation of policy regarding antenatal health care reform and to present an overview of the renewed perinatal health policy. The policy triangle framework for policy analysis by Walt and Gilson was applied. Actors, context factors, process factors and content factors were identified by triangulation of data from three sources: a document analysis, stakeholder analysis and interviews with key stakeholders. The analysis provided a chronological reconstruction of the policy process after perinatal mortality rates became apparent (between 2004 and 2011). Important process factors for agenda setting and formulation of policy were the quantification of the perinatal mortality problem, the openness of the debate and the nature of the subject. The nature of the subjects engaged a broad scope of actors. An accent in the contents of policy was that organizational change was neces-

sary in care throughout the full spectrum of perinatal healthcare. Furthermore there was a shift in responsibility from the curative setting towards the preventive setting as policy stated the importance of social and environmental determinants in health. This pointed out the necessity of municipal involvement. Important contextual factors were the Dutch tiered antenatal healthcare system and divergent views regarding perinatal healthcare providers.

However, it seemed challenging to make perinatal health a key priority amongst municipal health policy makers. The direction of public health identified the need for a dedicated project to set up such partnerships between the curative and preventive sector on municipal level to effectuate the local health policy. They sought for a field partner to execute their plans programmatically. After they identified the Ready for a Baby program in Rotterdam, they approached its executors to discuss a national program. The program was to have a municipal approach and to employ preventive measures. As a result a grant was provided to the Erasmus MC and the HP4All study was launched. The study was initiated in 2011 by the Erasmus University Medical Centre with support of the Ministry of Health, Welfare and Sport to implement strategies to improve perinatal outcomes with special focus on deprived areas. The Ready for a baby program provided the framework for this national study. The main purpose of the HP4All study was to evaluate the effectiveness of two interventions in 14 municipalities to prevent and reduce adverse pregnancy outcomes; (1) the preconception care sub-study, a population-based prospective cohort study focusing on the feasibility and effectiveness of customized preconception care, and (2) the risk assessment sub-study, a cluster randomized trial to investigate the feasibility and effectiveness of scorecard-based antenatal risk assessment to identify women early in pregnancy at risk for adverse pregnancy outcomes. The present thesis focuses on the risk assessment (RA) sub-study within the HP4All study.

In **chapter 3** we describe the thorough analysis that was performed to identify geographical areas in which adverse perinatal outcomes were high. These areas were regarded as eligible for either or both sub-studies as we hypothesized that interventions would have be most necessary. Therefore, the selection of municipalities was based on multiple criteria relevant to either the preconception care intervention or the antenatal risk assessment intervention, or to both. Accordingly, the following municipalities were selected: Utrecht, Amsterdam, Den Haag, Schiedam, Tilburg, Almere, Heerlen, Enschede, Nijmegen, Groningen, Delfzijl, Appingedam, Menterwolde en Pekela.

In **chapter 4** we describe the design and outline of the RA sub-study. Despite the increasing evidence for the influence of nonmedical risk factors (social status, lifestyle or ethnicity) on perinatal outcomes, standard risk assessment in antenatal healthcare does not include the assessment of non-medical risks of perinatal health. The intervention in the RA sub-study consisted of systematic scorecard-based risk selection using the R4U (Rotterdam Reproductive Risk Reduction) scorecard in pregnant women at the first

antenatal visit. Subsequent patient-tailored care pathways and consultation of professionals from different medical and social disciplines were offered in case risks were detected. The RA sub-study was designed as a cluster randomized controlled trial on municipal level. The municipalities (clusters) Amsterdam, Tilburg, Nijmegen, Enschede, Groningen and the four surrounding municipalities (one cluster) were assigned to the intervention group. The municipalities (clusters) Utrecht, Almere, Schiedam, Den Haag and Heerlen were assigned to the control group. The study aimed to investigate the effectiveness of systematic approach in antenatal health care on adverse pregnancy outcomes (primarily lowering prematurity and small for gestational age outcomes) and to investigate the efficacy of implementation (measured by the number of R4Us filled out by the healthcare professional, the performance of multidisciplinary deliberations and patient and healthcare professional satisfaction).

In **chapter 5** we investigate the implementation of the R4U sub-study. A complex structural intervention such as the RA sub-study depends on the participation of local healthcare professionals in the participating municipalities. These differences in context and setting made implementation monitoring essential. We used an existing framework for the development of a program implementation monitoring plan with specific attention to the setting and context of the program. We performed triangulation of data from multiple data sources and applied pre-specified criteria for evidence of implementation to examine the evidence for implementation. Six out of 11 municipalities (54%) met our criteria of implementation for the entire risk assessment program. The results of this process evaluation will be used to get a better understanding of the associations between specific program elements and program outcomes.

Part II: Non-medical risk factors in pregnancy

In **chapter 6** we presented the development of the R4U score card for early antenatal detection of risk factors and tailored prevention in an integrated care setting. The R4U scorecard covers 70 items divided into six domains (social status, ethnicity, care, lifestyle, and medical and obstetric history). The R4U scorecard gives a weighted score to every pregnant woman. If the score exceeded a predefined cut-off point, her risk profile was discussed in a multidisciplinary consultation (MC) between community midwives, gynaecologists and other invited non-obstetric care providers (e.g. social workers). Pilot-evidence from a cohort of 218 pregnancies in a multi-practice setting showed that a cut-off of 16 points implies that 20% of all cases were to be assessed in a multidisciplinary setting.

In **chapter 7** we study the current practices regarding assessment and care of non-medical risk factors in antenatal healthcare among community midwives from 139 midwifery practices and gynaecologists, hospital-based midwives, and trainees in obstetrics from 38 hospitals. Performance of systematic screening for non-medical risk factors was

rare and approaches were highly variable between community midwife practices and hospitals. Screening mostly addressed lifestyle risk factors, whereas the frequency of screening for social risk factors among healthcare professionals was highly variable. Because there is not a national guideline or protocol for the screening on non-medical risk factors, local protocols were reported to be used for this purpose. Caregivers stated that multidisciplinary protocols were a prerequisite for assessment of non-medical risk factors. Only one fifth of the caregivers used predefined criteria to define whether or not patients should be discussed multidisciplinary.

In **chapter 8** we examine the association between specific non-medical risk factors and socio-economic status and ethnicity. We also explored whether risk accumulation of these non-medical factors could be demonstrated as independent contributors to major adverse perinatal outcomes. Women in the lowest SES category and women of non-western descent were at a substantially increased risk for adverse pregnancy outcomes. The risk factors 'single parentship', 'low family income', 'low education level', 'no preconception folic acid supplementation' were all significantly more present among these groups. However, when we adjusted the effect of SES on adverse perinatal outcome for non-western ethnicity, the effect of SES became non-significant. This suggests that there might be an independent effect of ethnicity. We observed a gradual increase in prevalence of adverse perinatal outcome (overall perinatal morbidity and SGA and PTB separately) regarding the severity of a risk factor category, going from the least to the more favourable category of the risk factor. Apparently risk accumulation explains perinatal inequalities between groups. The risk impact of non-medical risk factors on adverse perinatal outcome was proportionally related to the number of non-medical risk factors; there was an up to three-fold increased risk of adverse outcome in case of three factors.

Part III: Perinatal outcomes on neighbourhood level

In **chapter 9** we studied the separate contribution of several socio-demographic risks on perinatal health inequalities between municipalities and neighbourhoods. All included municipalities showed higher rates of perinatal morbidity and mortality than the national average. Patterns in perinatal health inequalities differ on both the municipal and neighbourhood level. Some municipalities show overall high rates of adverse perinatal outcomes, while others show large differences between neighbourhoods. Considerable differences in low socio-economic status between municipalities were apparent. For some municipalities, socio-demographic risk factors were a strong predictor for the observed inequalities, while in other municipalities these factors were very weak predictors. If all socio-demographic determinants were set to the most favorable value in a predictive model, combined perinatal morbidity would decrease with 15% to

39% in these municipalities. These different patterns of inequality suggest differences in etiology.

Chapter 10 we summarize the evidence form observational studies on the relation between neighbourhood deprivation and the risks for preterm birth, small for gestational age, and stillbirth. This meta-analysis indicated that neighbourhood deprivation was significantly associated with all three perinatal outcomes separately.

Chapter 11 we summarize and discuss the main findings of this thesis and its recommendations for the clinical field and policy. This thesis provided an intervention strategy in which high perinatal risk regions were targeted. Taking the evidence from the present study and previous studies on non-medical risk factors and risk accumulation into account, it makes sense to organize tailor-made antenatal healthcare responsive to women's needs with local initiatives and in close collaboration with Public Health services to approach these risk factors. Early detection (preferably at the intake) may contribute to the improvement of perinatal outcomes either by increased awareness or the ability of risk modification. Given that prevalence of medical risk factors in women living in deprived neighbourhoods is already higher, non-medical risk factors require active screening and active intervention amongst these women. We believe that the emerging knowledge on the predictive role of both medical and non-medical risk factors, and risk accumulation justifies the implementation of structural risk assessment in antenatal healthcare.

NEDERLANDSE SAMENVATTING

Perinatale gezondheid kreeg in Nederland hoge prioriteit door de verschijning van twee opeenvolgende rapporten waaruit bleek dat ons land ongunstig scoort op perinatale sterftecijfers ten opzichte van omliggende landen. Naast deze relatief ongunstige positie werden er ook verschillen in perinatale sterftecijfers binnen Nederland geobserveerd. De prevalentie van ongunstige zwangerschapsuitkomsten was hoger in achterstandswijken en werd geassocieerd met sociaaleconomische en etniciteit gerelateerde risicofactoren, zoals een laag inkomen of verminderde integratie in de samenleving.

Onderzoek liet zien dat perinatale morbiditeit in 85% van de gevallen voorafgaat aan perinatale sterfte. Perinatale morbiditeit werd gedefinieerd als het voorkomen van vroeggeboorte (geboorte < 37 weken), dysmaturiteit (geboortegewicht < 10^{e} percentiel), lage Apgar score (score < 7 gemeten 5 minuten na de geboorte) en / of congenitale afwijkingen, ook wel de 'Big 4 aandoeningen' genoemd. Daarnaast liet onderzoek zien dat niet-medische risicofactoren (sociale en leefstijl gerelateerde risicofactoren) een belangrijke rol spelen in ongunstige zwangerschapsuitkomsten. Tot slot werd een opstapeling van deze risicofactoren (risicocumulatie) geassocieerd met een extra verhoogd risico op een ongunstige zwangerschapsuitkomst. Niet-medische risicofactoren en risicocumulatie werden vaker gezien bij zwangeren die wonen in achterstandswijken.

Deze nieuwe inzichten zorgden ervoor dat perinatale sterfte werd herkend als een belangrijk politiek en maatschappelijk probleem. Dit heeft geleid tot veel lokale en landelijke initiatieven op het gebied van perinatale gezondheidszorg.

Dit proefschrift heeft drie hoofddoelen: 1) de evaluatie van een aantal initiatieven in Nederland die tot doel hebben om perinatale uitkomsten te verbeteren, 2) onderzoek naar de bijdrage van niet-medische risicofactoren op zwangerschapsuitkomsten en hoe hier in de huidige verloskundige zorg aandacht aan wordt besteed, 3) onderzoek naar de invloed van achterstandswijken op zwangerschapsuitkomsten. Dientengevolge worden de resultaten gepresenteerd in drie delen.

Deel I: initiatieven om perinatale gezondheid te verbeteren

In **hoofdstuk 2** beschrijven we het beleidsproces en daaropvolgende beleidsaanpassingen in het perinatale gezondheidsbeleid als reactie op de relatief ongunstige perinatale sterftecijfers in Nederland. We hadden tot doel om de actoren, inhoudsfactoren, contextuele factoren en procesfactoren die de agendasetting hebben beïnvloed te identificeren en het hernieuwde beleid chronologisch in kaart te brengen. Hiertoe maakten we gebruik van drie databronnen: een documentanalyse van alle kamerstukken gepubliceerd van 2004 (verschijning 1^{e} report) tot 2011 (initiatie nieuw beleid), een stakeholder analyse en interviews met de geïdentificeerde stakeholders. Belangrijke

procesfactoren voor de agendasetting en beleidsaanpassingen waren het inzichtelijk worden van de cijfers (kwantificatie van het probleem), het openlijke debat (media) en het onderwerp babysterfte waarbij een groot aantal actoren betrokken waren. Een belangrijke inhoudelijke factor was het inzicht in een noodzakelijke organisatieverandering door de gehele keten. Daarnaast werd een deel van de verantwoordelijkheid van perinatale gezondheidszorg ondergebracht onder de preventieve zorg, omdat duidelijk werd dat sociale en omgevingsfactoren ook een belangrijke rol speelden in perinatale gezondheid. Hierdoor werd de rol van gemeenten ook steeds duidelijker en belangrijker. Belangrijke contextuele factoren waren de huidige organisatie van de verloskundige zorg in Nederland met het 3-lagig systeem (1e, 2e en 3e lijn) en de uiteenlopende opvattingen tussen de beide beroepsgroepen (verloskundigen en gynaecologen).

De actieve participatie van gemeenten in perinatale gezondheid bleek een uitdagend voorstel en daarom ging men opzoek naar partners in het veld om samenwerkingsverbanden tussen curatieve en preventieve zorg op lokaal niveau te realiseren. Hiertoe werden de uitvoerders van het programma Klaar voor een Kind uit Rotterdam benaderd. Dit programma werd op gemeenteniveau in samenwerking met het Erasmus MC uitgevoerd en had tot doel de perinatale morbiditeit en mortaliteit in Rotterdam terug te dringen. De focus lag op wijken met de hoogste sterftecijfers. Het Erasmus MC schreef een projectvoorstel om deze aanpak ook in andere gemeenten met hoge perinatale morbiditeits- en sterftecijfers te implementeren. Het project genaamd Healthy Pregnancy 4 All (HP4All) werd in 2011 met ondersteuning van het ministerie van Volksgezondheid, Welzijn en Sport in 14 gemeenten in Nederland uitgevoerd. Ook in dit project lag de focus op wijken met de meest ongunstige zwangerschapsuitkomsten. Strategieën en instrumenten uit het programma Klaar voor een Kind werden op nationaal niveau verder uitgewerkt, geïmplementeerd en geëvalueerd met aandacht voor lokale voorzieningen. Het belangrijkste doel van HP4All was de evaluatie van twee interventies om perinatale morbiditeit en mortaliteit te reduceren in deze 14 gemeenten. Het project is opgebouwd uit twee deelstudies, te weten 1) de preconceptiezorg sub-studie, een prospectief cohort onderzoek met de focus op de haalbaarheid en effectiviteit van preconceptiezorg en 2) de risicoselectie sub-studie, een zogenoemd 'cluster randomised controlled trial' waarin de haalbaarheid en effectiviteit van systematische risicoselectie vroeg in de zwangerschap op zwangerschapsuitkomsten wordt geëvalueerd. Dit proefschrift is gebaseerd op de Risicoselectie (RS) sub-studie binnen HP4All.

In **hoofdstuk 3** voeren we een analyse uit om geografische gebieden (wijken) met hoge zwangerschapsuitkomsten te identificeren. Hiertoe gebruikten we meerdere selectiecriteria met als doel wijken te identificeren waarin vrouwen maximaal zouden profiteren van de interventies in beide experimenten. De gemeenten Utrecht, Amsterdam, Den Haag, Schiedam, Tilburg, Almere, Heerlen, Enschede, Nijmegen, Groningen, Delfzijl, Appingedam, Menterwolde en Pekela werden op basis van deze criteria geselecteerd.

In **hoofdstuk 4** beschrijven we het onderzoeksprotocol van de RS sub-studie. Ondanks toegenomen kennis over niet-medische risicofactoren (sociale en leefstijl gerelateerde risicofactoren) in relatie tot zwangerschapsuitkomsten, werd in de verloskundige zorg niet standaard gescreend voor deze risicofactoren. De interventie bestond uit risicosignalering met het instrument 'Rotterdam Reproductive Risk Reduction scorecard' (R4U scorekaart) tijdens de eerste antenatale controle bij elke nieuwe zwangere. Aansluitende zorgpaden en multidisciplinair overleg zorgden voor juiste zorgtoeleiding en afgestemd antenataal beleid. Het onderzoek werd uitgevoerd in de vorm van een cluster randomised controlled trial in verloskundigenpraktijken en ziekenhuizen gelegen in de geselecteerde wijken van de 14 deelnemende gemeenten (10 clusters). De gemeenten Amsterdam, Tilburg, Nijmegen, Enschede en Groningen en de vier omringende gemeenten (1 cluster) waren zogenoemde interventie clusters. De gemeenten Utrecht, Almere, Schiedam, Den Haag en Heerlen waren controle clusters. Geëvalueerd werd 1) de haalbaarheid van de implementatie (o.a. aantal zwangeren waarbij de R4U werd afgenomen, het aantal vrouwen dat multidisciplinair werd bespreken en de tevredenheid onder zorgverleners en zwangeren) 2) de effectiviteit van de interventie op ongunstige zwangerschapsuitkomsten te weten laag geboortegewicht (< p10) en prematuriteit (zwangerschapsduur <37 weken).

In **hoofdstuk 5** onderzoeken we de haalbaarheid van de implementatie met procesevaluatie. Een complexe interventie als de RS sub-studie is afhankelijk van de deelname van lokale zorgverleners in de 14 geselecteerde gemeenten. Verschillen in context en achtergrond maakten monitoring van de implementatie noodzakelijk. Voor deze monitoring maakten we gebruik van een bestaande methode voor het monitoren en evalueren van zulke complexe interventies. Door triangulatie van data afkomstig uit verschillende bronnen en vooraf samengestelde criteria werd per gemeente geëvalueerd of aan de implementatie criteria werd voldaan. Hiermee werd de vraag beantwoord of de interventie succesvol was geïmplementeerd. Zes van de 11 clusters (Groningen stad en omringende gemeenten werden afzonderlijk geëvalueerd) voldeden aan de gestelde criteria voor implementatie. De resultaten van de procesevaluatie worden gebruikt om de verschillende verbanden tussen programma-elementen en uitkomsten in perspectief te kunnen plaatsen.

Deel II: niet-medische risicofactoren in de zwangerschap

In **hoofdstuk 6** presenteren we de ontwikkeling van de R4U scorekaart voor vroegtijdige signalering van risicofactoren en aansluitende zorgpaden ter ondersteuning van integrale geboortezorg. De R4U scorekaart omvat 70 risicofactoren onderverdeeld over 6 domeinen (sociale, psychische, leefstijl, algemeen medische, obstetrische en zorg gerelateerde risicofactoren). Na het invullen ontstaat een gewogen risicoscore. Bij een score boven de drempelwaarde wordt geadviseerd een zwangere in multidisciplinair

verband te bespreken met verloskundigen, gynaecologen, andere zorgverleners en hulpverleners uit het niet-medische domein. Uit een pilotstudie met 218 zwangeren concludeerden we een risicoscore boven de 16 punten er op neerkomt dat 20% van de zwangeren besproken dient te worden in een multidisciplinaire setting.

In **hoofdstuk 7** onderzoeken we de huidige manier van risicoselectie en zorgtoeleiding voor niet-medische risicofactoren in de verloskundige zorg bij eerstelijnsverloskundigen uit 139 praktijken en gynaecologen, klinisch verloskundigen en arts-assistenten uit 38 ziekenhuizen. Hieruit bleek dat systematische risicoscreening voor niet-medische risicofactoren vrijwel nooit werd uitgevoerd en grote verschillen in de aanpak bestond tussen eerstelijns verloskundigen en gynaecologen. De meerderheid van de respondenten gaf aan wel naar leefstijl gerelateerde risicofactoren te vragen, maar voor de screening op sociale risicofactoren bestonden grote verschillen tussen de respondenten. Er is geen landelijke richtlijn voor de screening op niet-medische risicofactoren en werden vaak lokale protocollen gebruikt. Zorgverleners gaven aan dat ze een multidisciplinaire richtlijn voor niet-medische risicofactoren nodig hebben. Een vijfde van de respondenten gebruikte vooraf gestelde criteria om te besluiten of een zwangere multidisciplinair besproken zou moeten worden.

In **hoofdstuk 8** kijken we naar de associatie tussen niet-medische risicofactoren, socio-economische status en etniciteit. Daarnaast onderzoeken we of risicocumulatie een onafhankelijke rol speelt bij het ontstaan van ongunstige zwangerschapsuitkomsten. Vrouwen met een lage socio-economische status en vrouwen van niet-westerse afkomst bleken een substantieel verhoogd risico op ongunstige zwangerschapsuitkomsten te hebben. De risicofactoren 'alleenstaand', 'laag gezinsinkomen', 'laag opleidingsniveau', 'geen preconceptioneel foliumzuurgebruik' waren allemaal significant vaker aanwezig in deze groep. Wanneer we corrigeerden voor socio-economische status op ongunstige zwangerschapsuitkomsten bij de groep niet-westerse zwangeren verdween dit effect. Dit suggereert dat er mogelijk een onafhankelijk effect voor etniciteit bestaat. We observeerden een geleidelijke toename in de kans op deze ongunstige uitkomsten naarmate er meer risicofactoren aanwezig waren. De resultaten konden deels verklaard worden door risicocumulatie. Concluderend was de impact van niet-medische risicofactoren proportioneel gerelateerd aan het aantal risicofactoren bij een zwangere, oplopend tot een drievoudig verhoogd risico indien er drie niet-medische risicofactoren aanwezig waren.

Deel III: zwangerschapsuitkomsten op wijkniveau

In **hoofdstuk 9** onderzoeken we de afzonderlijke bijdrage van verscheidene socio-demografische risicofactoren op perinatale gezondheidsverschillen tussen verschillende gemeenten en wijken in deze gemeenten. Deelnemende gemeenten toonden allemaal hogere morbiditeits- en sterftecijfers dan het landelijk gemiddelde. Hieruit bleek dat

patronen in perinatale gezondheidsverschillen zowel op gemeente als op wijkniveau verschillend waren: in sommige gemeenten waren de zwangerschapsuitkomsten in alle wijken verhoogd, terwijl in andere gemeenten grote verschillen tussen wijken bestonden. Daarnaast speelde socio-economische status in sommige gemeenten een belangrijke rol in de verklaring van ongunstige zwangerschapsuitkomsten, maar in andere gemeenten niet. De bijdrage van socio-demografische risicofactoren hebben we met een voorspellingsmodel gekwantificeerd. Hieruit bleek dat indien alle socio-demografische risicofactoren werden omgezet naar gunstige factoren (vb. een hoge socio-economische status i.p.v. een lage socio-economische status), de perinatale morbiditeit met 15% tot 39% kan afnemen in gemeenten. Dit verschil laat zien dat er verschillende oorzaken zijn voor perinatale gezondheidsverschillen in gemeenten.

In **hoofdstuk 10** hebben we door de resultaten van verschillende observationele onderzoeken samen te voegen gekeken naar de associatie tussen achterstandswijken en de zwangerschapsuitkomsten vroeggeboorte, dysmaturiteit en perinatale sterfte. Uit deze meta-analyse bleek dat wonen in een achterstandswijk significant is gerelateerd aan zowel vroeggeboorte, dysmaturiteit en perinatale sterfte.

Hoofdstuk 11 presenteert een samenvatting en discussie van de hoofdbevindingen en conclusies dit proefschrift, en voorziet in klinische en beleidsgerelateerde aanbevelingen en implicaties voor het veld. Dit proefschrift biedt een interventie strategie gericht op zwangeren wonend in potentieel hoog risico wijken. Naar aanleiding van dit proefschrift in combinatie met eerdere studies aangaande niet-medische risicofactoren en risicocumulatie verdient systematische screening op medische en niet-medische risicofactoren en een toespitste, individuele interventie naar onze mening de aandacht in de huidige antenatale zorg bij deze groep zwangeren. Bij voorkeur in samenwerking met de publieke gezondheidssector op landelijk en lokaal niveau. Vroege detectie (bij voorkeur tijdens het eerste zwangerschapsconsult) zou kunnen bijdragen aan de verbetering van de perinatale gezondheidsuitkomsten door toegenomen bewustzijn bij zorgverleners en het vroegtijdig (multidisciplinair) aanpakken van risicofactoren.

Chapter 13

Authors and affiliations
List of publications
PhD portfolio
About the author
Dankwoord

AUTHORS AND AFFILIATIONS

Erwin Birnie, Gouke J. Bonsel, Semiha Denktaş, Lieke de Jong-Potjer, Annemiek Leeman, Jashvant Poeran, Anke Posthumus, Eric A.P. Steegers, Sabine van Voorst, Adja Waelput from the Department of Obstetrics and Gynaecology, Division of Obstetrics and Prenatal Medicine, Erasmus MC, University Medical Centre Rotterdam, The Netherlands

Semiha Denktaş, Department of Social Sciences, Erasmus University College, Erasmus University, Rotterdam, The Netherlands

Gouke J. Bonsel and Gerard Borsboom from the Department of Public Health, Erasmus MC, University Medical Centre Rotterdam, The Netherlands

Gouke J. Bonsel and Mieke J. van Veen from the Midwifery Academy, Rotterdam University ofApplied Sciences, Rotterdam, The Netherlands

Erwin Birnie from the Institute of Health Policy and Management, Erasmus University, Rotterdam, The Netherlands

Jashvant Poeran, Institute for Healthcare Delivery Science, Department of Population Health Science & Policy and Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, United States of America

LIST OF PUBLICATIONS

Manuscripts related to this thesis

1. **Vos AA**, Bonsel GJ, Steegers EAP. Foetal and neonatal mortality in a European perspective: improvement of perinatal health care in the Netherlands still necessary [in Dutch: Foetale en neonatale sterfte in Europees perspectief: verbetering van de verloskundige zorg in Nederland blijf nodig]. Nederlands tijdschrift voor geneeskunde 2014;158:A7594.

2. **Vos AA**[‡], van Voorst SF[‡], Steegers EAP Steegers, Denktaş S. Analysis of policy towards improvement of perinatal mortality in the Netherlands. Submitted.
   [‡]Shared first authorship

3. Denktaş S, Poeran J, van Voorst SF, **Vos AA**, de Jong-Potjer LC, Waelput AJ, et al. Design and outline of the Healthy Pregnancy 4 All study. BMC Pregnancy Childbirth 2014;14:253.

4. **Vos AA**, van Voorst SF, Waelput AJ, de Jong-Potjer LC, Bonsel GJ, Steegers EAP, Denktaş S. Effectiveness of score card-based antenatal risk selection, care pathways, and multidisciplinary consultation in the Healthy Pregnancy 4 All study (HP4ALL): study protocol for a cluster randomized controlled trial. Trials 2015;16(1):8.

5. **Vos AA**, van Voorst SF, Posthumus AG, Waelput AJ, Denktaş S, Steegers EAP. Implementation of score card-based antenatal risk selection, care pathways, and interdisciplinary consultation (the Healthy Pregnancy 4 All study). Submitted

6. **Vos AA**, van Veen MJ, Birnie E, Denktaş S, Steegers EAP, Bonsel GJ. An instrument for broadened risk assessment in antenatal health care including non-medical issues. International journal of integrated care 2015;15:e002.

7. **Vos AA**, Leeman A, Waelput AJM, Bonsel GJ, Steegers EAP, Denktaş S. Assessment and care for non-medical risk factors in current antenatal healthcare. Midwifery.2015 Jun 22.

8. **Vos AA**, Denktaş S, Steegers EAP, Bonsel GJ. Non-medical risk factors and risk accumulation in relation to perinatal outcomes (the Healthy Pregnancy 4 All study). Submitted

9. **Vos AA**, Denktaş S, Borsboom JJM, Bonsel GJ, Steegers EAP. Differences in perinatal morbidity and mortality on the neighbourhood level in Dutch municipalities: a population based cohort study. BMC Pregnancy and Childbirth.2015 Jun, 15:201

10. **Vos AA**, Posthumus AG, Bonsel GJ, Steegers EAP, Denktaş S. Deprived neighborhoods and adverse perinatal outcome: a systematic review and meta-analysis. Acta obstetricia et gynecologica Scandinavica 2014;93(8):727-40.

Other scientific publications

– van Voorst SF, **Vos AA**, de Jong-Potjer LC, Waelput AJ, Steegers EA, Denktaş S. Effectiveness of general preconception care accompanied by a recruitment approach: protocol of a community-based cohort study (the Healthy Pregnancy 4 All study). BMJ open 2015;5(3):e006284.

– Prick BW, **Vos AA**, Hop WC, Bremer HA, Steegers EA, Duvekot JJ. The current state of active third stage management to prevent postpartum hemorrhage: a cross-sectional study. Acta obstetricia et gynecologica Scandinavica. 2013;92(11):1277-83.

– Denktaş S, Waelput AJM, van Voorst SF, **Vos AA**, Bonsel GJ, de Jong-Potjer L, Steegers EAP. Healthy Pregnancy 4 All: Preconception care and risk assessment during pregnancy [in Dutch: Preconceptiezorg en risicoselectie tijdens de zwangerschap]. Tijdschrift sociale geneeskunde. 2012;90(8):479-483.

– Posthumus AG, Schölmerich VLN, Waelput AJM, **Vos AA**, De Jong-Potjer LC, Bakker R, Bonsel GJ, Groenewegen P, Steegers EAP, Denktaş S. Bridging between professionals in perinatal care: towards shared care in the Netherlands. Maternal Child Health Journal.2012;(12).

– **Vos AA**, Bruinse HW. Congenital adrenal hyperplasia: do the benefits of prenatal treatment defeat the risks? Obstetrical & gynecological survey. 2010;65(3):196-205.

Health reports

Waelput AJM, Rosman AN, Van Voorst SF**, Vos AA**, Lagendijk J, Sijpkens MK, Van Veen-van Belle DW, De Jong-Potjer LC, Bonsel GJ, Steegers EAP. 'Project Healthy Pregnancy 4 All. Aanpak babysterfte in Nederlandse gemeenten' The Healthy Pregnancy 4 All study. Approach to perinatal mortality in the Netherlands. Rotterdam: Erasmus MC, may 2015. (Report for the Ministry of Health, Welfare and Sports, report in Dutch)

PHD PORTFOLIO

Summary of PhD training and teaching activities

Name PhD candidate:	Amber Amanda Vos
Erasmus MC Department:	Obstetrics & Gynaecology - Div of Obstetrics and Prenatal Medicine
Research school:	Netherlands Institute for Health Sciences (NIHES)
PhD period:	September 2011 – June 2014
Promotores:	Prof. dr. Eric A.P. Steegers
	Prof. dr. Gouke J. Bonsel
Co-promotor:	Dr. Semiha Denktaş

	Year	Workload (ECTS)
1. PhD Training		
General and specific courses		
Biostatistics for clinicians	2012	1
Regression analysis for clinicians	2012	1.9
Multilevel analysis with R (CARMA)	2012	1
Logistic regression	2012	1.4
Clinical epidemiology	2012	5.7
International conferences		
First International Congress on Fetal Growth, Birmingham, United Kingdom: poster presentation	2012	1
60th Annual meeting of the Society for Gynecologic Investigation, Orlando, USA: oral presentation	2013	1.5
61th Annual meeting of the Society for Gynecologic Investigation, Florence, Italy: 2 poster presentations	2014	2
National conferences		
NCVGZ Dutch Annual Public Health Conference (in Dutch: 'Nationaal Congres Volksgezondheid'), Utrecht, The Netherlands: poster presentation	2012	1
DOHaD satellite meeting, Rotterdam, The Netherlands: poster presentation	2012	1
Conference 'Kennispoort Verloskunde', Utrecht, The Netherlands: oral & poster presentation	2014	2.5
Healthy Pregnancy 4 All Final symposium, The Hague, the Netherlands: oral presentation	2014	1.5

Presentations

Numerous oral presentations (> 60) at Regional Obstetric Collaboration meetings (VSVs), Lunch meetings, Case presentations, Research meetings, and other meetings to introduce, implement, and discuss the progress of the Healthy Pregnancy 4 All study to midwives and gynaecologists	2011-2014	15

Seminars, workshops, research meetings

Attending weekly and quarterly research meetings of the Department of Obstetrics and Gynaecology (and Urology) with 3 oral presentations	2011-2014	5
Attending the annual meetings of the Collaboration of Rotterdam Regional Gynaecologists' Teaching Hospitals (in Dutch: RGOC) 'Wladimiroff Symposium	2011-2014	0.6
Attending the symposium 'Urban Perinatal Health (in Dutch: Grootstedelijke Perinatale Gezondheid)', Rotterdam, The Netherlands	2011	0.2
Preparing and attending the Kick-off meeting of the Healthy Pregnancy 4 All (HP4All) project, Utrecht, the Netherlands	2011	1
Attending the symposium 'Cluster Randomisation', Rotterdam, the Netherlands	2012	0.2
Attending the symposium on behalf of the 2.5 year anniversary of the 'Sophia Birth Centre', Rotterdam, the Netherlands	2012	0.2
Workshop giver 'Urban Perinatal Health' to GP's, midwives, physicians and pharmacists (The Hague)	2013	1
Attending the Final symposium of 'Ready for a Child (in Dutch: Afsluitend symposium Klaar voor een Kind)', Rotterdam, the Netherlands	2013	0.2
Workshop giver: 'Collaboration in Antenatal Health care: Practical use of risk assessment instruments and care pathways' to midwives, gynaecologists and social workers (The Hague)	2014	1
Attending the Sophia Children's hospital Research days poster presentation	2014	0.2

Other: Organizer, contact person and chair of 10 working groups

Development and implementation of local care pathways for medical and non-medical risk factors in work groups together with midwives, gynaecologists and social workers in the participating HP4All municipalities	2011-2014	20

2. Teaching activities

Lecturing

Lecture on 'Perinatal Health' for Medical students: minor 'Circle of Life'	2012	1
Lectures on Perinatal Health, Risk Assessment, Care pathways, and Policy implications for Clinical Midwives Master's candidates (Rotterdam)	2012 & 2014	2
Lecture on 'Risk Assessment and Care pathways' for community midwives Master's candidates (Amsterdam)	2012	1
Lecture on 'Ethnic origin, social disadvantage and poverty: antenatal risk assessment' for NIHES Master's candidates; course 'Urban Perinatal Health and Health care' (Rotterdam)	2012	1

Tutoring

Tutoring midwives, research nurses, and gynaecologist in the practical use of a new antenatal risk assessment instrument (R4U score card) in 14 municipalities in the Netherlands	2012-2014	7

Supervising Master's theses

Medical student Annemiek Leeman, title 'Assessment and Care for Non-Medical Risk Factors in Current Antenatal Healthcare', Erasmus Medical Center	2013	2
Medical student Mijke Hofhuis, title 'Process evaluation of the implementation of scorecard-based antenatal risk selection, care pathways, and interdisciplinary consultation', Erasmus Medical Center	2013	2
Medical student Sehrash Mahmood, title 'Process evaluation of the implementation of scorecard-based antenatal risk selection, care pathways, and interdisciplinary consultation', Erasmus Medical Center	2014	2
Medical student Varsha Jehrap, title 'Non-medical risk factors and risk accumulation in relation to perinatal outcomes', Erasmus Medical Center	2014	2

ABOUT THE AUTHOR

Amber Vos was born on 9th of April 1986 in Deventer, and she grew up in Epse and Schijndel. After graduation of pre-university education (Atheneum, Elde College, Schijndel) in 2004, she attained a bachelor degree in Nutrition and Health at the Wageningen University in 2007. In September 2007, she was accepted into the Selective Utrecht Medical Master (SUMMA) program at the University of Utrecht, where she attained her medical and clinical investigator's degree in September 2011. During her studies, her early interest in Obstetrics and Gynaecology brought her to do a clinical internship in the Kalafong hospital in Pretoria, South Africa. She also got involved in research at the department of Obstetrics and Gynaecology, division of Obstetrics and Prenatal Medicine, where her interest was triggered for urban perinatal health inequalities and social obstetrics.

In 2011, the Dutch Ministry of Health, Welfare and Sports commissioned an intervention program to reduce inequalities in perinatal mortality rates within the Netherlands. This resulted in the Healthy Pregnancy 4 All study. Amber was dedicated to the design, implementation and evaluation of the Risk Assessment sub-study between September 2011 and July 2014 in the 14 participating municipalities. Her PhD thesis was supervised by prof. dr. E.A.P. Steegers (promotor), prof. dr. G.J. Bonsel (promotor), and dr. S. Denktaş (co-promotor). In September 2014, she started working as a ANIOS in Obstetrics and Gynaecology at the Diakonessenhuis in Utrecht (dr. N.W.E. Schuitemaker). As of 1 January 2016 she will start with much enthusiasm as a resident in Obstetrics and Gynaecology (AIOS) at the Onze Lieve Vrouwe Gasthuis in Amsterdam (dr. E.M. Kaaijk) and the VU University Medical Center (prof. dr. J.I.P. de Vries).

Amber Vos is married to Patrick Meulstee and lives in Utrecht.

DANKWOORD

Als geneeskunde student raakte ik geïnspireerd door een voordracht over perinatale gezondheidsverschillen in Rotterdam. Het leek mij de ultieme combinatie: verloskunde en Public Health. 'Maar waar vind je nóg zo'n project?' dacht ik toen nog. Niet wetende dat ik een half jaar later zou starten bij het Healthy Pregnancy 4 All project.

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Daarnaast wil ik graag mijn promotores - prof. dr. Eric A.P. Steegers & prof. dr. Gouke J. Bonsel - en copromotor – dr. Semiha Denktaş – in het bijzonder bedanken.
Professor Steegers, beste Eric, jij was degene die de sociale verloskunde nieuw leven heeft ingeblazen en ervoor gezorgd heeft dat ik toch bij het Erasmus MC bleef plakken. Door je rol als programmadirecteur en promotor hebben we vaak samen gesproken. Ondanks je drukke agenda was je altijd goed bereikbaar. Het was ook leuk om je van een andere kant te leren kennen door de feestelijke borrels en tijdens etentjes en sportwedstrijden op congressen.

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Lieve meiden uit Schijndel, lieve Roos, Evelien, Yvon en Lieke, ik vind het onbetaalbaar dat we nog steeds zo'n goede vriendinnen zijn. Wie had dat ooit gedacht bij de totstandkoming van RY(P)ELA in 1999. Ik hoop dat we onze gezellige etentjes, weekendjes en borrels nog héél lang gaan voortzetten.

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Lieve paranimfen, wat een eer dat jullie vandaag naast mij staan. Lieve Sabine, ik zal je altijd blijven herinneren aan jouw favoriete uitspraak 'wie is hier nou de snackbar'. Het geeft exact weer hoe wij ons vaak hebben gevoeld. Ik waardeer je enorme doorzet-

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Lieve Lou, zie je ons nog zitten bij de 'wok-to-go' in Eindhoven voor onze eerste wijncursus? Ik was ervan overtuigd dat ik alle tijd van de wereld zou hebben voor nieuwe hobby's met een 36-uurs contract. Memorabel. We zijn het promotie-avontuur samen begonnen, ik in Rotterdam en jij in Maastricht, en ik vind het een eer om het met jou af te mogen sluiten. Wijn bleek het centrale thema de afgelopen 4 jaar, in voor- en tegenspoed. En die vinologen opleiding, die gaat er komen voor ons!

Lieve papa en mama, bedankt voor jullie onvoorwaardelijke liefde, steun en vertrouwen. Mam, zonder jou was ik nooit geneeskunde gaan studeren, ik ben je hier eeuwig dankbaar voor. Bedankt dat je er altijd voor me bent en altijd in me blijft geloven.

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Lieve Patrick, mocht je nog een carrière-switch overwegen, kan dit altijd binnen de verloskunde. Jou is inmiddels alles wel bekend in dit wereldje. Dit betekent niets anders dat ik je enorm mag bedanken voor je luisterend oor en betrokkenheid. Een hoogtepuntje van mijn promotietijd was toch wel een bruiloft organiseren samen met jou. Dit was een ambitieuze, maar zeer welkome afwisseling in de laatste fase. Bedankt voor je relativeringsvermogen, nuchtere blik als 'buitenstaander' en onvoorwaardelijke steun in alle beslissingen die ik neem. Het was niet altijd gemakkelijk, maar je hebt mij enorm geholpen. Wij regelen het wel samen, ik ben erg gelukkig dat ik nu je vrouw ben.

ADDENDUM

R4U SCORE CARD

✂ Name		Study ID		G: P:	Date of Birth	
Name of practice	Zip Code		Date of booking visit		Due date	□ LMP □ US □ IVF

SOCIAL			action
Social situation	YES	NO	
Single mother			
Relationship problems > 3 months			
Experience of inadequate social support			
Domestic violence			
Previous referral to children's social services			
Work and income	YES	NO	
Unemployed (> 3 months)			
Standing labour			
Working hours > 32 and stressful			
Netto family income < 1000 euro			
Irredeemable Financial debts			
Partner unemployed			
Education	YES	NO	
Low education level (< 7 years) or illiterate			
Neighbourhood	YES	NO	
Housing problems			
Deprived neighbourhood*			
(*ZIP code classification present in script)			
ETHNICITY			
Ethnicity	YES	NO	
Surinamese - Hindo			
Surinamese - Creole			
Surinamese - Javanese			
Antillean / Aruban			
Cape Verdian			
Turkish			
Maroccan			
Non-Western other			
Language / communication	YES	NO	
Language barrier (limited Dutch or English)			
Exclusively communication by interpreter			
Mentally disabled			
REPRODUCTIVE FACTORS			
General	YES	NO	
Uninsured			
Family planning / age	YES	NO	
Unwanted pregnancy			
Unplanned, but wanted pregnancy			
Assisted reproduction (ICSI/IVF/IUI/oocyte donation)			
Teenage pregnancy (≤ 18 yeas)			
Advanced maternal age (≥ 40 jaar)			
Obstretical	YES	NO	
Start antenatal care 12 - 14 weeks			
Late start antenatal care > 14 weeks			
LIFESTYLE			
Intoxication	YES	NO	
Preconceptional smoking (past 6 months)			
Smoking during first trimester			
Smoking during second trimester			
Preconceptional alcohol use (past 6 months)			
Alcohol use during first trimester			
Alcohol use during second trimester			
Preconceptional illicit drug use (past 6 months)			
Illicit drug use during first trimester			
Illicit drug use during second trimester			
Nutrition	YES	NO	
Vegetarian, vegan or macrobiotic diet			
No daily vegetable intake			
No daily fruit intake			
Body weight	YES	NO	
BMI < 18			
BMI 30 - 35			
BMI > 35			

GENERAL HISTORY			action
Disorders	YES	NO	
Chronic maternal illness (as described in script)			
Annual consultation GP or physician			
Hemoglobinopathy			
Refuses blood transfusion (Jehovah's Witness)			
Medication	YES	NO	
Prescribed medication			
Over-the-counter drugs			
No preconceptional folic acid use			
Infectious diseases	YES	NO	
(Treated for) sexually transmitted disease last year			
Promiscuity			
At risk for Toxoplasmosis			
At risk for Rubella			
Psychiatry	YES	NO	
History of psychiatric admission / positive family history (1st degree)			
Current use of psychiatric medication			
Current psychiatric problems			
OBSTETRIC HISTORY			
History	YES	NO	
Nulliparous			
Recurrent miscarriage (2 or more)			
Interpregnancy interval < 6 months			
Preterm birth (< 37 weeks)			
Low Apgarscore < 7 after 5 minutes			
Small for gestational age (<p10)			
Previous child with major congenital anomalies			
Stillbirth (22 weeks - 7 days postpartum)			
Shoulder dystocia			
Instrumental delivery			
Caeserean section			
Gestational diabetes			
Manual placental removal / postpartum haemorrhage			
Placental abruption			
(Pre)eclampsia or HELLP syndrome			
Family	YES	NO	
Major congenital anomaly in first degree relative			
Other (as described obstetric indication list)			
Result booking bloods	POS	NEG	
Irregular antibodies			
Hepatitis B			
HIV			
Lues			

Preconception consult

□ Yes midwife date (mm/yy): □ Yes GP date (mm/yy): □ No

Plus factor

Result

Domain	Score
Social	
Ethnicity	
Care	
Life style	
General history	
Obstetrical history	
Lab results booking bloods	
CUMULATIVE score	

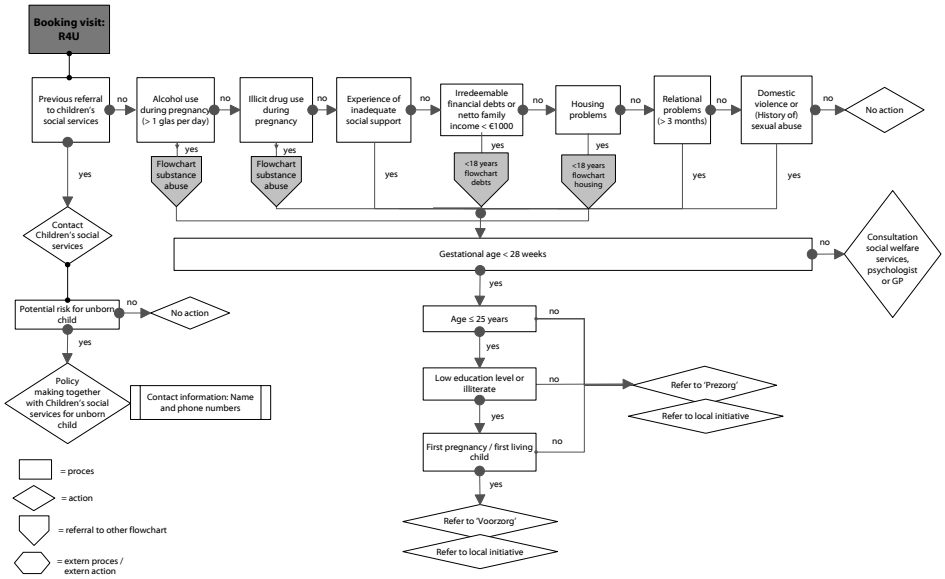
Time start consult (hh:mm)	
Time end consult (hh:mm)	

Partner present	YES	NO	NA

Additional notes

Care pathway example

Domain social and lifestyle - Care pathway 'psychosocial'



Short description care pathway 'Psychosocial'

Background

Construction of this care pathway is mainly based on the programs 'VoorZorg' and 'Prezorg'. Unfortunately, these initiatives were not enrolled in every municipality of the Netherlands. Therefore, the proposed care pathway is a typical example of blueprint. The definitive version will depend on local organizations and initiatives which are offered in a particular municipality.

For pregnant women younger than the age of 18 that are not eligible for these two programs, we refer to the flowcharts regarding teenage pregnancy (described further on in this document). If a health care professional has a strong suspicion for substance abuse (alcohol or drugs) and a pregnant woman is again not eligible for 'VoorZorg' or 'Prezorg', we refer to the flowchart 'substance abuse in pregnancy'.

The program 'VoorZorg' is based on the American 'Nurse Family Partnership' program. Nulliparous women younger than 25 years and low educated are eligible for this program. The main goals are primary prevention of child abuse, improving mother health during pregnancy (i.e. cigarette smoking), improving child's health and development by helping parents to provide more competent care and improving mother's own personal development. The program provides approximately 10 home visits during pregnancy conducted by trained nurses. The visits are more frequent during the first month of the intervention, which will start from on the 16th week of gestation, and the six weeks postpartum. The program finishes two years after child birth[1-3].

Prezorg is a less intensive program for those women not eligible for 'VoorZorg' or in case the program is expected to be too intensive. The main purpose of Prezorg is to inform and prepare future parents on parenthood to reduce stressful events. Prezorg stops directly after child birth. After child birth, the family will be referred to a special program ('Stevig Ouderschap' (strong parenthood)) offered by the Center of Youth and Family in the Netherlands. These Youth and family centres are operating nationwide[4].

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4. 'Strong Parenthood' (Stevig ouderschap), www.stevigouderschap.nl, 14 december 2011