PRECONCEPTION CARE

FROM POLICY TO PRACTICE AND BACK

SABINE FRANCISCA VAN VOORST

Preconception care: from policy to practice and back
PhD thesis, Erasmus University Rotterdam, The Netherlands

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GENERAL INTRODUCTION

GENERAL INTRODUCTION

Preconception Care

Preconception care (PCC) is care for women or couples that contemplate pregnancy. It aims to promote health of the future child by reducing or eliminating risks for adverse pregnancy outcomes, prior to conception and in early pregnancy. Where risks cannot be reduced, PCC aims to inform prospective parents to enable them to make informed decisions about pregnancy.

The content of PCC encompasses a vast amount of risk factors associated with adverse perinatal health outcomes, which are important to address prior to conception to ascertain the most benefit. These risk factors can be categorized within 13 domains: health care promotion (e.g. unplanned pregnancy), immunization (e.g. inadequate protection against rubella), infection (e.g. sexually transmitted diseases or toxoplasmosis), chronical medical conditions (e.g. diabetes), psychiatric conditions (e.g. depression and anxiety disorders), maternal exposures (e.g. alcohol and tobacco), genetic risks (e.g. genetic carriership of hemoglobinopathies), nutrition (e.g. obesity), environmental exposures (e.g. solvents in paint), psychosocial stressors (e.g. domestic violence), reproductive history (e.g. obstetric history of premature birth (<37 weeks of gestation)) and risks within special groups (e.g. immigrant and refugee populations).[1]

The rationale for preconception care

Embryonic health is the basis for a healthy start in life, a healthy childhood and health in adulthood.[2-4] Preconception care is an essential addition to conventional perinatal health care for several reasons.

Firstly, conventional antenatal care does not provide the opportunity for primary prevention. It can only address risk factors when the foetus has already been exposed to risks for adverse pregnancy outcomes as the first consultation during antenatal care occurs at best between the 8th and 12th week of pregnancy. By then, key events in embryonic growth and development have already taken place. At about the 10th week of pregnancy approximately all organs and the placenta have been developed. Developmental rates during the first trimester are even the highest during ones' entire lifetime.[5] Not only are organs formed and does the embryo grow, foetal programming occurs, during which functions of cells are determined. These three events are crucial to the health of the foetus during pregnancy and its extra-uterine life. Addressing preconception risk factors during antenatal care is simply too late, as preconception risk factors may already have irreversibly affected embryonic health. These early exposures may give rise to the so-called 'Big 3' perinatal morbidities (small for gestational age (SGA), prematurity and congenital abnormalities), which precedes mortality in 82% of the cases.[6] It has been estimated that perinatal morbidity and/or mortality can be reduced substantially with preconception care.[7-10]

Secondly, PCC can promote health in later life. Perinatal mortality and morbidity are the first consequences of risk exposure in embryonic period. If preconception risk factors result in permanent alterations in the structure and function of organs, the result of the affected embryonic health is not only limited to perinatal mortality and morbidity, affected embryonic health can

contribute to higher risks for diseases in childhood and adulthood (e.g. risks for cardiovascular and metabolic disease).[11] PCC's potential to prevent early exposure to risks provides an opportunity for primary prevention of morbidity in later life.

Lastly, PCC can provide additional benefits for parental health. Becoming a parent can be seen as an extra screening moment for health risks and can be an ultimate motivator to change health behaviors. A well-known example is that many women say they will stop smoking if they are pregnant. Smoking cessation reduces a woman's' risk of developing restrictive lung disease, (lung) cancer and cardio metabolic diseases. In other words, utilizing the life event of parenthood can provide a momentum for health promotion.

Organization of PCC in the Netherlands

It has been acknowledged to be a true challenge to select the optimal delivery strategy for PCC.[12] In the Netherlands, the Health Council of the Netherlands has categorized preconception care into collective preconception care (e.g. national campaigns) and individual preconception care (e.g. consultations (risk assessment and consequent intervention during an individual consultation).[13] Individual preconception care is subcategorized into general PCC (individual consultations for women or couples with undefined risks) and specialized PCC (individual consultations for women or couple with defined risks for adverse pregnancy outcomes).

Individual consultations provide the opportunity for professional led broad risk assessment. Other forms often opportunistically address single risk factors when women present themselves with specific questions or seek specific information. These forms therefore rely on women's own risk perception, which is known to be low.[14] Given the advantages individual consultations, research in this thesis focusses on organization and implementation of preconception care in the form of individual consultations.

Point of departure for this thesis

The debate about the high perinatal mortality rate in the Netherlands as of 2004 ultimately resulted in the awareness of the need to innovate in the organization of perinatal health care and to emphasize preventive measures. Within this process, it was suggested that the nationwide introduction of individual PCC consultation for the general public should be implemented in primary care as of 2007.[13]

Although prerequisites were met for the delivery of general preconception care within primary care (e.g. guidelines and risk assessment tools), nationwide introduction of individual PCC for the general public was stalled. It was thought that more evidence was needed regarding whether PCC approaches would reach high-risk women and would be effective in terms of risk reduction or reduction of perinatal mortality.

In 2009 the Erasmus Medical Center initiated the Ready for a Baby Program or the 'Klaar voor een Kind' program as it is referred to in Dutch. In this program new collaborations were formed between the public health domain and caregivers from the curative health domain, to improve perinatal health in disadvantaged neighbourhoods. Interventions were designed to address

each step in the chain of perinatal health: from the preconception phase to early childhood. The experiences from this Rotterdam-based program provided the incentive to experiment with programme-based preconception care, new risk selection during pregnancy and accessing high-risk groups in other communities in the Netherlands nationally.[15] This incentive met the agenda of the Ministry of Health. In 2011 the Dutch Ministry of Health financed a national program to improve perinatal health in disadvantaged neighbourhoods. This resulted in the Healthy Pregnancy 4 All (HP4All) study. Given the insights in the importance of embryonic health and involvement of public health, this program was designed to improve perinatal health by intervening before and in early pregnancy. The program consisted of two interventions (1) programmatic preconception care within primary care and (2) broadened risk selection with the Rotterdam Reproductive Risk Reduction (R4U) instrument and multidisciplinary care pathways. Both interventions are evaluated iteratively.

This thesis is based on studies conducted within or parallel to the HP4All – Preconception care sub-study between (september 2011 – december 2014). This study formed the basis to reflect upon the organization and implementation of preconception care in the form of individual consultations, in this thesis.

AIMS OF THIS THESIS

The aims can be summarized as follows (see Figure 1):

- To evaluate the policy process and to review the evidence which led to selection of PCC as an intervention to reduce perinatal mortality (Part I - Agenda setting and intervention selection).
- To develop a programmatic PCC intervention strategy in high risk municipalities – Healthy Pregnancy 4 All (Part II – Designing an intervention strategy).
- To evaluate current practice and implementation of these strategies with involved stakeholders (Part III –Implementation and evaluation).

THESIS OUTLINE

Part I – Agenda setting and intervention selection

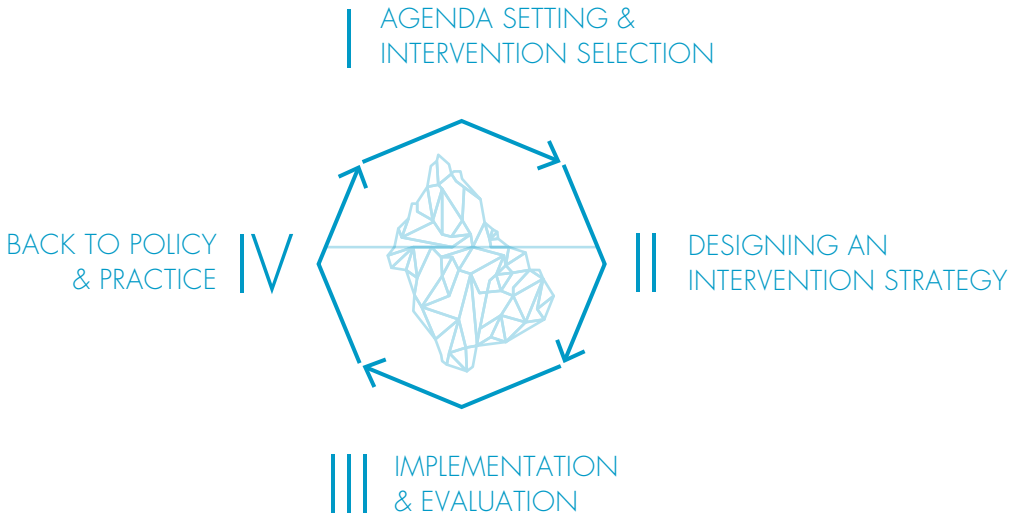
Chapter 2 addresses the question how the agenda setting emerged and led to the policy of the national government to intervene in the organization of perinatal healthcare to reduce perinatal mortality and morbidity. In order to answer this question a retrospective policy analysis was performed to investigate the process between 2004 and 2011.

Chapter 3 provides a summary of a National Summit on PCC in the Netherlands which took place in 2012. During this summit professionals were engaged to reflect upon the available evidence and knowledge gaps to frame future implementation of PCC.

Chapter 4 provides a thorough review of the evidence of lifestyle interventions. As lifestyle interventions are applicable to a large proportion of couples in the general population, their evidence is important to consider prior to the design of PCC programs.

FIGURE 1: Contents and central philosophy of this thesis.

Perinatal mortality is only the tip of the iceberg. Being born with perinatal morbidity can give rise to disease and illness in childhood and adulthood. Perinatal care should encompass preconception care (PCC) in order to promote perinatal health and a healthy society. Implementation of individual PCC consultations was advocated in response to the disadvantaged position of the Netherlands in perinatal health. With this thesis we look back upon the past decade and we draw lessons from research regarding the organization of individual PCC within the Dutch primary care and public health system. Content of this thesis is presented according to chronologic steps of a policy process depicted in this figure. Hence, the title of this thesis: 'Preconception care – from policy to practice and back'



Part II - Designing an intervention strategy

Chapter 5 and 6 reflect upon how an intervention approach was developed to address risks before and respectively during early pregnancy.

Part III – Implementation and evaluation

Within Part III the chapters reflect on what can be learned from the different stakeholders in general preconception care: primary caregivers (midwives and general practitioners), women contemplating pregnancy, municipal public health partners and peer health educators.

Chapter 7 focuses on what can be learned from the current preconception activities of primary caregivers. A cross-sectional inventory is performed regarding their activities, perceptions and prerequisites regarding delivery of (systematic) PCC in the future.

Chapter 8 looks into the preferences of the target population. A qualitative approach is used to assess preferences across the four essential components of the social marketing approach (Product, Place, Price and Promotion). Findings are important to tailor delivery of PCC consultations to the needs and preferences of women.

In **Chapter 9** an in depth study is presented regarding the implementation of peer health education in preconception care. Recommendations are made regarding future implementation strategies.

PART IV - Back to policy and practice

After addressing each question in the main section of this thesis, the general discussion (**Chapter 10**) elaborates on principle findings and strengths and weaknesses of the methodology regarding the organization of programmatic PCC in the future.

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PART I

AGENDA SETTING & INTERVENTION SELECTION

ANALYSIS OF POLICY TOWARDS IMPROVEMENT OF PERINATAL MORTALITY IN THE NETHERLANDS

(2004 - 2011)

S.F. van Voorst‡, A.A. Vos‡, E.A.P. Steegers, S. Denktaş
‡ Shared first authorship
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ABSTRACT

Objectives: 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.

Methods: The policy triangle framework for policy analysis by Walt and Gilson was applied.[11] 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.

Results: 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.

Conclusions: This study provides lessons which are applicable to health care professionals and policy makers in perinatal care or other multidisciplinary fields.

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 socioeconomic 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. Due to these numbers, the unique organization of perinatal care in the Netherlands was questioned in the open 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

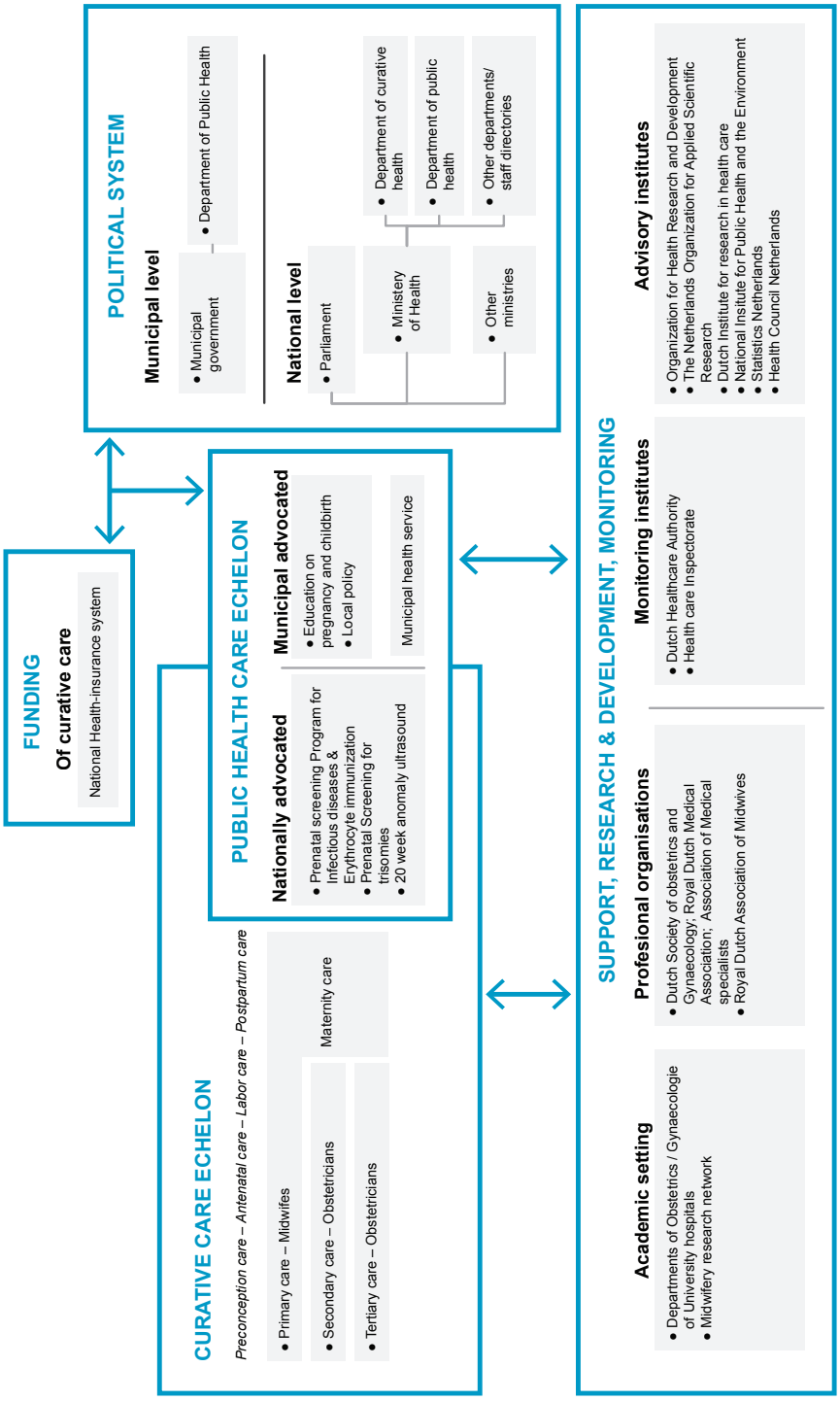
The policy process took place within a uniquely organized field: the Dutch perinatal health system. Figure 1 depicts the field that is involved in either formulating or implementing perinatal health policies.

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.

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 (80% of pregnancies start in the first tier of care). The fact that women typically start antenatal care with a

FIGURE 1: The health policy environment (adapted from Schafer et al. 2010 [26])



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 professional 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 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 setting 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 levels.

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 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 (initials removed). 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 was 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 (SVV and AV) 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.

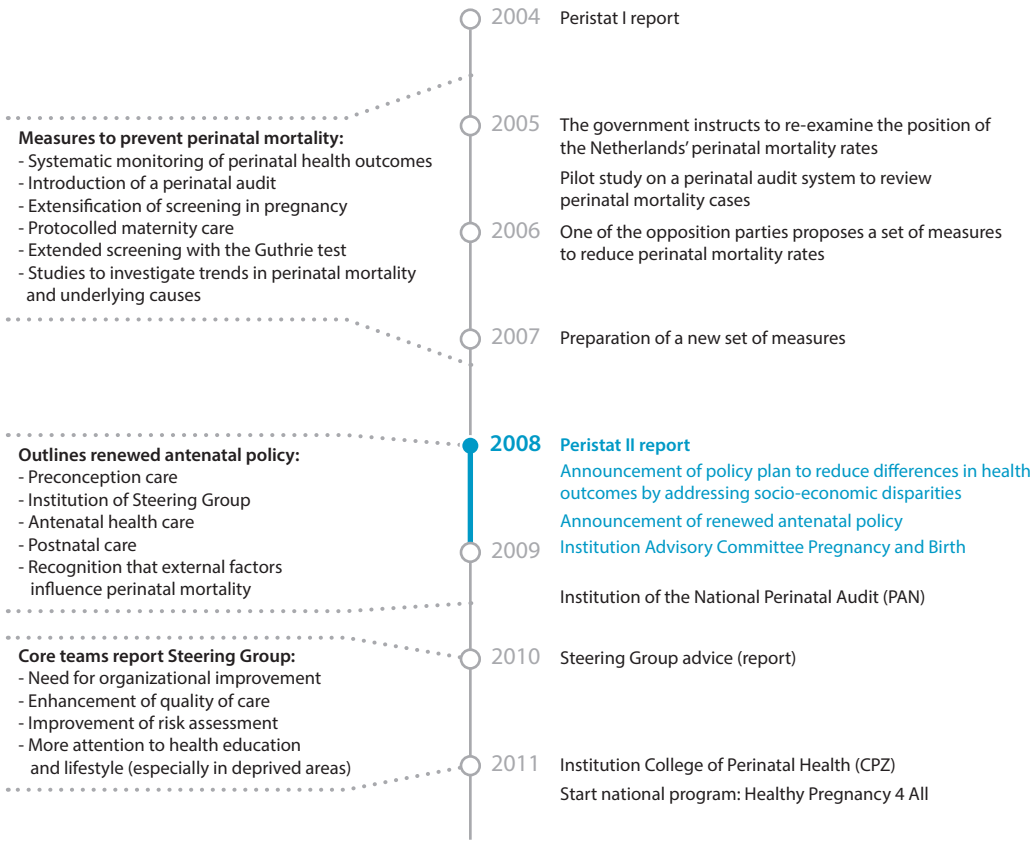
RESULTS

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 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 (individually or in pairs) varying from 30 – 90 minutes.

The identified content of governmental policy was organized in a chronologic time line (Figure 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 3.

FIGURE 2: Time line of governmental measures to improve perinatal outcomes in 2004-2011

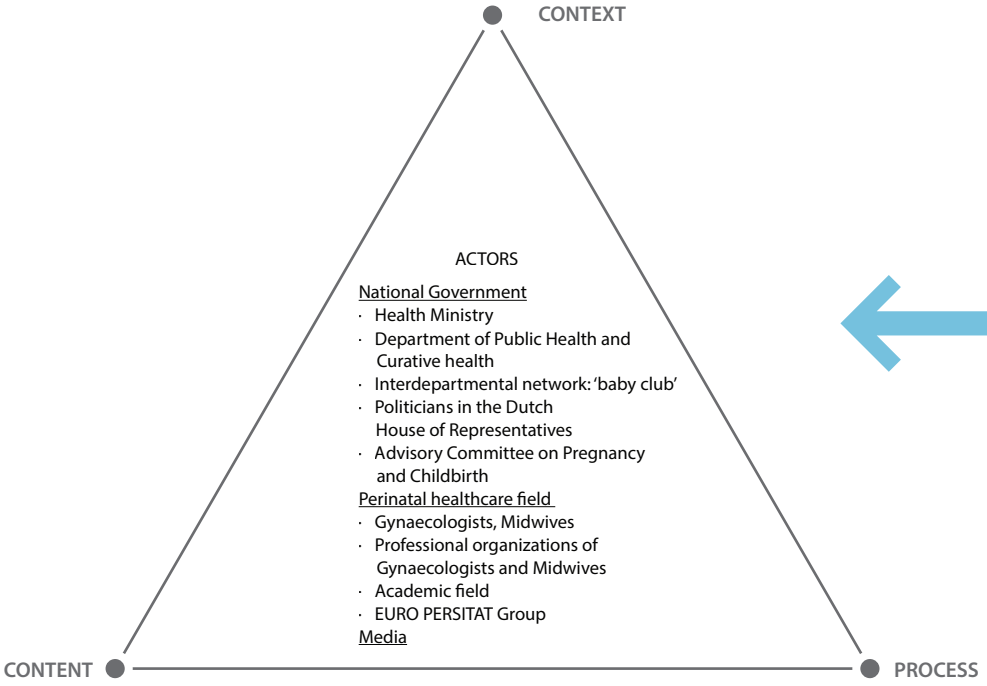


Policy process

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) 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 2010.

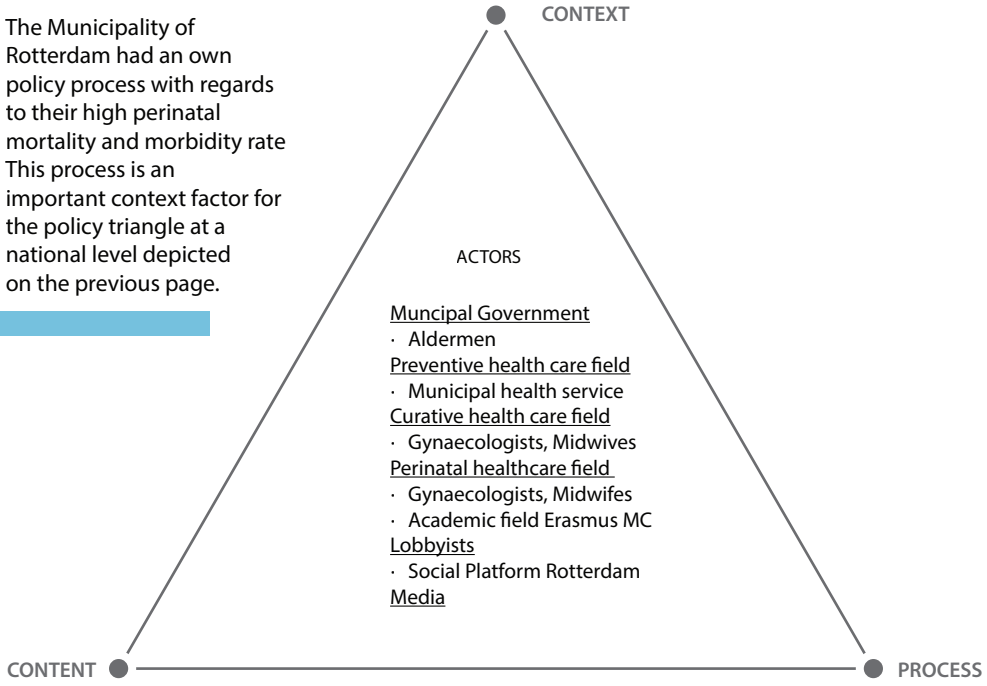
NATIONAL POLICY TRIANGLE



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.

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 depicted on the previous page.



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

FIGURE 3: Policy process: The policy triangle was used to summarize the policy process according to the policy triangle.

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 perinatal mortality became a 'key priority' at the Health Ministry. Parliamentary questions are questions asked by a member of parliament to the Minister in relation to parliamentary law and political decisions. These questions are answered during debates and by means of letters. Parliamentary questions are thus a way to get items on the political agenda and to initiate actions by departments.[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]

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

BOX 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 extra tariff).
4. Postnatal care: evaluation the current capability of maternity care, evaluation the implementation of extended neonatal screening.
5. External factors: reduction socio-economic related health differences

Ministry presented five main intervention themes (based on prior inquiries) in 2008 which are presented in Box 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 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 municipal policy triangle in Figure 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 Supplementary Box 1.

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 attempted 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 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 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.

CONFLICTS OF INTERESTS

The last two authors participated in the study as respondents. The research team has received funding from the Ministry of Health, Welfare and Sports in order to execute the Healthy Pregnancy 4 All study.

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SUPPLEMENTARY BOX 1: 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

SUPPLEMENTARY TABLE 1

This Table presents the results of the stakeholder analysis performed according to methods proposed by Varvaskovszky and co-authors.[17] This analysis was performed to assist the actual policy analysis in identifying key-informants and understanding their roles in the policy process. Characteristics of each of these stakeholders were identified based on preknowledge before the policy analysis and new insights as a result of triangulation of data from the document analysis and interviews. These characteristics are: (1) their interest in perinatal mortality, (2) their influence, (3) their position (supportive, opposed, and neutral) and (4) the impact of perinatal mortality on them.[27]

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


3

THE DUTCH NATIONAL SUMMIT ON PRECONCEPTION CARE:

A SUMMARY OF DEFINITIONS, EVIDENCE AND RECOMMENDATIONS

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ABSTRACT

Objectives: Preconception care is a primary preventive approach in which prepregnancy risk factors are addressed in order to prevent adverse pregnancy outcomes. Although benefits of preconception care are acknowledged, consensus on concepts of preconception care and approaches for implementation in the Netherlands are currently lacking. Due to the comprehensiveness and multidisciplinary nature of preconception care consensus could be a prerequisite to develop or implement approaches to deliver preconception care.

Methods: A literature-based consensus meeting was organized to achieve consensus about (I) the definition, (II) categories, (III) target groups, (IV) prepregnancy risk factors and interventions and (V) risk assessment instruments.

Discussion: Preconception care is only delivered in a small scale and consensus on the content and how the care should be delivered is not well documented. Consensus regarding the content and delivery of preconception care is necessary to upscale preconception care and to commit both curative and public health in their responsibility in preconception care.

Conclusions: This paper presents a summary of the reached consensus and the identified knowledge gaps during the meetings.

INTRODUCTION

Preconception care (PCC) is widely recognized as a way to optimize women's health through biomedical and behavioural change prior to conception, ultimately to improve pregnancy outcomes. In terms of prevention, PCC is primary prevention for the future baby and secondary prevention for prospective mothers. When these appropriate secondary and primary preventive measures are taken public health benefits are achievable by prevention and treatment of identified risk factors (e.g. smoking, alcohol abuse, obesity and infectious diseases) and improvement of perinatal health potentially leading to improvement of health later in life.

Despite recognition of the importance of PCC in the Netherlands within curative care and governmental policy makers,[1] PCC is still only delivered on a small scale and not in a uniform manner. Lack of consensus regarding the content and the delivery of the care seems to be an underlying cause. This consensus is important to provide caregivers with a foundation for further implementation of PCC. Consensus is also a necessary first step in creating of awareness among caregivers regarding their societal responsibilities in primary and secondary prevention. Therefore, a consensus meeting was organized to identify gaps and essential targets to contribute to policy thinking for implementation of PCC. Point of departure was a comprehensive literature study. This paper summarizes results of the meetings. These results can be used to create commitment and responsibility amongst curative care givers and public health policy makers to keep the debate going in the content of PCC.

METHODS

A comprehensive literature study was performed to provide a starting point to address five core subjects: 1) the definition of PCC, 2) categories of PCC, 3) relevant target groups and methods for outreach, 4) risk factors which should be taken up in PCC (an evidence update as of 2008) and effective interventions (evidence as of inception of databases), and 5) risk assessment instruments. Despite increasing evidence of paternal influence on pregnancy outcome and the crucial influence of men on their partners' health behaviours, this meeting – and therefore the literature study - firstly focussed on PCC for women.[2-4] This meeting does not have its focus specifically on lifestyle risk factors, however we would like to point out that we recently have published another systematic review regarding effectiveness of PCC interventions on lifestyle risk factors in the Preconception Phase.[5] The meeting, organised by the Erasmus MC in Rotterdam, consisted of two one day sessions (January 2012 and April 2012). Propositions for consensus – based on the literature - were presented as a starting point for the discussion. Participants included:

- Care givers (midwives, general practitioners, gynaecologists, clinical geneticists, an occupational health physician);
- Representatives from professional organizations of the care givers (Regional Organisational Support for Primary health care [ROS]);
- Governmental representatives (the Ministry of Health Welfare and Sport, the Commission for Perinatal Health [College Perinatale Zorg], a Municipal Health Service [GGD Rotterdam-Rijnmond]);

- Health insurance companies and the Health Care Insurance Board;
- Funders of scientific research (the Netherlands Organisation for Health Research and Development [Zon MW]);
- Providers of health care expertise (the Health Council of the Netherlands [Gezondheidsraad], the National Institute for Public Health and the Environment [RIVM], the Dutch National Genetic Resource and Information Center [Erfocentrum], the Dutch Foundation of Preconception Care, Organisation for Applied Scientific Research [TNO], the Dutch birth registry (Netherlands Perinatal Registry [PRN]);
- Patient-consumer federation (the Dutch Genetic Alliance of Parent and Patient organizations [VSOP]);
- Other relevant disciplines (department of medical ethics, epidemiology).
- Sessions were chaired by independent experts on PCC. Achieved consensus, lack of consensus and knowledge gaps were recorded. These records were verified by participants after each session.

EXPERTS DISCUSSION

Results will be presented per core subject in a fixed format: an introduction, the proposal, achieved consensus (in case of agreement), lack of consensus (if any) and identified knowledge gaps resulting in recommendations for future research.

I. DEFINITION OF PCC

Introduction

Various definitions for PCC have been formulated. The definition is an important take off point in the debate around the content of PCC. In 1992 the following definition was included in PubMed's Mesh database: "An organized and comprehensive program of health care that identifies and reduces a woman's reproductive risks before conception through risk assessment, health promotion, and interventions.[6] In 2005 the Centers for Disease Control and Prevention (CDC) and the March of Dimes recognized the need to state that PCC is a continuum of care throughout the various stages of the reproductive life of women. This was incorporated in their definition: "A set of interventions that aim to identify and modify biomedical, behavioural, and social risks to a woman's health or pregnancy outcome through prevention and management, emphasizing those factors that must be acted on before conception or early in pregnancy to have maximal impact."[7] In 2007 the Health Council of the Netherlands presented a definition in line with the CDC: "Preconception care is the entire range of measures designed to promote the health of the expectant mother and her child, which, in order to be effective, must preferably be adopted prior to conception." [1]

Proposition

To adapt the definition of the CDC and the March of Dimes, due to the different elements of risk factors, defined outcomes and the defined timeframe.

Consensus

- There was agreement with the proposition.
- To add that: PCC should be regarded as a programme and that PCC includes psychosocial risks, non-medical risks (e.g. financial problems and domestic violence) counselling and informed decision making.
- To replace 'woman's health' with 'parental health'.
- To replace 'pregnancy outcome' with 'the health of their future child', prolonging the timeframe targeted by PCC.
- A note should be added to the definition about the potential of PCC to reduce perinatal mortality and morbidity.
- The consensus meeting resulted in the following definition: "A set of interventions and/or programmes that aims to identify and enable informed decision-making to modify biomedical, behavioural, and (psycho)social risks to parental health and the health of their future child, through counselling, prevention and management, emphasizing those factors that must be acted on before conception and in early pregnancy, to have maximal impact and/or choice.
- Preconception care may be a good opportunity to reduce perinatal mortality and morbidity.

Knowledge gaps/recommended future research

- Although major steps are to be made in the implementation of PCC for women first, it is desirable to achieve consensus on PCC for men, in the future.
- Perinatal mortality and morbidity is a more important outcome for policy makers. Therefore trials should also address pregnancy outcomes (besides behavioural change) as an outcome measure of the effectiveness of PCC (see Figure I).

II. CATEGORIES OF PCC

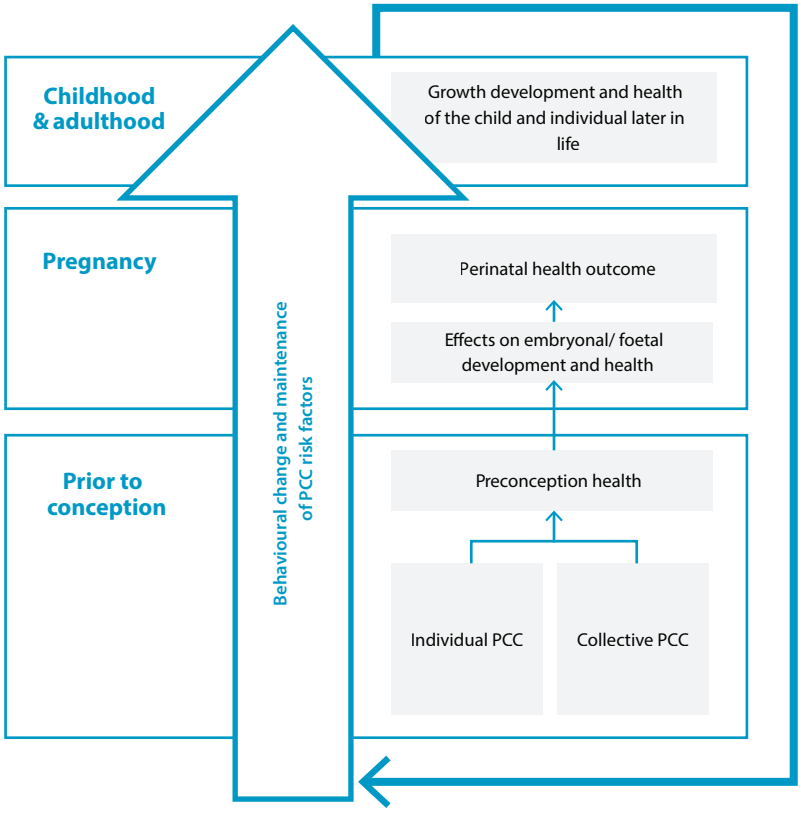
Introduction

PCC is meant to improve the health of mother and child in various ways. The Dutch Health Council provides the following categorization of methods for PCC delivery:

- Collective measures are aimed at the general population to improve preconception health. An example is campaigns on the use of folic acid.
- General individual PCC is detection and management or intervention on risk factors, in couples planning a pregnancy within the general population. The general nature resides from the fact that these couples mostly do not have a known or predefined preconception risk(profile).
- Specialist individual PCC is provided for a) couples with a known or predefined risk for an adverse pregnancy outcome (e.g. Diabetes) or b) couples who are referred from general individual PCC after risk assessment (e.g. when diabetes is detected).
- Recognition of the different forms of PCC is important in the implementation of PCC. Categorization provides a basis to identify professionals with core responsibilities in a category, to tailor a feasible recruitment approach and applicable target group.

FIGURE 1: Outcomes of PCC

Preconception risk factors potentially and behavioural change may influence foeto-maternal health throughout the periconception period, pregnancy as well as during childhood and adulthood. Health during reproductive age will subsequently affect the outcomes of subsequent pregnancies and the health of future generations.



Proposition

- Not to change the categorization of PCC.
- Addition of care pathways to the elements of PCC. They can facilitate implementation of individual PCC in a uniform and locally tailored manner. Care pathways are a means of achieving multidisciplinary agreements on organization and efficient shared care. They should be evidence based and in line with local guidelines and available care facilities.[8]

Consensus

- Care pathways were recognized to be valuable, specifically where they address socio-medical risk factors. Professional organizations should have a leading role in the development in care pathways, specifically to achieve multidisciplinary agreements.

Disagreement

- There is unclarity regarding which health care professional has a core responsibility in which category. The line between general individual PCC and specialized PCC is not very evident. There are caregivers that could address both general and specialized individual PCC. The difficulty lays in the education and/experience in addressing specialistic risk factors. As PCC has a very broad content; it seems merely impossible for one caregiver to address all risk factors.

Knowledge gaps/recommended future research

- There is a need to define the role of different professions within the Dutch Healthcare system within different categories of PCC. The collaboration between public and curative health, and delegation of tasks (e.g. to qualified physician assistants or nurses) should be explored further. This task can be fulfilled by the Commission for Perinatal Health (CPZ) which has now appointed a committee that will develop a consensus based multidisciplinary guideline. This guideline will explicate specific roles of health care workers.

III. REACHING TARGET GROUPS

Introduction

So far, no (inter)national consensus exists as to whom PCC should be offered. The target population can be divided into four major groups: (1) the general population, (2) all men and women of reproductive age (3) men and women aiming to conceive and (4) men and women with predefined high risk groups (e.g. due to previous pregnancy complications, genetic risks, chronic illness or medication use).

Reaching women and men before the onset of pregnancy is crucial for effective PCC. Women neither actively seek PCC consultation, nor do they accept the offer to attend a consultation.[9] In every day practice clinicians do not often initiate a PCC consultation, nor do they recommend it to women.[10,11] The curative setting and the public health setting in contact with women of childbearing age should be aware of the importance of preconception health promotion. However there is a lack of awareness or perhaps sense of responsibility under these professionals about their responsibility and potential role in preconception health promotion.

Research on why the outreach of PCC is limited and how this short-coming can be addressed, is scarce. Several studies have indicated that an important problem with reaching parents to be on time is that many women do not plan pregnancies.[12,13] Another challenge is adapting the PCC approach to reach specific target groups. The importance is recognized by trials evaluating outreaches of PCC programs.[14-16] Above all, research on effective (tailored) methods to reach target groups for PCC are lacking.[17,18]

Proposition

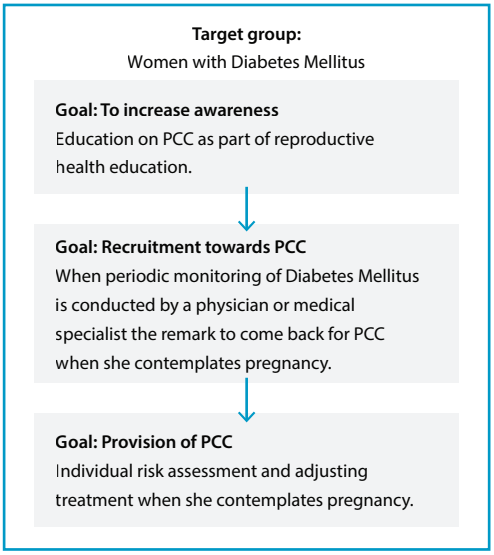
- Increased awareness and specification of their role in executing PCC should be contemplated by the following care givers/ organizations: governmental organisations, care providers (midwives, general practitioners, pediatricians, gynecologists and medical specialists in general), youth and family centers, peer educators, social welfare services, and schools.

Consensus

- There was consensus on the fact that preconception health promotion needs broad support from actors with different relations to the target group. The following actors in general were identified additional to the professionals above, either as a direct link to the target population or as a medium: municipal health service, paramedics (e.g. dieticians and dentists), pharmacists, occupational health physicians, all health promotional institutes in general that address people of childbearing age, institutes focusing on migrants, the social network around future parents (e.g. aunts, grandmothers), policy makers and means of communication (e.g. internet). The need for involvement and collaboration of curative health professionals and public health professionals is therefore acknowledged.
- Tailored approaches should be applied by actors for the different target groups of PCC. Specifically teenagers are a group of interest because early sensitisation could promote timely behavioural change or utilisation of PCC services later in life.

FIGURE 2: Target approach to reach women with Diabetes Mellitus

This figure shows a potential approach to improve preconception health and to target women with Diabetes Mellitus to utilize Preconception Care when they contemplate pregnancy later in life.



Knowledge gaps/recommended future research

- The consensus meeting concentrated on identifying actors to enlarge awareness and outreach of preconception health promotion amongst target groups. Feasible approaches should be developed per actor; per target group.
- There is a gap in practice as to how the above mentioned actors optimally could have a role. A potential schematic approach to reach women with Diabetes Mellitus is shown in Figure. 2.

IV. RISK FACTORS AND INTERVENTIONS AS PART OF PCC

Introduction

For the delivery of PCC there has to be consensus on the content. This should be based on known risk factors for adverse pregnancy outcomes and effective interventions to address them in the preconception period. A risk factor- and intervention review was conducted to form a basis for the discussions.

Risk factors

A review by Jack et al., was conducted in 2008 to provide evidence for risk factors to be taken up in PCC.[19] To update this review for the consensus meeting a search was conducted in PubMed, as of 2008. Selection was performed according to predefined criteria: the study assesses risk factor(s) which are present in the preconception period and the study reports an association with an adverse pregnancy outcome. Three reviewers independently assessed eligibility and performed data extraction. The search resulted in 2214 articles of which 178 articles were included.

Interventions

A systematic search was conducted to assess efficacy of available PCC interventions in PubMed, Embase and Web of Science from 1900 to January 2012. Selection was performed according to predefined criteria: the study assesses interventions, addressed in the preconception phase for an adverse pregnancy outcome. Two reviewers independently assessed eligibility of 678 articles and performed data extraction on 104 included articles.

Table 1 gives an update of the quality of the evidence for the risk factors per domain with interventions where available. Strength of evidence was assessed according to the Canadian Task Force on Preventive Health Care.[20]

Proposition

- Identified risk factors and available interventions with a level of evidence of I-A to II-3 should be included as part of evidence based PCC.
- Identified risk factors with a level of evidence of I-A to II-3, but without evidence based interventions, should be prioritized for development of interventions.

TABLE 1: Quality of the evidence for preconception risk factors and interventions to improve maternal and/or infant health and consensus on uptake in PCC

Risk domain	Risk factors	Outcome	Intervention	Consensus
Health care promotion	Interpregnancy intervals (<6 months and >60 months)	II-2		+
	Lack of physical exercise	II-2	I-a	+
	Unplanned pregnancy	III		+
Immunizations	Human Papilloma Virus (HPV)	II-2		-
	MMR	II-3	II-2	+
	Hepatitis B	III		-
	Varicella	III		+
	Influenza	III		-
	DTP	III		+
Infection	Syphilis	I-a		+
	HIV	I-b		+
	Periodontal disease	I-b		+
	Bacterial vaginosis	I-b		+
	Asymptomatic bacteriuria	II-1	I-a	+
	Herpes Simplex Virus (HSV)	II-1		+
	Chlamydia	II-2		+
	Toxoplasmosis	II-2		+
	GBS	II-2		+
	Tuberculosis	II-2		+
	Hepatitis C	III		+
	Cytomegalovirus (CMV)	III		+
	Parvovirus	III		+
	Malaria	III		+
	Gonorrhoea	III		+
Chronic medical conditions	Diabetes mellitus type 1 or 2	I-a	I-a	+
	Thyroid disease	II-1		+
	Phenylketonuria (PKU)	II-1		+
	Seizure disorders	II-2		+
	Hypertension	II-2		+
	Systemic Lupus Erytromatosus (SLE)	II-2		+
	Chronic renal disease	II-2		+
	Cardiovascular disease	II-2/II-3		+
	Thrombophilia	II-3		+
	Asthma	II-3		+
	Rheumatoid arthritis (RA)	III		+
Psychiatric conditions	Depression and anxiety disorders	II-2		+
	Bipolar disorder	II-2		+
	Schizophrenia	II-2		+
Maternal exposure	Alcohol	I-a	I-a	+
	Tobacco	I-a		+
	Illicit substances	II-2		+

TABLE 1 continued

Risk domain	Risk factors	Outcome	Intervention	Consensus
Genetic risks	Genetic disorder(s) or carrier ship in one of the prospective parents	II-2		+
	Ethnicity based risks	II-3		+
	Positive family history	II-3		+
	Recurrent miscarriages	III	II-2	
	Known genetic conditions	II-3		
Nutrition	Inadequate folate intake	I-a	I-a	+
	BMI > 30 kg/m2	I-b	I-a	+
	BMI < 18 kg/m2	II-2		+
	Insufficient vitamin B12	II-1		+
	Inadequate dietary intake	II-2	I-a	+
	Western Dietary pattern	II-2		+
	Excessive vitamin E intake	II-2		+
	Insufficient Vitamin D	II-3		+
	Insufficient or excessive vitamin A intake	III		+
	Eating disorders	III		+
Environmental exposures	Occupational exposure (e.g. chemicals, solvents)	II-2		+
	Household exposures (e.g. PCB's, solvents, metals (lead))	III		+
Psychosocial stressors	Inadequate financial resources	II-2		+
	Interpersonal violence	II-2		+
Medication	Prescribed medication	II-1		+
	Herbs / herbal products / weight loss products	II-1		+
	Over the counter drugs	III		+
Reproductive history	Prior preterm birth	I-a		+
	Prior miscarriage	I-a		+
	Prior fetal growth restriction	II-2		+
	Prior caesarean delivery	II-2		+
	Prior stillbirth	II-2		+
	Uterine anomalies	II-3		+
Special groups	Immigrant and refugee populations	II-2		
	Women who survived cancer	II-2		
	Women with disabilities	III		

*Quality of evidence

I-a: at least 1 properly conducted randomized controlled trial BEFORE pregnancy

I-b: at least 1 properly conducted randomized controlled trial not necessarily before pregnancy

II-1: well-designed controlled trials without randomization

II-2: cohort or case-control studies

II-3: multiple time series with or without intervention or dramatic results in uncontrolled experiments

III: opinions: clinical experience, descriptive statistics, case reports or reports of experts committees

Consensus

- Table 1 shows the consensus achieved per risk factor, regarding the uptake as part of PCC.
- There were remarks considering the uptake of the following risk factors in PCC:
  - Group B streptococcus (GBS): Due to the recurrence of GBS colonisation after treatment, it is not considered beneficial to screen all women preconceptionally for GBS. However, PCC can identify women with previous GBS infection or neonatal complications due to GBS colonization. For these women a management plan for their pregnancy and delivery can be formulated.
  - HPV immunization: Although HPV carrier status is common, fetomaternal transmission rates and consequent neonatal outcomes are infrequent; there was consensus not to incorporate HPV carrier detection and immunization in PCC.
  - Hepatitis B immunization: Where Hepatitis B infection is present in one of the future parents, routine clinical care was thought to be sufficient together with the local policy in pregnancy regarding vaccination of the neonate after birth.
- Although the review did not point out the following risk factors; the experts noted the following risk factors to be taken up as part of PCC:
  - Chronic medical conditions: such as inflammatory bowel disease (Colitis, Crohn's disease), women with organ transplants, previous thrombotic event or embolism.
  - Genetic risks: consanguinity.
  - Exposures: Occupational exposure to working shifts and stress, sauna, diving and passive smoking as part of household exposure.
  - Psychosocial stressors: adverse childhood events.
  - Reproductive history: subfertility, prior pregnancy complications, prior congenital anomalies, prior neonatal complications and advanced maternal age (defined as older than 36 years).
  - The discussion about risks that should be addressed by the PCC provider set aside, prospective parents may have questions (e.g. with regards to fertility and sexual health). PCC providers should assess needs and inform or refer where necessary.
- The current proposal focuses on individual risk factors. The participants agreed that the effect of risk accumulation should be recognized. Risk accumulation is the phenomenon that combinations of risk factors augment the total risk of the individual to a larger extent than the sum of the individual risks.[21]

Knowledge gaps/recommended future research

- More research is needed regarding the Population Attributable Risks (PAR) of preconception risk factors and combined effects of risk factors.
- A remark can be made by the risk factor 'unplanned pregnancy.' It is unclear whether this considers unplanned pregnancies that are welcome or not welcome. This might be an important factor affecting pregnancy outcome as risky behaviour is more likely to happen

when a pregnancy is unwanted. More insight is necessary in the contributory risk component in unplanned pregnancy: unwantedness versus the unplanned nature.

- As the possible content of PCC is growing, there is a need for prioritization in the interventions for a woman's specific risk profile. There is no method to identify the best core of action and a fixed format is not feasible due to inter-individual differences. PCC providers are subjected to 'common sense' in the prioritization of risk factors. This should be based on the impact of risk factors and the feasibility of interventions.

V. RISK ASSESSMENT INSTRUMENTS

Introduction

Assessing preconception risk factors within all domains is time consuming and to stimulate a uniform risk assessment; risk assessment instruments are necessary.

Available risk assessment instruments were identified:

- ZwangerWijzer is the most widely used instrument in the Netherlands.[22,23] It is a validated tool based on the Preconception Health Assessment form developed by Cefalo and Moos.[24] It is self-administered online questionnaire that assesses and informs about medical-, genetic-, environmental- , occupational-, nutritional-, and lifestyle risk factors. The identified risks can be emailed to a caregiver – to provide an agenda for individual PCC. A supportive program provides the caregiver with a preconception patient record with protocols to address each identified risk factor.[25]
- Slimmer Zwanger is a personal screening and coaching program provided by mobile phone app.[26] The application assesses nutrition and lifestyle behaviours by a self-administered questionnaire. The application then provides motivational text messages and e-mail messages to change risky behaviours. Effectiveness is currently being assessed.

Proposition

- To include generic risk assessment instruments suitable for the local setting in PCC.

Consensus

- Instruments with a wide range of detecting risk factors to limit the amount of questionnaires are preferable.
- Risk assessment instruments can lead to awareness and therefore can function as an intervention themselves.

Knowledge gaps/recommended future research

- Appropriate evidence-based standardised risk assessment instruments remain to be developed or existing tools should be optimized (e.g. multilingual) and validated.

SUMMARY

In conclusion, consensus was achieved on the majority of the key elements of PCC, including the definition, the categorisation, institutes and health care professionals which should play a role in reaching target groups, the content and delivery and the need for development of evidence-based risk assessment instruments. These elements give further insight in what should be resolved in order to enlarge the scale at which PCC is delivered. Furthermore, these can be used as starting points for policy makers and other relevant actors that take responsibility to develop implementation strategies for PCC.

In order to develop a tailored PCC program, the needs of specific populations should be known and resources should be in line with setting specific characteristics.

This consensus paper is based on current evidence. Biannual update on the evidence of preconception risk factors and management is recommended to keep the debate going. This debate is necessary to hold the commitment amongst the broad scope of professionals in the curative setting and the public health care setting to collaborate regarding PCC.

CONFLICTS OF INTEREST

The last two authors participated in the study as respondents. The research team has received funding from the Ministry of Health, Welfare and Sports in order to execute the Healthy Pregnancy 4 All study.

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EVIDENCE-BASED PRECONCEPTIONAL LIFESTYLE INTERVENTIONS

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ABSTRACT

Objectives: Although the evidence for the associations between preconceptional risk factors and adverse pregnancy outcomes is extensive, the effectiveness of preconceptional interventions to reduce risk factors and to improve pregnancy outcomes remains partly unclear. The objective of this review is to summarize the available effectiveness of lifestyle interventions prior to pregnancy for women in terms of behavior change and pregnancy outcome.

Methods: A predefined search strategy was applied in electronic databases, and citation tracking was performed. Study selection was performed by 2 independent reviewers according to predefined criteria for eligibility: The intervention was performed preconceptionally on women regarding alcohol use, smoking, weight, diet/nutrition, physical activity, and folic acid status (fortification and supplementation) to achieve behavior change and/or improve pregnancy outcome. Quality and strength of evidence were assessed by 2 independent reviewers.

Results: A total of 4,604 potentially relevant records were identified, of which 44 records met the inclusion criteria.

Conclusion: Overall, there is a relatively short list of core interventions for which there is substantial evidence of effectiveness when applied in the preconception period.

INTRODUCTION

Worldwide efforts are made to reduce adverse pregnancy outcomes. As many women do not realize they are pregnant until the fifth week of pregnancy—when essential fetal processes have already commenced—the first antenatal visit is relatively late to address perinatal risk factors[1]. As these risk factors can mostly be identified, managed, or treated when they are detected preconceptionally to prevent or limit fetal exposure, preconception care (PCC) has been identified as a promising form of care to improve pregnancy outcomes. [2, 3]

PCC is defined as "a set of interventions that aim to identify and modify biomedical, behavioral, and social risks to a woman's health or pregnancy outcome through prevention and management, emphasizing those factors that must be acted on before conception or early in pregnancy to have maximal impact".[4]

Effective PCC interventions could be an opportunity to improve pregnancy outcomes. Although the amount of evidence for preconceptional risk factors associated with adverse pregnancy outcomes is growing, PCC is still based largely on the assumption that elimination of the risk factor will reduce the chances of adverse perinatal outcomes rather than on evidence for the effectiveness of the preconceptional interventions itself. Risk factors in PCC are very diverse, reflecting the diverse pathophysiology in the periconceptional period. Risk factors, from both parents, can be of genetic, environmental, or behavioral origin. Therefore, a broad approach in PCC is necessary to optimize perinatal health. In many countries, preconceptional health assessment focuses on women with predefined risk factors, such as diabetes. PCC is offered much less frequently to women in the general population without previously identified risk factors. Assessment of the general lifestyle and behavioral risks such as alcohol consumption, smoking, the use of drugs, and nutritional diet and folic acid supplementation seems to be offered mostly to these women with predefined risk factors. More evidence is needed regarding the effectiveness of interventions aimed at general lifestyle risk factors that are applicable to a large proportion of the couples aiming to conceive. This evidence would not only help women with predefined risks but also be a boost for implementation of PCC for the general population.

Furthermore, evidence for preconceptional health interventions is necessary to embed PCC as an available health service—for professionals and for couples wishing to conceive— among the general population. Also, concrete evidence is necessary to motivate policy makers, insurers, and health-care providers themselves. Although it is challenging to reach target groups for PCC, PCC is regarded to be a very welcome health service by couples wishing to conceive[5]. In order to address these general risk factors in PCC, evidence-based preconceptional interventions to reduce or eliminate these general risk factors are needed. Besides a Cochrane review in 2009[6] restricted to randomized controlled trials, no systematic review comprising observational studies has been conducted to address preconceptional lifestyle interventions for women. A systematic review including observational studies is deemed valuable as the majority and most prominent studies are observational because of the behavior changes that are included in PCC.

The objective of this review is to provide an up-to-date overview of the effectiveness of predefined lifestyle interventions on behavior change and improved pregnancy outcomes among preconceptional women in the general population.

MATERIALS AND METHODS

Search strategy

Studies were identified initially with an electronic search in the databases Medline, Embase, and Web of Science from inception to March 2012, restricted to the following languages (English, Dutch, German, French, and Spanish) and to humans. The electronic search encompassed keywords referring to the preconceptional time period, health-care promotion or intervention, the mother/ father or couple, and predefined risk factors. The detailed search is available in the Appendix. Furthermore, citations of identified reviews were screened for eligible records.

Study selection

The following criteria for eligibility were applied to select studies: 1) The study included any kind of intervention (e.g., varying from individual consultation to group education sessions performed preconceptionally) regardless of duration or amount of visits of preconceptional women; 2) the intervention focused on health promotion or on modification of any of the following risk factors: alcohol, smoking, weight, diet/ nutrition, physical activity, folic acid fortification, and folic acid supplementation (in relation to anomalies other than neural tube defects); and 3) reported outcome(s) were behaviour change and/or risk factor modification and/or pregnancy outcome (e.g., miscarriages, birth defects, premature birth, birth weight, low birth weight and/or small for gestational age, and perinatal deaths). Regarding birth defects, development of neural tube defects was not regarded as an outcome for folic acid supplementation, as this is already considered evidence based in numerous studies[7]. Although fertility is an important outcome of preconceptional interventions, this was regarded as a subgroup of interventions and was not included in this systematic review. Records were assessed for eligibility on the basis of title and abstract. The full manuscripts of these abstracts and of potentially relevant articles identified with citation tracking were then evaluated to determine whether inclusion criteria were met. Additionally, identified reviews were screened for potentially relevant references. Study selection was performed independently by 2 reviewers (ST and SVV) with a third reviewer (SD) for adjudication of discrepancies.

Data extraction

Predefined characteristics that were extracted were title; author(s); aim; intervention (how, when, and by whom) per group (if applicable); study design; inclusion and exclusion criteria; participant recruitment (time period of study, country, recruitment site, patient sampling method if specified); methods of randomization/case or control selection/matching if applicable; data collection/ follow-up (prospectively or retrospectively, sources of data, method and timeframe of assessment,

and blinding when specified); flowchart of participants; loss to follow-up (number and reasons stated); baseline characteristics of the study population; setting of the intervention; definitions of prespecified outcomes (of interest to this review); and the corresponding results (if applicable confounder-adjusted estimates were given, with confounders for which was adjusted stated). Items were extracted largely from the Strengthening the Reporting of Observational Studies in Epidemiology ("STROBE") statement[8] and the Cochrane Handbook[9]. When there were questions regarding these items, the authors of the articles in question were contacted for clarification.

Study quality and assessment of the strength of evidence. A quality assessment checklist was constructed on the basis of the results of a systematic review evaluating tools for assessing quality and susceptibility to bias in observational studies and the Cochrane Handbook regarding quality assessment for randomized controlled trials[9,10]. Nine criteria were used across 5 quality domains. The criteria for quality assessment can be found in Appendix Table 1. Studies were considered as highly susceptible to bias if 2 or more of the 5 domains were scored as susceptible to bias, or if 3 or more of the 5 domains were scored as unclear. The strength of the evidence for each intervention was assessed by 2 reviewers (ST, SVV) according to predefined criteria adapted from the Canadian Task Force on the Periodic Health Examination[11]. In case of disagreement, a third reviewer (SD) was asked to resolve the discrepancy. The applied classification for the strength of evidence can be found in Appendix Table 1.

Data analysis

Because of presumed clinical heterogeneity, no attempt for a meta-analysis was prespecified.

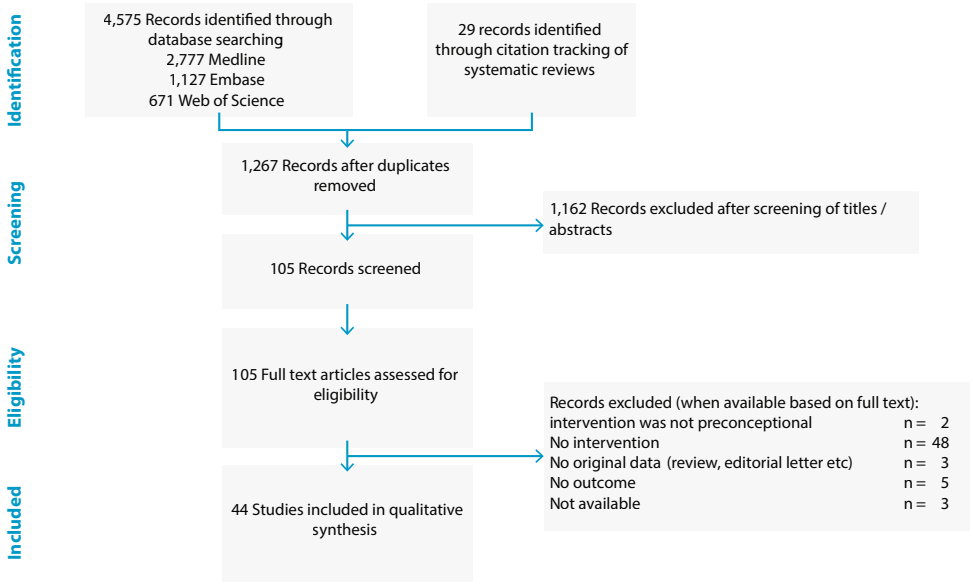
RESULTS

Study identification and selection

From the search for articles related to preconceptional lifestyle interventions in women and behavior change and/or risk factor modification and/or pregnancy outcome, 105 fulltext articles were retrieved from 4,604 references (2,777 from Medline; 1,127 from Embase; 671 from Web of Science; and 29 references from reviews). After exclusion of 61 full-text articles for stated reasons, 44 articles fulfilled the selection criteria (Figure 1).

Table 1 summarizes the included studies. Results are classified as follows. First, studies were grouped by the core risk factor that the interventions address and report. Multiple risk factor studies with multiple outcomes were classified separately. The rationale for this approach is to give a structured overview and classification between studies addressing and reporting a single risk factor versus multiple risk factor studies. Second, interventions were classified into individual (individual consultation of a patient/couple), group-based (consultation of patients/couples performed in groups), or collective interventions (interventions targeted at a group of people as a whole, e.g., iodizing salt in prevention of hypothyroidism)[12]. The majority of studies focused on individual interventions[13–38], 3 studies focused on group interventions[39–41], 1 study focused on a mix of individual and group intervention[42], and 14 studies focused on collective interventions[43–56].

FIGURE 1: Flowchart: identification, screening, and selection process of studies for inclusion in review.



Of the 44 studies identified, 25 of those studies reported on pregnancy outcome[13–23,30,34,44–54,56], 18 studies reported on behavior change regarding the risk behavior(s)[24–29,32,33,35–43,55], and 1 study reported on both pregnancy and behavior change outcome.[31] Behavior change was most often based on self-reported outcomes[25–27,31,33,36,39,41–43]; 1 study measured behavior change with biomarkers only[29], and 8 studies measured behavior change by using a combination of self-report and biomarkers[24,28,32,35,37,38,40,55]; 19 randomized controlled trials[13–22,25,26,30,31,36,38–41], 22 cohort studies[24,27–29,32,35,37,42–56], 1 case-control study[34], 1 cohort controlled trial[23], and 1 cross-sectional study[33] were identified. Results are presented in Appendix Table 2 and discussed per (risk) behavior in the following section.

Alcohol

One randomized controlled trial reported on the effectiveness of a program to reduce alcohol-exposed pregnancies by reducing risky drinking (8 drinks/week or >5 drinks on 1 occasion) in women in whom conception could occur. Floyd et al.[36] assessed the effectiveness of a prevention program consisting of 4 counselling sessions with personalized feedback and goal setting regarding risky drinking. Participants also received a counselling session on contraception. The comparison group received written information regarding alcohol risks and women's health. The study population (n = 830) consisted of women of childbearing age not planning pregnancy who were engaged in risky drinking. Women who received motivational counselling sessions and counselling about contraception had significantly higher odds to be at reduced risk for an alcohol-

exposed pregnancy up to 9 months after intervention (odds ratio = 2.11, 95% confidence interval (CI): 1.47,3 .03). This outcome is based on self-reported behavior change. Because the trial was conducted in a population with a high predefined risk of alcohol consumption, results are limited in generalizability. Regarding other criteria, the study quality was good resulting in a low risk of bias overall. Considering the aims of the review, this study was not conducted specifically with women planning a pregnancy. The strength of evidence is I-a.

Smoking

Three studies reported on the effectiveness of the advice to quit smoking: 1 randomized controlled trial[38] and 2 cohort studies[29,35]. One study assessed the effectiveness of a preconceptional health program in terms of behaviour changes with a biomarker. Czeizel assessed smoking cessation rates with urinary cotinine.[29] The intervention, smoking cessation advice at a preconceptional consultation, resulted in a decrease of smoking rates after 3 months (17.9% vs. 12.4%). In the report by Hughes et al.[38], the effectiveness of a "stage of change"– oriented, scripted hand out and counselling at the hospital's cessation clinic was assessed. The comparison group received information about the impact of prepregnancy smoking. De Weerd et al.[35] evaluated provision of advice to stop smoking. Both studies were performed in a hospital-based population; Hughes et al. also included pregnant women. Outcomes were self-reported behavior change and were verified with exhaled carbon monoxide measurements in the report by Hughes et al. and with the biomarker cotinine in by de Weerd et al. With only advice to stop smoking, 88% of the self-reported smokers reduced smoking; however, none ceased smoking. The stages of change-oriented counselling in the report by Hughes et al. was not proven effective in the short term; however, after 12 months, women in the intervention group were significantly more likely to maintain smoking cessation than those in the control group. Although the selection of the study population was unclear in the study by Czeizel[29], overall susceptibility to bias was low. The study by de Weerd et al.[35] is susceptible to an attrition bias: how loss to follow-up is dealt with is unknown. As data collection was based on a letter, items of quality assessment were unclear. Both Hughes et al.[38] and de Weerd et al.[35] sampled patients within a hospital-based setting. The strength of evidence is I-a [38] and II-2. [29,35]

Nutrition

Three studies focused on the effectiveness of a nutritional intervention program: 1 randomized controlled trial[39] and 2 case-control studies.[34,42] Caan et al.[34] assessed the effect of long-term enrollment in the Women, Infants, and Children (WIC) supplemental food program with short-term enrollment among women with low income and nutritionally at risk in their interpregnancy interval. Long-term (5–7 months) WIC support was associated with a positive effect on birth weight and birth length. Cena et al.[39] assessed the effect of nutrition lessons regarding folate among low-income, nonpregnant women. The comparison group underwent a lesson about resource management. Nutrition lessons led to increased selfreported intake of dietary folate.

Doyle et al.[42] assessed the effectiveness of a preconception nutrition counselling program (educational group events, and nutrition newsletters) among women with pregnancy intention

TABLE 1 Characteristics of studies reporting on the effectiveness of preconceptional interventions included in this systematic review (n=44; 1987-2012 Australia, Canada, China, Denmark, Finland, France, Germany, Hungary, Israel, the Netherlands, Norway, Union of Soviet Socialist Republics, United Kingdom, United States)

				Reported	outcome	
	Study	**Study design**	**Study population**	**Behavioral change**	**Pregnancy outcome**	**High susceptibility to bias**
I Alcohol						
Individual Interventions	Floyd 2007 [35]	RCT	N= 593	Self reported	No	
II Smoking						
Individual Interventions	Hughes 2000 [38]	RCT	N= 204	Self reported and biomarkers	No	
	de Weerd 2001 [35]	Cohort	N= 111	Self reported and biomarkers	No	Yes
III Nutrition						
Individual interventions	Caan 1987 [34]	CC	N= 703	Not reported	Yes	
	Hammiche 2011 [37]	Cohort	N= 110	Self reported and biomarkers	No	
Group interventions	Cena 2008 [39]	RCT	N= 153	Self reported	No	
Mixed individual and group interventions	Doyle 1999 [42]	Cohort	N= 41	Self reported	No	
IV Folic acid						
Individual interventions folic acid advice and provision	MRC Vitamin Study Research Group, 1991 [13]	RCT	N= 1,817	Not reported	Yes	Yes
	Czeizel 1992 [14]	RCT	N= 5,453	Not reported	Yes	Yes
	Czeizel 1993 [15]	RCT	N= 5,453	Not reported	Yes	Yes
	Czeizel 1993 [17]	RCT	N= 4,156	Not reported	Yes	
	Czeizel 1994 [20]	RCT	N= 5,453	Not reported	Yes	Yes
	Czeizel 1996 [16]	RCT	N= 5,453	Not reported	Yes	
	Czeizel 1998 [18]	RCT	N= 4,823	Not reported	Yes	Yes
	Rolschau 1999 [21]	RCT	N= 14,021	Not reported	Yes	
	Ulrich 1999 [22]	RCT	N= 8,184	Not reported	Yes	
	Czeizel 2003 [20]	RCT	N= 5,453	Not reported	Yes	Yes
	Czeizel 2004 [23]	CCT	N= 6,138	Not reported	Yes	
	Watkins 2004 [24]	Cohort	N= 165	Self reported and biomarkers	No	

	Robbins 2005 [25]	RCT	N= 280	Self reported	No
	Schwarz 2008 [26]	RCT	N= 265	Self reported	No
	Morgan 2009 [27]	Cohort	N= 322	Self reported	No
Individual Interventions Folic acid advice	de Weerd 2002 [28]	Cohort	N= 111	Self reported and biomarkers	No
Collective interventions: public campaign	Chan 2001 [43]	Cohort	N= 512	Self reported	No
	Myers 2001 [44]	Cohort	N= 222,314	Not reported	Yes
	Gindler 2001 [45]	Cohort	N= 23,806	Not reported	Yes
Collective interventions fortification	Gucciardi 2002 [46]	Cohort	cases=3,207	Not reported	Yes
	Honein 2001 [47]	Cohort	N= 39,434,211	Not reported	Yes
	Persad 2002 [48]	Cohort	N= 107,851	Not reported	Yes
	Ray 2002 [49]	Cohort	N= 218, 977	Not reported	Yes
	Williams 2002 [50]	Cohort	cases=5,630	Not reported	Yes
	CDC 2004 [51]	Cohort	N= 6.9 million	Not reported	Yes
	Liu 2004 [55]	Cohort	N= 780	Self reported and biomarkers	No
	Canfield 2005 [53]	Cohort	N= 9,729,763	Not reported	Yes
	Botto 2006 [52]	Cohort	N= 1.5 million	Not reported	Yes
	Yazdy 2007 [56]	Cohort	N= 38,232	Not reported	Yes
	de Wals 2007 [54]	Cohort	N= 1.9 million	Not reported	Yes
Programs					
Individual Interventions	Czeizel 1999 [29]	Cohort	N= 8,837	Biomarkers	No
	Lumley 2006 [30]	RCT	N= 786	Not reported	Yes
	Elsinga 2008 [31]	RCT	N= 460	Self reported	Yes
	Ockhuijsen 2011 [32]	Cohort	N= 101	Self reported	No
	Williams 2012 [33]	CSS	N= 30,481	Self reported	No
Group interventions	Hillemeier 2008 [40]	RCT	N= 360	Self reported and biomarkers	No
	Weisman 2011 [41]	RCT	N= 268 at 12 months N=262 at 6 months	Self reported	No

and history of a prior low birthweight baby and an inadequate dietary intake. The interventions led to higher intake of certain micronutrients, except for folic acid from diet.

Doyle et al.[42] sampled women in a hospital-based setting. Overall, the quality criteria were assessed as good, resulting in a low risk of bias. The strength of evidence is II-2 [34,42] and I-a.[39]

Folic acid

Thirty studies were identified as reporting on the effectiveness of folic acid supplementation and fortification. Sixteen studies were individual-based programs, of which 12 were randomized controlled trials[13–22,25,26], 1 was a cohort controlled trial[23], and 3 were cohort studies[24,27,28]; 14 cohort studies[43–56] were collective interventions, namely, folic acid fortification or public campaigns. Regarding individual-based programs, 16 studies[13–28] provided folic acid supplements. No studies were restricted to advising only folic acid supplements.

From the 15 studies that provided supplements, there were 3 trials that provided folic acid supplements as well as counselling on folic acid: A significant beneficial effect of selfreported folic acid supplement use was shown.[25–27]

Counselling varied from brief folic acid counselling to a computerized educational session. Only Morgan et al.[27] succeeded in showing a significant increase in self-reported daily multivitamin intake. Morgan et al. and Schwarz et al.[26] showed an increase of self-reported use up to 6–10months after the counselling and provision of supplements. Two trials, those by Watkins et al.[24] and de Weerd et al.[28], assessed the effectiveness of folic acid supplement provision and counselling with biomarkers in addition to selfreported outcomes. Watkins et al. did not show a significant increase in folic acid use based on self-reported outcomes and serum folate levels before and after the intervention. De Weerd et al. reported a significant increase of self-reported supplement use among women planning a pregnancy. An elevated red cell folate level 4 months postintervention was found. All trials were conducted among women of childbearing age; pregnancy intention was not always specified. Susceptibility to bias was assessed as low; the strength of evidence is I-a [25,26] and II-2.[24,27,28] Besides the effect of individual folic acid interventions on behavior change, 11 studies reported on the effect on pregnancy outcome. No significant difference in miscarriage rates was shown in 1 study.[13] Nine studies showed associations with a lower risk for certain congenital anomalies (e.g., urinary tract anomalies, cardiovascular anomalies, limb deficiencies, oral facial clefts, and urinary tract defects, talipes, and hypospadias).[14–20,22,23] One study reported a lower incidence of low birth weight in the folic acid supplementation group; the trial did not show an effect on gestational birth weight or preterm birth.[21] Studies reporting on pregnancy outcomes varied in study quality. In those by the Medical Research Council Vitamin Study Research Group[13] and Czeizel et al.[14–17,19,20], many quality items were not clarified. Therefore, these studies were assessed as highly susceptible to bias. The strength of evidence is I-a[13–22] and II-2.[23]

Of 14 collective folic acid intervention studies, 3 cohort studies reported on the effectiveness of a folic acid campaign.[43–45] Chan et al.[43] reported on behavior change, and Myers et al.[44] and Gindler et al.[45] reported on pregnancy outcome.

Chan et al. investigated the effect of a folate campaign (information regarding the importance

of folic acid in the reduction of neural tube defects and pamphlets advertising available resources) targeted to interconceptional women of reproductive age as well as health-care professionals. Selfreported consumption of folate-rich food and folic acid tablet use periconceptionally increased from 12% to 18.6% and from 10.1% to 26.7% 1 year after the campaign.

Myers et al.[44] and Gindler et al.[45] evaluated the effect of a public health campaign targeted to women attending a premarital examination. The intervention in both studies included the advice for women to take folic acid daily from the premarital examination until the end of the first trimester of pregnancy. In Myers et al., supplementation was associated with a risk reduction of 41% in imperforate anus of the child. The study of Gindler et al. showed a higher relative risk of miscarriages for women with folic acid use (relative risk = 1.03, 95%CI: 0.89, 1.20). Susceptibility to bias was assessed as low; the strength of evidence is II-2.[43–45]

Regarding collective interventions, 11 large cohorts[46–56] were included and reported on the effectiveness of folic acid fortification. One study reported on behavior change assessed with biomarkers[55], and 10 studies evaluated changes in prevalence rates of congenital anomalies.[46–54,56]

Liu et al.[55] evaluated the effectiveness of folic acid food fortification among women of childbearing age and seniors over 65 years, recruited prefortification through a random telephone survey. Postfortification, the annual rate of neural tube defects was decreased by 78%, red blood cell folate was significantly increased, and the proportion of women taking a vitamin supplement containing folic acid was significantly increased from17% to 28%. Susceptibility to bias was assessed as low; the strength of evidence is II-2.[55]

Eight large cohorts assessed the effectiveness of fortification in reduction of neural tube defect prevalence rates[46–52,54]. Cases were retrospectively selected from birth certificate information and registered databases. All studies showed a decline, ranging from 10% to 54%, in the incidence of neural tube defects postfortification. Not all studies included stillborn and terminated pregnancies in the time period assessed. Furthermore, subgroup analysis of spina bifida and anencephaly showed a decrease in prevalence varying between 16% and 60%. Susceptibility to bias was assessed as low; the strength of evidence is II-2 [46–52,54].

Canfield et al.[53] assessed prevalence rates of other congenital abnormalities besides neural tube defects postfortification. A decrease in prevalence rates was noted for anencephaly, spina bifida, transposition of the great arteries, cleft palate, pyloric stenosis, upper limb reduction defects, omphalocele, and obstructive genitourinary defects. Susceptibility to bias was assessed as low; the strength of evidence is II-2.[53]

Yazdy et al.[56] showed a significant decline of 6% in orofacial clefts following folic acid fortification in a subgroup of non-Hispanic whites. Susceptibility to bias was assessed as low; the strength of evidence is II-2.[56]

Multiple risk factors

Seven studies were identified that reported on the effectiveness of multiple risk factors. The majority of these studies were individual-based programs, of which 2 were randomized controlled trials[30,31], 2 were cohort studies[32,37], and 1 was a cross-sectional study[33]; there were 2 group-based

randomized controlled trials.[40,41]

Williams et al.[33] retrospectively assessed the effectiveness of receipt of PCC with regard to preconceptional health behaviors. PCC was defined as any form of contact with a health-careworker to prepare for a healthy pregnancy. The population consisted of interconceptional women planning a pregnancy. Although the definition of PCC was broad, any receipt of PCC (content undefined) led to a higher self-reported intake of multivitamins 1 month before pregnancy and cessation of alcohol during the 3 months before pregnancy. Susceptibility to bias was assessed as low; the strength of evidence is II-2.[33]

Hammiche et al.[37] assessed the effectiveness of a tailored lifestyle and dietary consultation in a hospital-sampled subfertile population that was planning pregnancy. Couples that attended a second counselling session after 3 months reported a higher intake of fruit and fish and reduction of their dietary risk score based on self-reported behaviors and biomarkers. However, only a selection of the sampled subfertile patients within a hospital-based setting attended the second consultation. Susceptibility of bias was assessed as low; the strength of evidence is II-2.

Ockhuijsen et al.[32] assessed the effectiveness of PCC consultation in smoking cessation and weight reduction among subfertile women. The outcome was self-reported smoking cessation and self-reported weight reduction. With consultations every 4 weeks during a follow-up period varying between 3 months and 1 year, 15 of 30 (50%) obese women lost weight (mean = 6.1 kg, standard deviation, 3.6) and 7 of 23 (30%) women quit smoking. Because the follow-up period varied among study participants, there is a susceptibility to a detection bias, as the study results are applicable only to a hospital-based population of subfertile women. Overall susceptibility of bias was assessed as low; the strength of evidence is II-2.

Two different multiple risk factor studies assessed effectiveness regarding pregnancy outcomes.[30,31] Lumley and Donohue[30] assessed the effect of a home visit with prepregnancy information, advice, and counselling given by midwives among low-income women in a community setting. The intervention was compared with a postpartum home visit in which peripartum experiences were discussed. Although birth weight was 97.4 g lower in the intervention group, there was no significant difference in the outcomes: preterm birth (<32 weeks); low birth weight (<2,500 g); and small for gestational age (birth weight, <10th percentile). Quantitative outcomes showed a higher occurrence of preterm birth, low birth weight, and perinatal deaths. Because of recruitment of women who were at high risk for poor birth outcomes, there is susceptibility for a selection bias. Overall, the study was assessed as low susceptibility to bias; the strength of evidence is I-a.

Elsinga et al.[31] investigated the effectiveness of systematic PCC risk detection and intervention compared with the standard care given by general practitioners among women contemplating pregnancy. The study population consisted mainly of Dutch and high-educated women. The outcome was self-reported behavior change and an adverse outcome of subsequent pregnancy. Systematic counselling and intervention led to a significantly higher intake of folic acid and lower alcohol consumption before pregnancy. Adverse pregnancy outcome (defined as premature birth (<37 weeks), low birth weight (<2,500 g), small for gestational age (growth, <P2,3 (−2 standard

deviations)), and congenital anomalies) was 16.2% in the intervention group versus 20.2% in the control group. The odds ratio for an adverse pregnancy outcome after preconception counselling was 0.77 (95% CI: 0.48, 1.22). Susceptibility to bias was assessed as low; strength of evidence is I-a.

Hillemeier et al.[40] assessed the effectiveness of a preconceptional group-based intervention program regarding nutrition and physical activity among women "capable of becoming pregnant." The comparison group did not undergo any intervention. Women in the intervention group were more likely to read food labels, to use a daily multivitamin that contains folic acid, and to meet recommended levels of physical activity. However, half of the study population did not attend the follow-up consultation and was excluded. Weisman et al.[41] performed a follow-up study to assess the maintenance of the aforementioned behavior changes 12-months after the intervention. After 12 months, women in the intervention group were more likely to use a daily multivitamin containing folic acid and to have a lower body mass index. Intervention effects on physical activity were not maintained, and effects on reading food labels for nutritional values diminished between the 6- and 12-month follow-up periods.

Allocation concealment in the studies by Hillemeier et al.[40] and Weisman et al.[41] was unclear, and patient sampling was unclear, resulting in a potential selection bias. Overall susceptibility to bias was assessed as low; the strength of evidence is I-a.

Physical activity and weight loss

No studies reporting a specific intervention targeting physical activity and weight loss in a preconceptional population were found. Numerous studies did find that, when preconceptional health was addressed, this had a beneficial effect on physical activity in the short run[37,40] and weight loss.[32]

DISCUSSION

Regarding alcohol consumption, only 1 single risk factor study was available. Women who engaged in risky behaviors reduced their alcohol consumption to less risky levels following a relatively intensive intervention.[36] However, a multiple risk factor approach in which reduction of alcohol consumption was one of the targeted health behaviors in women contemplating pregnancy was shown to be effective among highly educated women.[31] The identified studies to assess the effectiveness in altering behavior regarding alcohol consumption are proven effective for only a selective group, and therefore more evidence is needed to justify that this intervention be embedded in routine care. No studies reported on the effectiveness regarding pregnancy outcome.

The effectiveness of PCC in reducing preconceptional smoking cessation is not clear. Hughes et al.[38] reported only maintenance of smoking cessation, verified by a biomarker, in the long term and only among a small subpopulation. A "stages of change" approach does not seem effective in terms of cessation in the short term but could be considered to achieve maintenance of smoking cessation. Results from other studies using a biomarker showed contradictory results: a decrease in initial smokers[29] versus no smoking cessation.[35] However, a large proportion reduced smoking.[35] No

studies reported on the effectiveness regarding pregnancy outcome.

Nutritional interventions seemed to be effective in changing dietary health behavior. However, alterations were assessed only among a selective group of women, for example, women living on food stamps with prior adverse pregnancy outcomes.[39,42] Regarding the effect on pregnancy outcome, longterm nutritional support was associated with a positive effect on birth weight.[34] The interventions provided in the available studies are proven effective only for a selective group, and therefore more evidence is needed to justify that they be embedded in routine care for the general public contemplating pregnancy.

Folic acid interventions were differentiated in individual advice and/or provision of folic acid supplements and in collective interventions, such as public campaigns and food fortification studies. Folic acid interventions proved to be effective in achieving self-reported intake of folic acid when folic acid supplements were provided.[25–27] The studies that assessed effectiveness of provision of folic acid with serum folate as a biomarker were conflicting. However in one of these studies, the self-reported outcomes did not support folic acid provision either.[24] The other study did show a slight increase in self-reported folic acid use and maintenance of levels biologically shown by erythrocyte folic acid 4 months post intervention.[28] On the basis of interventions provided in the available studies, it remains unclear whether sole advice to take folic acid supplementation is sufficient to achieve folic acid supplementation compared with the provision of folic acid supplements. To compare the effectiveness of sole advice versus advice including provision of folic acid supplements, a randomized controlled trial would need to be conducted, preferably using biomarkers. Eleven randomized controlled trials reported on the effect of individual folic acid advice, mostly including provision on pregnancy outcomes. On the basis of 1 study (with nonsignificant outcomes), there does not appear to be an effect on the miscarriage rate.[13] Nine studies showed associations with a lower risk for certain congenital anomalies.[14–20,22,23] One study showed a lower incidence of low birth weight.[21] Study quality items were unclear in a majority of these studies; it is unclear to what extent results are applicable for the general public. Because folic acid is widely proven to be effective in reduction of the risk for neural tube defects, this evidence should be considered as further support for interventions to achieve folic acid supplementation preconceptionally. The findings of the effectiveness of collective approaches regarding folic acid are in line with findings from the individual interventions, described above, regarding the behavior outcomes and effect on pregnancy outcomes. An increase of folic acid intake due to food fortification was further supported by the finding that folate biomarkers increased among women postfortification.[55] Furthermore, a folate campaign was also effective in increasing self-reported consumption of folate rich food and folic acid supplementation.[43] Similar to the individual folic acid studies, the campaigns and fortification studies showed reduced occurrence of congenital anomalies, mainly neural tube defects.[44,46–54,56]

Studies on multiple risk factors in reducing risky health behaviors all seemed to be effective in 1 or more targeted risk behaviors, for example, weight loss, reduction of the number of cigarettes smoked, a higher daily consumption of fruit, fish, and multivitamins, and cessation of drinking.[31,32,37,40] However, the contents of the interventions were often not specified. One trial

succeeded in showing the effectiveness of a multiple risk factor approach on adverse pregnancy outcomes among a higher educated group of women in the Netherlands.[31] Further evidence is necessary regarding the beneficial effects of a multiple risk factor approach for PCC above single intervention studies.

Strengths and limitations

As the studies identified in the review contained clinically heterogeneous data, they therefore could not be pooled. Clinical heterogeneity was a result of differences in interventions applied to different (sub)populations in different settings. Tailoring interventions seems to be very important in order to meet the demands of different populations; however, it does not allow meta-analysis regarding this topic. The timeframe of the intervention within the pregnancy planning scheme was often undefined or classified differently. The duration, method of follow-up, and reported outcomes were reported differently by studies. For the aforementioned reasons, this review is descriptive in nature.

The evidence from the studies included in this review is likely to be at some risk of bias. Although studies made efforts to reduce bias by aspects of study design such as accounting for loss to follow-up and reporting predefined outcomes, the risk associated with unclear patient sampling and unclear allocation concealment could not easily be addressed. Follow-up was insufficient in a number of studies to measure change in health behavior. Missing data are a particular problem in studies where women are followed over time, but they are mostly excluded from the analysis. Possible outcomes become difficult to interpret and apply only for a subset of the study population. Findings for those women who are followed up at all data collection points may not be applicable to those women with missing data. For instance, missing data could reflect the fact that an intervention was not feasible for all participants. As a result of missing data, overestimation of the effect could be measured, because the subset of the study population is not representative of the wider population. Ten[25–27,31,33,36,39,41–43] of the 19 studies relied only on self-report for information on behavior change postintervention. Self-reported outcomes may not be reliable.[57] In this review, the more recent studies introduced the use of biomarkers to assess behavior change. This seems a very welcome introduction that should be integrated in further research on this topic. A drawback with biomarkers is the diagnostic value regarding the degree to which behaviors have changed. Furthermore, not all studies elaborated on the cutoff levels they applied in the interpretation of biomarkers.[29,38,40,55] As the majority of studies did not include follow-up of subsequent pregnancies after the preconceptional intervention or maintenance of health behaviour change, the effect on pregnancy outcome could often not be assessed. Because some studies were conducted in specific populations (e.g., hospital based with subfertile women, women at higher risk for adverse pregnancy outcomes, and low-income women), it is not clear how easy it would be to transfer interventions to other settings or the general population.

Regarding adequate implementation of interventions, it should also be noted that many studies do not describe the details of the intervention thoroughly. More information is necessary, such as who delivered the intervention and how the intervention was exactly implemented to

ensure adequate implementation of interventions in the future.

Study populations often comprised women of childbearing age, without further elaboration of pregnancy intention. It may be that the period with pregnancy intention is a window of opportunity to change risky health behaviors.[36] Women are potentially more motivated to change their behaviour in order to have a healthy child. This motivation could be very crucial in the effect of the intervention in achieving and maintaining behavior change.

Besides population and intervention characteristics, as stated above, organizational factors in the setting are of great importance. These organizational factors are largely dependent on the nation's health-care infrastructure, insurance system, and socioeconomic factors.[1] Articles in this field often lack these details or lack reflection on the relation of these factors to the reported findings. Transfer of this knowledge seems very valuable.

CONCLUSION

As evidence for preconceptional risk factors associated with adverse pregnancy outcomes is large, there is a need for effective interventions to reduce these risk factors and improve pregnancy outcomes. However, overall, on the basis of the available evidence, there is a relatively short list of core interventions for which there is substantial evidence of effectiveness when applied in the preconception period. Regarding alcohol, evidence is lacking for interventions in the preconceptional period. Regarding nutrition, preconceptional interventions are effective in terms of dietary change and birth weight. Smoking interventions are effective in achieving smoking reduction in the preconception period. Regarding folic acid, individual interventions and collective interventions to increase folic acid use are effective in terms of behavioral change and improvement of pregnancy outcomes. The additional benefits of a programmatic approach above a single intervention approach remain difficult to assess; there were no comparative studies. Integration of single interventions into care is a challenging discussion for which implementation studies are necessary.Naturally, despite the relatively short list of core interventions, health-care providers should continue with information provision about the consequences and risks of risky behaviour to couples wishing to conceive.

Recommendations for future research are as follows. Include 1) follow-up of pregnancy outcomes; 2) confirmation of self-reported outcomes, for instance, with biomarkers; 3) description of determinants (such as contemplation of pregnancy) that are associated with effective or ineffective treatment outcomes to supply information on the generalizability of findings; and 4) provision of specific information regarding the content of interventions and the setting to guide implementation of interventions.

CONFLICTS OF INTEREST

None declared.

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APPENDIX 1: Search Strategy

PubMed:

PubMed: (preconception*[tw] OR pre-conception*[tw] OR prepregnan*[tw] OR pre-pregnan*[tw] OR pregestation*[tw] OR pre-gestation*[tw] OR periconception*[tw] OR peri-conception*[tw] OR interconception*[tw] OR inter-conception*[tw] OR interpregnan*[tw] OR inter-pregnan*[tw] OR intergestation*[tw] OR inter-gestation*[tw] OR internatal*[tw] OR inter-natal*[tw]) AND (education*[tw] OR promotion*[tw] OR care[tw] OR cares[tw] OR caring*[tw] OR healthcar*[tw] OR campaign*[tw] OR counsel*[tw] OR wellness*[tw] OR intervent*[tw]) AND (matern*[tw] OR mother*[tw] OR paternal*[tw] OR father*[tw] OR parent*[tw] OR man[tw] OR men[tw] OR woman[tw] OR women[tw] OR couple*[tw]) AND (eng[la] OR dut[la] OR ger[la] OR fre[la] OR spa[la]) NOT (animals[mesh] NOT humans[mesh])

Embase:

((preconception* OR prepregnan* OR pregestation* OR periconception* OR interconception* OR interpregnan* OR internatal* OR intergestation* OR pre-conception OR pre-conceptional OR pre-pregnancy OR pre-pregnant OR pre-gestation OR pre-gestational OR peri-conception OR peri-conceptional OR inter-conception OR inter-conceptional OR inter-pregnancy OR inter-pregnant OR inter-gestation OR inter-gestational OR inter-natal) NEXT/2 (education* OR promotion* OR care OR cares OR caring* OR healthcar* OR campaign* OR counsel* OR wellness* OR intervent*)):ti,ab,de AND (matern* OR mother* OR paternal* OR father* OR parent* OR man OR men OR woman OR women OR couple*):ti,ab,de AND ([english]/lim OR [dutch]/lim OR [german]/lim OR [french]/lim OR [spanish]/lim) NOT ([animals]/lim NOT [humans]/lim)

Web of Science:

((preconception* OR prepregnan* OR pregestation* OR periconception* OR interconception* OR interpregnan* OR internatal* OR intergestation* OR pre-conception OR pre-conceptional OR pre-pregnancy OR pre-pregnant OR pre-gestation OR pre-gestational OR peri-conception OR peri-conceptional OR inter-conception OR inter-conceptional OR inter-pregnancy OR inter-pregnant OR inter-gestation OR inter-gestational OR inter-natal) NEAR/2 (education* OR promotion* OR care OR cares OR caring* OR healthcar* OR campaign* OR counsel* OR wellness* OR intervent*)) AND (matern* OR mother* OR paternal* OR father* OR parent* OR man OR men OR woman OR women OR couple*) NOT (animal* NOT [human*) AND ([english]/lim OR [dutch]/lim OR [german]/lim OR [french]/lim OR [spanish]/lim)

APPENDIX TABLE 1: Quality Assessment Criteria and Assessment of Strength of Evidence

Quality assessment criteria: adapted from (9-10)		
Domain	***Criteria***	
I Methods for selecting study participants	The source population was appropriate AND in- or exclusion criteria were defined.	
II Methods for measuring exposure and outcome variables	Methodology was adequate to detect stated outcomes	
III Design specific sources of bias	a)	randomized controlled trials: allocation was concealed
	b)	selection bias: patient selection and sampling (and in case of a case-control or cross sectional study case selection or when applicable matching) was adequate
	c)	detection bias: the length of follow-up was adequate to detect outcome and equally applied amongst all groups
	d)	attrition bias: loss to follow-up/ drops outs were reported and handled appropriately in analysis
	e)	reporting bias: outcomes were pre-specified and there was no selective report on outcomes
IV Statistical methods	Statistical procedures were described adequately and if applicable adjustment for confounding factors was reported	
V Conflicts of interest	Source of funding or conflicts of interests were reported	
Classification of strength of evidence adapted from the Canadian Task Force for Preventive Medicine (11)		
I-a: at least 1 properly conducted randomized controlled trial BEFORE pregnancy		
I-b: at least 1 properly conducted randomized controlled trial not necessarily before pregnancy		
II-1: well-designed controlled trials without randomization		
II-2: cohort or case-control studies		
II-3: multiple time series with or without intervention or dramatic results in uncontrolled experiments		

APPENDIX TABLE 2: Findings From Studies Reporting on the Effectiveness of Preconceptional Interventions per (Risk) Behavior (N=44)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
I Alcohol					
Individual interventions					
Floyd 2007[35]	Aim: Assessment of efficacy of motivational counselling to reduce the risk of an alcohol-exposed pregnancy. Intervention: In the intervention group: four motivational counselling sessions (advice to reduce risky drinking, with personalised feedback and goal setting) and a contraception counselling visit about effective contraception use. The comparison group received written information on alcohol and women's health.	Design: Randomized controlled trial. Recruitment: Prospectively during 2002-2004 in six community-based settings (primary care, hospital clinics, and jails) by media and presentations. Follow-up: Assessment at baseline and at three, six, and nine months following the intervention by interview.	In- exclusion criteria: (1) Women aged 18-44 years old capable of becoming pregnant; (2) sexual intercourse in the previous three months without contraception with a fertile man; (3) no condition causing infertility; (4) not pregnant or planning pregnancy at time of the intervention; (5) engaged in risky drinking; and (6) available for the follow-up period. Study population: N= 830 (intervention group n=416; comparison group n=414). Loss to follow-up: N=125 in the intervention group (63% attended all four counselling sessions); comparison group n=112. These women were excluded in analysis. Setting: Community-based setting: Florida, Texas, and Virginia, USA.	Outcomes: Odds for an alcohol exposed pregnancy (risky drinking: eight drinks/week or >five drinks on one occasion and ineffective contraception). Results: Women in the intervention group had higher odds to be at reduced risk for an alcohol exposed pregnancy: - At three months follow-up (OR 2.31; 95% CI 1.69-3.20); - At six months follow-up (OR 2.15; 95% CI 1.52-3.06); and - At nine months follow-up (OR 2.11; 95% CI 1.47-3.03).	I-a
II SMOKING					
Individual interventions					
Hughes 2000[38]	Aim: Assessment of effectiveness of a motivational intervention to cease smoking and maintain cessation. Intervention: The intervention group received scripted advice, "stage-of-change" orientated hand-outs and a visit to a smoking cessation clinic. The control group received 'standard care' about the impact of smoking.	Design: Randomized controlled trial. Recruitment: Prospectively from 1996 until 1999. Data collection/ Follow-up: Questionnaire and exhaled carbon monoxide measurements at six and twelve months for both groups.	Inclusion criteria: Newly referred infertile and pregnant patients who had smoked ≥three cigarettes in the past six months; not attending for genetic counselling or habitual abortion. Study population: N=94 infertile women (intervention group n=47; comparison group n=47) and n=110 pregnant women (intervention group n=56; comparison group n=54) Loss to follow-up: None. Setting: Three university teaching hospitals in Hamilton, Ontario, Canada.	Outcomes: Self-identified "stage-of-change" and rate of maintenance of cessation after twelve months. Results: Intervention and comparison were similarly effective; the rate of maintained cessation rose significantly from 4% to 24% over twelve months, with a mean delta "stage-of-change" 0.28.	I-a
De Weerd 2001[34]	Aim: Assessment of efficacy of smoking cessation advice	Design: Cohort study. Recruitment: Prospectively between 1997 and 1999. Women scheduled for an ap-	In- exclusion criteria: Non-pregnant women scheduled for a preconception care appointment on the fertility clinic.	Outcomes: Smoking cessation or reduction by self-report and by cotinine levels. Results: No self-reported smoking cessa	II-2

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
	Intervention: Smoking cessation advice during a preconceptional consultation three-four monthly.	pointment were approached by letter for inclusion. Patient sampling: consecutively. Data collection/ Follow-up: Questionnaire and blood sample at baseline and four-six weeks later and every three-four months until the sixth, eighth and twelfth week of pregnancy.	Study population: 16 self-reported smokers and 24 smokers based on cotinine in the serum ((cotinine >5µg/L) within a cohort of 111 women. Baseline characteristics: unknown. Loss to follow-up: Not known for the smoking group. (Loss to follow-up in the initially included population was N=33.) Setting: Tertiary care setting, the Netherlands.	tion, however 88% of self-reported smokers and 75% of cotinine validated smokers reduced smoking.	
III NUTRITION					
Individual interventions					
Caan 1987[34]	Aim: Assessment of efficacy of the WIC programme on birth outcomes. Intervention: WIC support (food supplementation and nutrition education) during prior pregnancy and five to seven months postpartum (intervention group) and up to two months postpartum (comparison group).	Design: Case-control study. Recruitment: Prospectively. Data collection/ Follow-up: Until subsequent pregnancies up to 27 months after the index birth were analysed. Data was collected from medical and WIC records.	In- exclusion criteria: Women that had received WIC support during their first pregnancy and that gave birth to their first infant after august 1981 Study population: N =897. Study and control groups were significantly different in terms of race, underweight status, parity, birth weight of the first child and birth intervals. Correction was applied for these confounders. Loss to follow-up: N=178 were excluded form analysis due to missing outcome data, n=16 were excluded because of foetal death or multiple birth. Setting: 48/86 urban and rural Californian local WIC agencies.	Outcomes: The impact of five to seven months of WIC support compared to up to two months of WIC support on birth outcomes. Results: Five to seven months of WIC participation was associated with a positive effect on: - Birth weight (grams) adjusted for gestational age (3461±26, 6 vs. 3341±27, 8; p=0,003). - Birth length (inch) (19,8±0,076 vs. 20,1±0,008; p=0,01).	II-2
Hammiche 2011[37]	Aim: Assessment of the efficacy of tailored preconception counselling to modify dietary and lifestyle behaviors. Intervention: A tailored dietary and lifestyle consultation (focusing on folic acid use, medication, alcohol, caffeine, drugs, physical exercise, infection risk, body mass index, waist circumference, waist to hip ratio, blood pressure, vitamin B12, avoidance of raw milk cheeses /raw meat or fish, and rubella vaccination status).	Design: Cohort study. Recruitment: Prospectively between 2007 and 2009. Data collection/ Follow-up: Three months after the consultation by questionnaires, anthropometric measurements, and biomarkers. Data was used to formulate a personal Preconception Dietary Risk score (PDR score) and a Rotterdam Reproductive Risk Score (R3 score).	Inclusion criteria: Couples planning pregnancy that visited an outpatient academic Obstetrics and Gynaecology clinic. Study population: N=419 couples. Baseline characteristics: median age 31 year; 56% Dutch ethnicity; 35% high educated; and 93.8% of the couples were subfertile. Loss to follow-up: 309 couples did not attend the follow-up consultation. Setting: Tertiary Obstetrics and Gynaecology clinic in the Netherlands.	Outcomes: Change in dietary and lifestyle behaviors and changes in the PDR- and R3-score in women. Results: - Intake of fruit increased from 65 to 80% in women. - Recommended intake of fish increased from 39 to 52% in women. - Median PDR score decreased in women: from 2.6 (95% CI 2.4-2.9) to 2.4 (95% CI 2.1-2.6)	II-2

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
				- Median R3 score decreased in women from 4.7 (95% CI 4.3-5.0) to 3.1 (95% CI 2.8-3.4) due to less alcohol use (-14.6%), more physical exercise and folic acid use.	
Group interventions					
Cena 2008[39]	Aim: Evaluation of the effect of learner-centered nutrition education on folate intake and food-related behaviors. Intervention: The intervention group underwent a learner-centered nutrition lesson with group discussions, participatory activities, worksheets, visual aids, cooking demonstrations, and instructor explanations regarding recommended folate intake and suppletion. The control group received a lesson about resource management.	Design: Randomized controlled trial. Recruitment: Prospectively starting in 2006 (duration unclear). Recruitment sites were food stamp program offices; WIC clinics; low-income schools; and community programs that serve low-income families or individuals. Data collection/ Follow-up: Data was collected at baseline and four weeks after each lesson, by questionnaire.	In- exclusion criteria: (1) Non-pregnant women with a low-income (<185% of federal poverty level); (2) aged 18-45 years; (3) English or Spanish understanding and reading; and (4) primary purchaser of food for herself or her family. Study population: N=155 (intervention group n=77; comparison group n=78). Loss to follow-up: N=2. Group not specified. Setting: Trained Food Stamp Nutrition Education staff in five Californian counties (urban and rural).	Outcomes: Increases in folate intake (natural food folate, synthetic folic acid from fortified foods, synthetic folic acid from supplements, total synthetic folic acid, and total folate from all sources) and food related behaviors compared to baseline. Results: - Significant increase in natural food folate intake (p=0.009) and total folate from all sources (p=0.045), compared to women in the control group. - Other results (synthetic folic acid from fortified foods, synthetic folic acid from supplements, and total synthetic folic acid) were not significantly different.	I-a
Mixed individual and group interventions					
Doyle 1999[42]	Aim: Assessment of efficacy of a preconception nutrition counselling programme. Intervention: Nutritional assessment followed by four to six weekly consultations to strive to attain Reference Nutritional Intakes (RNI) and additional monthly educational group events.	Design: Cohort study. Recruitment: Prospectively from 1995 to 1996. Women were recruited during postpartum hospital stay. Data collection/ Follow-up: Seven-day dietary diary at baseline and six months later.	In- exclusion criteria: Mothers who had delivered a singleton baby weighing <2.5 kg (independent of gestational age), who intended to have further pregnancies and whose diets were assessed as being inadequate. Study population: N=111. Baseline characteristics: mean age 29.1; ethnic origin African 27%, Asian 12%, Caucasian 41%, and West Indian 20%. Loss to follow-up: 70 women did not fill in the follow-up dietary diary, they were excluded. Setting: Dieticians and co-workers at a Mother and Baby clinic.	Outcomes: Changes in dietary intake (Reference Nutritional Intakes). Results: Post-intervention: - A significant increase in the intake of protein, zinc, niacin equivalents and vitamin B6. - A small increase in the proportion of mothers who met the dietary reference values for energy and for 11 of the 15 nutrients considered (significance not tested).	II-2

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
IV FOLIC ACID					
Individual interventions: folic acid advice and provision					
Medical Research Council Vitamin Study Research Group 1991[13]	Aim: To assess the efficacy of folic acid and/ or multivitamin supplementation in the prevention of neural tube defects. Intervention: The following groups were composed: (A) mineral+ folic acid, (B) mineral + folic acid + multivitamin, (C) mineral + placebo, (D) mineral + multivitamin (no folic acid).	Design: Randomized controlled trial. Recruitment: Prospectively between 1983 and 1991 from 33 participating centres. Randomization: Method not specified. Data collection/ follow-up: Clinical follow-up was three monthly until the twelfth week of pregnancy. At each visit number of capsules taken was counted; blood and urine samples were taken. Outcome of pregnancies and health in first years of life was assessed with annual questionnaires.	In-exclusion criteria: Women with a previous pregnancy affected by a neural tube defects (not associated with the autosomal recessive disorder or Meckel's syndrome), planning another pregnancy and not already taking vitamin supplements. Women with epilepsy were excluded. Study population: N=1,817 (group A n=449, group B n=461, group C n=454, group D n=453). Baseline characteristics: no significant differences amongst groups. Loss to follow-up: not reported. Setting: Multicentre study in the United Kingdom, Australia, Hungary, Israel, Canada, France and USSR.	Outcomes: Miscarriage rate. Results: No significant differences were seen in miscarriage rates: RR=1.06; 95% CI 0.79-1.43, p=0.70 for groups A+B vs. C+D.	I-a
Czeizel 1992[14]*; Czeizel 1993*[15]*; Czeizel 1994*[17] *and Czeizel 2003*[20]	Aim: To assess the efficacy of preconceptional multivitamin use in reduction of first occurrence of NTD's and other congenital defects. Intervention: All women attended a Hungarian family planning pregnancy program (a check up, consultation three months later and consultation during pregnancy) The intervention group received a box with multivitamin tablets (0.8 mg folic acid, twelve vitamins, four minerals and 3 trace elements) with recommendation for 1 tablet a day preconceptional up to at least the second missed menstrual period. The control group: was recommended to take a tablet with trace elements (manganese, copper, zinc and a low dose of vitamin C) daily.	Design: Randomized controlled trial. Recruitment: Prospectively, between 1984 and 1992. Women that visited the Hungarian family clinic were recruited. Randomization: Patients were asked if they agreed to their allocation on the basis of the randomization table. Data collection/ Follow-up: Clinical follow-up was three monthly until pregnancy. Self-reported supplement use, number of tablets left was assessed. Pregnancy outcomes were collected from certificates filled in by women and verified by their physician. . Follow-up regarding congenital abnormalities not specified.	In-exclusion criteria: Women < 35years planning pregnancy; not infertile, no previous wanted pregnancy. Study population: N= 7,905 participants in 5,502 women a pregnancy was confirmed (n=2,793 in the intervention group; n= 2,660 in the control group). Baseline characteristics intervention group vs. trace element group: age (mean years; ±SD) 27, ±3 vs. 27± 3; primiparous 88% vs. 89%; prepregnancy body weight 57.1kg ±7.7kg vs. 57.3 ±7.3 kg. Loss to follow-up: 49/5,502 pregnancy outcomes could not be clarified. Setting: Hungarian Family planning clinics, care delivered by qualified nurses in Hungary.	Outcomes: Pregnancy outcome: termination rates, miscarriage rate (undefined), still birth (> 28 weeks GA), live birth rate, low birth weight rate (not defined), preterm birth rate (not defined). Results: Birth outcomes: - First trimester termination: n=6 (0.2%) vs. n=6 (0.2%); second trimester termination after diagnosis of fetal defect: n=3 (0.1%) vs. n=13 (0.5%). - Miscarriage: n=301 (10.8%) vs. n=251 (9.4%) (X2=2.69, p=0.10) - Stillbirth n=11 (0.4%) vs. n=9 (0.3%). - Live birth: n=2410 (86.3%) vs. n=2337 (n=87.9). - Low birth weight rate: n-178 (7.5%) vs. n=166 (7.2%) (X2=1.86, p=0.17). - Preterm birth n=178 (7.5%) vs. n=166 (7.2%) (X2=0.21, p=0.64). Congenital anomalies: in the article of Czeizel, 1992; Prevalence's of congenital malformations intervention group (n=2104	I-A

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
				in this subset) vs. comparison group (n=2052 in this subset): - Cardiovascular malformation: n=6 vs. n=9. - Cleft lip and/or palate: n=4 vs. n=5. - Hypospadias: n=1 vs. n=1. - Obstructive defects of urinary system n=1 vs. n=2. - Congenital postural deformity: n=2 vs. n=0. - Limb reduction defect: n=1 vs. n=5; - Foramina parietale permagna: n=0 vs. n=2. - Exomphalos and gastroschisis: n=1 vs. n=1. - Hemangioma in the face: n=3 vs. n=1. - Other: n=4 vs. n=7.	
Czeizel 1993[16]	Aim: Assessment of effect of periconceptional multivitamin supplementation on neural tube defects (NTDs) and other congenital abnormalities. Intervention: Intervention group: daily multivitamin supplementation (containing vitamins -including 0.8 mg of folic acid – minerals and trace elements) preconceptional until at least two months after conception. The control group received a daily trace element preconceptional until pregnancy.	Design: Randomized controlled trial. Recruitment: Prospectively. Women were recruited via the Hungarian family planning programme. Randomization: Method not reported. Data collection/ Follow-up: until the end of pregnancy (self-reported pregnancy outcome. confirmed by their physician). Infants were followed up with physical examination.	In-exclusion criteria: Women < 35years planning pregnancy; not infertile, no previous wanted pregnancy. Study population: N=4,753 confirmed pregnancies (intervention group n=2,420; comparison group n=2,333). Baseline characteristics intervention group vs. comparison group maternal age mean 26.8 [SD 3.4] vs. 26.7 [SD 3.3]; 94.5% vs. 94.0% primiparous women. Loss to follow-up: 13% in the intervention group and 12% in the comparison group did not report pregnancy outcomes. The analytic sample consisted of 4,156 women (intervention group n=2,104; comparison group n=2,052) and 3,713 infants (intervention group n=1,876; comparison group n=2,032). Setting: Qualified nurses of the Hungarian family planning programme.	Outcomes: Number of major and mild congenital abnormalities. Results: - The rate of major congenital abnormalities other than NTDs and genetic syndromes was 9.0/1000 in pregnancies with known outcome in the vitamin group and 16.6/1000 in the trace element group (RR=1.85; 95% CI 1.02-3.38), difference 7.6/1000. - The rate of all major congenital abnormalities other than NTDs and genetic syndromes diagnosed up to the eight month of life was 14.7/1000 informative pregnancies in the vitamin group and 28.3/1000 in the trace element group (RR=1.95; 95% CI 1.23-3.09), difference 13.6/1000.	I-a

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
Czeizel 1996[18]	Aim: Assessment of effect of periconceptional multivitamin supplementation on neural tube defects and other congenital abnormalities. Intervention: Intervention group: daily multivitamin supplementation (containing 12 vitamins -including 0.8 mg of folic acid – minerals and trace elements) preconceptional until at least two months after conception. The control group received a daily trace element preconceptional until pregnancy.	Design: Randomized controlled trial. Recruitment: Prospectively. Women were recruited via the Hungarian family planning programme from 1984 to 1992. Randomization: unclear Data collection/ Follow-up: until the end of pregnancy (self-reported pregnancy outcome. confirmed by their physician). Infants were followed up with physical examination.	In-exclusion criteria: Women < 35 years planning pregnancy; not infertile, no previous wanted pregnancy. Infants with minor anomalies were excluded. Study population: N=5,502 confirmed pregnancies (intervention group n=2,819; comparison group n=2,683). Baseline characteristics intervention group vs. comparison group: maternal age mean 26.9 [SD 3.4] vs. 26.9 [SD 3.3]; 88.3% vs. 89.9% primiparous women. Loss to follow-up: Dropout rate 0.9% in both groups. The analytic sample consisted of 5,453 women (intervention group n=2,793; comparison group n=2,660) and 4,862 infants (intervention group n=2,471; comparison group n=2,391). Setting: Qualified nurses of the Hungarian family planning programme.	Outcomes: Number of major congenital abnormalities. Results: - Major congenital abnormality: rate in the intervention group: RR=0.51; 95% CI 0.36-0.71, p<0.0001; after exclusion of neural tube defects: - After the exclusion of NTDs, the RR for a major congenital abnormality in the intervention group: 0.54; 95% CI 0.39-0.76, p=0.0003.	I-a
Czeizel 1998[19]	Aim: To study the relation between periconceptional use of multivitamins and birth defects. Intervention: All women attended a Hungarian family planning programme. Intervention group: daily multivitamin supplementation (containing vitamins -including 0.8 mg of folic acid – minerals and trace elements) preconceptional until at least two months after conception. The control group received a daily trace element preconceptional until pregnancy.	Design: Randomized controlled trial. Recruitment: Prospectively between 1985 and 1993. Women were recruited via the Hungarian family planning programme. Randomization: method not reported. Data collection/ Follow-up: until the end of pregnancy (self-reported pregnancy outcome. confirmed by their physician). Infants were followed up with physical examination.	In- exclusion criteria: women planning pregnancy, not infertile. Study population: N=4,862 (intervention group n=2,471, comparison group n=2,391). Baseline characteristics: not reported. Loss to follow-up: Intervention group 0.9%, comparison group 0.9%. Setting: Qualified nurses of the Hungarian family planning programme.	Outcomes: Association of birth defects with maternal periconceptional multivitamin use containing folic acid. Results: Daily maternal periconceptional multivitamin use was associated with: - A non-significant risk reduction for orofacial clefts: OR=0.77; 95% CI 0.22-2.69. - A non-significant increased risk for cleft lip with or without cleft palate: OR=1.29; 95% CI 0.32-5.22. - A non-significant risk reduction for cleft palate only: OR=0.19; 95% CI 0.01-4.03. - A significant risk reduction for heart defects: OR= 0.42; 95% CI 0.19-0.98. - A non-significant risk reduction for outflow tract defects: OR= 0.48; 95% CI 0.04-5.34. - A significant risk reduction for conotruncal defects: OR= 0.29; 95% CI 0.09-0.97. - A non-significant risk reduction for limb deficiencies: OR=0.19; 95% CI 0.03-1.18.	I-a

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
				- A non-significant risk reduction for hypertrophic pyloric stenosis: OR=0.24; 95% CI 0.05-1.14. - A significant risk reduction for urinary tract defects: OR= 0.21; 95% CI 0.05-0.99. - A significant risk reduction for obstructive and renal agenesis: OR=0.12; 95% CI 0.02-0.69.	
Rolschau 1999[21]	Aim: To study the effect of two doses of folic acid suppletion on birth outcomes Intervention: The intervention group received free folic acid supplements (2,5mg) for daily use; the control group received free supplement (1.0mg) for daily use.	Design: Randomized controlled trial. Recruitment: Prospectively from 1983 to 1986. By campaign (mailings, media, and involved health care professionals) addressing all women 18-35 years. Randomization: Not specified. Not all women were randomized. Data collection/ Follow-up: A registration form was completed by the General practitioner/ midwife/ doctor and kept by the pregnant woman. Length of follow-up: up to the infant's medical examination at 5 months.	In-exclusion criteria: (1) Women aged 18-35, (2) planning pregnancy or already pregnant (3) registered resident in the county of Funen (4) that have not had a prior baby with a NTD (5) multiples and abortions were excluded. Study population: N=8,184 women were randomized; N=14,533 pregnancies in 8,184 women over the course of three years, data was available regarding 14,021 pregnancies with 14,185 infants (13860 single pregnancies; 161 pluri pregnancies with 325 infants). This study gives results of 13,860 single born infants. Baseline characteristics: Total size of groups and characteristics per group not presented. Loss to follow-up: Not accounted for. Setting: Funen country, Denmark.	Outcomes: Birth weight, incidence of preterm, low birth weight (≤2,500 gram) and small for gestational age (weight for gestational age <2SD than the average, excluding congenital anomalies and stillborn). Results: Intervention versus control group versus no folic acid: - Birth weight at gestational age: no significant differences in gestational weight (results not given); when FA was started preconceptionally gestational birth weight was higher. - Preterm birth (excluding congenital abnormalities and perinatal deaths): no difference between different doses. - Low birth weight: 40.9% vs. 51.5% and 59.8% p=0.01. There was no difference between users of 2.5mg and 1.0 mg FA. - SGA: 14.7‰ when FA was started preconceptionally and 17.4‰ when started during the first 19 weeks of pregnancy. No difference was observed between 2.5 and 1.0 mg FA.	I-a
Ulrich 1999[22]	Aim: To study prevalence of congenital abnormalities in a subset of Rolschau 1999. Intervention: see Rolschau 1999.	Design: subset of the study of Rolschau 1999, a randomized controlled trial. Recruitment: See Rolschau 1999. Randomization: Only randomized women in Rolschau 1999 were included in this subset.	In-exclusion criteria: See Rolschau et al. Study population: N=8,293 infants born from 8,184 pregnancies. Baseline characteristics: Folic acid use before pregnancy: n=1,359 (16.6%) and during the first 19 weeks of pregnancy in n=6,825 pregnan	Outcome: Selected congenital anomalies (neural tube defects (omitted from our report) cardiovascular anomaly, limb reduction defects, urinary tract anomalies, oral clefts, talipes, hypospadias). Results: 2.5mg folic acid versus 1.0mg folic	I-a

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
		Data collection/ Follow-up: Complementary to the data collection for Part I of the study (see Rolschau 1999) information on congenital malformations was extracted from (1) the European Registration of Congenital Anomalies and Twins (Eurocat) and, (2) hospital records.	cies (83.4%). There were n=224/8,293 infants with congenital abnormalities. Loss to follow-up: Not accounted for. Setting: See Rolschau 1999.	acid: - Cardiovascular anomalies: 15/4165 versus 12/4128 versus. 13/2742. - Limb reduction defects: 1/4165 versus 2/4128 versus 2/2742. - Urinary tract anomalies: 9/4165 versus 4/4128 versus 2/2742. - Oral clefts: 13/4165 versus 7/4128 versus 6/2742. - Talipes: 3/4165 versus 6/4128 versus 6/2742. - Hypospadias: 5/4165 versus 7/4128 versus 5/2742.	
Czeizel 2004[23]	Aim: To compare informative offspring of women that used multivitamin supplements and women that did not. Intervention: The intervention group received periconceptional suppletion with daily multivitamin (containing 0.8 mg folic acid) from at least one month before conception. Supplements were provided. The comparison group did not use suppletion.	Design: Cohort controlled trial. Recruitment: Prospectively from 1993 to 1996. Supplemented women were recruited from a Hungarian Preconceptional clinic. Unsupplemented women were recruited at antenatal care clinics between the 8th and 12th week of pregnancy. Matching: Unsupplemented women were matched to supplemented women on base of age, socioeconomic status, place of residence and year of pregnancy. Data collection/ Follow-up: Questionnaires, interview, personal notes, counting of remainder of tablets. Pregnancy outcomes were extracted from a pregnancy outcome certificate. Congenital defects were detected in neonatal follow-up up to the twelfth month and in autopsy reports of infant deaths or stillborn infants.	Inclusion criteria: (1) Not sterile or subfertile women; (2) capable of conception within one year; (3) not currently pregnant (4) women that didn't use supplements longer than 7 days were excluded. Study population: N=6,246 pregnant women (n=3,123 supplemented and n=3,123 unsupplemented). Baseline characteristics: not reported. Loss to follow-up: Pregnancy outcomes could not be clarified in 54 supplemented and 47 unsupplemented women. There were 3,069 pregnant women analysable in each cohort. Setting: 31 countryside centers in Hungary.	Outcomes: Occurrence of congenital abnormalities (urinary tract anomalies, cardiovascular anomalies, pyloric stenosis, limb deficiencies, and oral facial clefts) amongst folic acid supplemented and unsupplemented women in live born or still born or terminated pregnancies in 2nd and 3rd trimester. Results: Supplemented vs. unsupplemented: - Cardiovascular malformations: n=31 vs. n=50 (OR=0.60; 95%CI 0.0.38-0.96); Ventricular septum defect: n=5 vs. n=10 (OR=0.26; 95%CI 0.08-0.73); Conotruncal defects (transposition of great vessels, Fallot): n=3 vs. n=1 (OR=3, 95% CI 0.24-15.0); Atrial septum defects Type II: n=9 vs. n=13 (OR=0.69; 95% CI 0.27-2.76). - Urinary tract congenital anomalies: Renal dysgenesis: n=2 vs. n=0; Cystic kidney: n=2 vs. n=0; Obstructive congenital anomalies: n=2 vs. n=19 (OR=0.52; 95%CI 0.24-1.13). - Congenital pyloric stenosis: n=0 vs. n=2. - Limb deficiencies: n=1 vs. n=3 (OR=0.33; 95%CI 0.01-3.71). - Orofacial clefts: n=4 vs. n=3 (OR=1.33; 95%CI 0.23 – 9.11).	II-2

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
Watkins 2004[24]	Aim: To determine if folic acid consumption is influenced by providing free folic acid supplements or fortified breakfast cereal to non-pregnant women of childbearing age. Intervention: Provision of folic acid pills (400 mcg), educational materials about folic acid, and super-fortified cereal (fortified with 400 mcg of folic acid per serving).	Design: Cohort study. Recruitment: Prospectively between 2000 and 2001 from six family clinics in Georgia. Patient sampling: unclear. Data collection/ Follow-up: Brief survey and blood sample after each clinic visit.	In-exclusion criteria: Non-pregnant women aged 18-45 years. Study population: N=1,093. Baseline characteristics: age 87.5% <35 years; race/ethnicity 54.1% White, 40.5% Black, 4.9% Other; 48.9% high school graduate or less; 32.4% smoker. Loss to follow-up: N=928 visited only once; response rate of 15.1%. Setting: Six family planning clinics in Georgia.	Outcomes: Change in the self-reported use of folic acid and change in mean serum folate levels. Results: The interventions did not significantly influence self-reported folic acid consumption (OR= 1.18; 95% CI 0.76-1.83) or mean serum folate levels (results not shown, p-values >0.1).	II-2
Robbins 2005[25]	Aim: To assess efficacy of a physician-based intervention during routine gynaecologic visits on women's folic acid supplementation. Intervention: The intervention group received folic acid counselling and 30 folic acid tablets from the gynaecologist at start, a reminder phone call from a research nurse 1 to 2 weeks after the counselling and a pamphlet. The control group received counselling on non-pregnancy related preventive health behaviors; a pamphlet on folic acid and a coupon for free folic acid.	Design: Randomized controlled trial. Recruitment: Prospectively. Women were recruited via four clinics (two were academic and 2 were private practiced). Randomization: At patient level – method not described. Data collection/ Follow-up: Self-reported folic acid use at baseline and assessed by phone interview 2 months later.	In-exclusion criteria: (1) Non-pregnant women aged 18-45 years capable of becoming pregnant; (2) attending a routine gynaecologic visit (not for preconception care); (3) understanding English (4) women with a pregnancy affected with a neural tube defect in the past were excluded. Study population: N=322 (intervention group n=162; comparison group n=160). Loss to follow-up: 13% (follow-up telephone interview unsuccessful n=40 and refused to complete the follow-up n=3). 279 patients completed the study (87%). Setting: 2 academic and 2 private clinics.	Outcomes: Changes in daily (7 days/week) and weekly (at least 1 day/week) folic acid use. Results: - Weekly folic acid intake increased in the intervention group by 68% vs. 20% in the comparison group (p=0.008). - No significant differences were found in daily intake.	I-a
Schwarz 2008[26]	Aim: To assess efficacy of a one-time 15-minute computer-assisted counselling with provision of 200 free folate tablets in increasing women's use of folate supplements. Intervention: Computerized counselling about periconception folate supplementation with nine questions and answers in the form of short video segments. Each subject was provided with 400 mcg folate with written instructions to use daily. The control group received counselling on emergency contraception. Emergency	Design: Randomized controlled trial. Recruitment: Prospective recruitment from two urgent care clinics in San Francisco in in 2005. Randomization: Allocation occurred with computer-generated sequences. Data collection/ Follow-up: A phone survey six months post enrolment.	In-exclusion criteria: English-speaking women aged 18-45 years. Women unlikely to become pregnant were excluded (she was currently pregnant/ she had undergone a hysterectomy or tubal ligation/ intrauterine device in place/ vasectomized partner) as were women without a phone Study population: N=583 women were screened; exclusion criteria applicable to n=137; n=446 were randomized (intervention group n=227, comparison group n=219). Baseline characteristics: not specified, except that 4% stated that they were	Outcomes: Folate supplements use In intervention group compared to the control group. Results: Folate supplement use in the intervention group vs. the control group: 32% vs. 21%, RR=1.54; 95% CI=1.12-2.13; p=0.007.	I-a

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
	contraception was provided with instructions.		trying to become pregnant. Loss to follow-up: Intervention group n=89, control group n= 92. Women were less likely to complete the follow-up if they were enrolled at the county clinic, had lower incomes, had not completed a college education, and were self-identified as black. Setting: Two semiprivate urgent care clinics in San Francisco.		
Morgan 2009[27]	Aim: To determine if vitamin consumption is influenced by providing a free bottle of multivitamins to non-pregnant women of childbearing age. Intervention: Verbal counselling, provision of written materials, and free bottles of multivitamins containing 400 mcg folic acid.	Design: Cohort study. Recruitment: Prospectively in 2004 from 24 participating health departments. Patient sampling: a proportional-to-size sampling design gathered 3,500 consent forms of which 14% were randomly chosen. Data collection/ Follow-up: Eight to ten months after the intervention a phone call for an eight-question survey and sometimes a written survey was conducted.	In-exclusion criteria: Non-pregnant females of childbearing age were included. Study population: N=500. Baseline characteristics: ethnic origin 60.3% White, 26.6% Latino/Hispanic, 7.5% African American, 2.8% American Indian and 3.4% Other/unknown; age 51.6% <25 years, 34.8% 25-34 years, 13.6% >34 years. Loss to follow-up: N=178 did not completed the survey and were excluded of the analysis (response rate of 64.4%). Setting: Nurses provided care in 24 local county health departments in Western North Carolina.	Outcomes: Change in the self-reported use of multivitamins at eight to ten months follow-up. Results: A greater than two-fold increase (PR=2.1; p<0.001) of daily multivitamin use (25% vs. 53%).	II-2
Individual Interventions: folic acid advice					
de Weerd 2002[28]	Aim: To assess whether counselling of women planning pregnancy to start or continue folic acid supplementation improves folate status. Intervention: Preconceptional advice to take multivitamin containing 400µg of folic acid daily as part of a preconceptional health program containing health promotion (smoking cessation, nutritional habits, information on the antenatal care system).	Design: Cohort study. Recruitment: Prospectively in 1997-1999. Couples were recruited from the fertility clinic or clinic for preconception care clinic. Data collection/ Follow-up: (1) A questionnaire at baseline (2) blood samples before the first consultation and every three - four months after counselling and in the sixth, eighth and twelfth week of pregnancy.	Inclusion criteria: Women planning pregnancy and visiting preconception care clinic (because of previous obstetric complications or other maternal risk factors) or fertility clinic. Study population: N=111. Baseline characteristics: mean age (±SD) 32.5 ±3.5 years; nulliparous 59.5%; White race 97.3%; education level low 13.3%, middle 40%, high 23.8%. Loss to follow-up: Eligible women n=168. Withdrawal: n=23 (reasons not stated), n=33 losses to follow-up (unspecified), n=1 participant was excluded (missing data). Setting: University hospital setting in the	Outcomes: Changes in self-reported folic acid supplementation (any frequency) and red cell folate level (user status was defined as ≥590 nmol/L) and serum folate (user status defined as levels ≥20 nmol/L). Results: - Self-reported supplement use four months after counselling: 54% (compared to 56% of the women at baseline). - Red cell folate level amongst non-users four months after counselling: 680 nmol/L (SD 52 nmol/L) (compared to 540 nmol/L SD± 30 nmol/L). P<0.01. - After one year no significant changes were seen in folate status compared to	II-2

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
			Netherlands. Counselling was performed by a physician.	initial precounselling folate levels: women that already used supplementation pre-counselling maintained their folate use.	
Collective interventions: public campaign					
Chan 2001[43]	Aim: To study the effect of a folate campaign towards targeted health professionals and women of reproductive age. Intervention: Key messages of the folate campaign were: 1) folate/ folic acid intake by women of reproductive age reduces NTD's in the offspring; 2) green leafy vegetables, fruit, cereals contain the most folate; 3) folate/ folic acid intake is important in the periconceptional phase. These messages were incorporated into information leaflets for professionals, consumer pamphlets, guidelines, newsletter, study curricula, presentations towards professionals.	Design: Cohort study. Recruitment: Retrospectively from 1994-1998. Recruitment of two groups: (1) women through random dialling and (2) women post-delivery consecutively. Data collection/ follow-up: Folic acid intake by computer assisted telephone interviews pre-campaign (1994) and during the campaign (1995, 1996 and 1998) and folate use with postnatal questionnaires (delivery: 1996-1998).	Inclusion criteria: Women aged 15-44, postnatal, that delivered in 1995 and 1996. Study population: N=512. Baseline characteristics not provided; characteristics are reported to be the same in all pre- and post-campaign measurements. Baseline characteristics: not reported. Loss to follow-up: Not applicable. Setting: Health professionals approached for the campaign were general practitioners, pharmacists, dieticians, nurse and medical staff of the child and youth health service in South Australia.	Outcomes: Folate consumed before and in the first three months of pregnancy. Results: - Women reported to have increased folate rich food consumption: in 1995 12.0% vs. 18.6% in 1996. - Self-reported periconceptionally folic acid use of women increased: 1995 10.1%, 1996 26.7%, 1998 46.1%.	II-2
Myers 2001[44]	Aim: To evaluate the effect of public health campaign with periconceptional maternal daily consumption of 400 mcg of folic acid and the risk for imperforate anus in the offspring. Intervention: Intake of daily one pill containing 400 mcg of folic acid from the time of premarital examination of women and until the end of the first trimester of pregnancy.	Design: Cohort study. Recruitment: Prospectively between 1993 and 1995. Women were recruited from the pregnancy monitoring system. Follow-up/ data collection: Free bottles of folic acid to women; three blinded pediatricians reviewed birth reports of liveborn and stillborn infants of at least 20 weeks' gestation.	In-exclusion criteria: All women who registered with the pregnancy monitoring system were included. Multiple pregnancies were excluded. Study population: N=222,314 (n=126,783 women taking periconceptional folic acid; n=95,531 not taking periconceptional folic acid). Baseline characteristics North vs. South: mean age 25.2 years vs. 25 years. Loss to follow-up: Not applicable. Setting: Village health care workers in two provinces of China.	Outcomes: Association of imperforate anus with maternal periconceptional folic acid supplementation. Results: Periconceptional daily 400 mcg folic acid supplementation was, after controlling for maternal age, associated with a risk reduction of 41% in imperforate anus of the child (OR=0.59; 95% CI 0.33-1.07).	II-2

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
Gindler 2001[45]	Aim: To evaluate the effect of public health campaign with periconceptional maternal daily consumption of 400 mcg of folic acid and the occurrence of miscarriages. Intervention: Intake of daily one pill containing 400 mcg of folic acid from the time of premarital examination of women and until the end of the first trimester of pregnancy.	Design: Cohort study. Recruitment: Prospectively between 1993 and 1995 from the pregnancy monitoring system. Follow-up/ data collection: Free bottles of folic acid to women; booklet with data on past pregnancy history, the prenatal period and delivery.	Inclusion criteria: (1) Women residing in Jiaxing City who had a premarital examination, (2) primigravid (3) who registered with the pregnancy monitoring system. Study population: N=23,806 (n=21,935 women taking periconceptional folic acid; n=1,871 not taking periconceptional folic acid). Baseline characteristics periconceptional folic acid use vs. no use of folic acid: age at pregnancy 23.5 years SD 1.5 vs. 23.8 years SD 2.1; BMI mean 20.4 SD 2.2 vs. 20.5 SD 2.2; high school education 5.3% vs. 11.4%; farmer 55.6% vs. 54.8%. Loss to follow-up: Not applicable. Setting: Village health care workers in China.	Outcomes: Association of miscarriages with maternal periconceptional folic acid use. Results: Compared with women who had no folic acid use, the RR of miscarriage for women with periconceptional folic acid use was 1.03; 95% CI 0.89-1.20.	II-2
Collective interventions: fortification					
Gucciardi 2002[46]	Aim: To study trends in the total incidence of open neural tube defects in Canada capturing the fortification period. Intervention: Folic acid fortification of grain is mandatory as of 1998.	Design: Cohort study. Recruitment: Population based retrospectively from 1986 to 1999 from the Canadian Congenital Anomalies Surveillance System and hospital data. Data collection/ follow-up: Collection of the total incidence of NTDs by combining the numbers of NTDs occurring in live births, stillbirths and therapeutic abortions.	Inclusion criteria: All live births, stillbirths and therapeutic abortions with neural tube defects registered in the databases and hospital data. Therapeutic abortions in free-standing abortion clinics were not included. Study population: Total neural tube defects n=3,207 (live births n=1,503; stillbirths n=425; therapeutic abortions n=1,279). Baseline characteristics: not reported. Loss to follow-up: Not applicable. Setting: Ontario, Canada.	Outcomes: Changes in neural tube defects birth incidence per 10,000 (live births and stillbirths only). Results: - Total neural tube defect incidence rate increased by 38% from 1986 to 1995 (11.7 to 16.2/10000 pregnancies, p<0.001); decreased by 47% from 1995 to 1999 (8.6/10000 pregnancies, p<0.001). – neural tube defect birth incidence decreased by 50% from 1986 to 1999 (10.6 to 5.3/10000 births, p<0.001). - Rate of neural tube defects in live births declined by 50% from 8.6/10000 live births in 1986 to 4.3/10000 live births in 1999 (p<0.001). - The rate of stillbirths with a neural tube defect decreased by 53%, from 33.6/1000 stillbirths in 1986 to 15.9/1000 stillbirths in 1999 (p<0.001). - From 1986 to 1995 the rate of therapeutic abortions in which a neural tube defect or hydrocephalus was detected rose 190%,	II-2

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
				from 17.5 to 50.7 per 10000 abortions (p<0.001). By 1999 it had fallen by 43% to 28.7/10000 abortions (p<0.001). This resulted in a decrease in the ratio of neural tube defect-affected births to therapeutic abortions from 3:1 in 1986 to 1:1 in 1999.	
Honein 2001[47]	Aim: To study the effect of folate food fortification with folic acid on neural tube defect birth prevalence. Intervention: Folic acid fortification of grain is mandatory as of 1998. The comparison group was born prior to the fortification period.	Design: Cohort study. Recruitment: Population based retrospectively between 1990 and 1999. Patient sampling: pre-fortification group (infants born from October 1995-1996) vs. post-fortification group (infants born from October 1998-1999). Data collection/ Follow-up: Cases with infants with spina bifida and anencephaly were collected from birth certificate information.	In- exclusion criteria: (1) Infants with spina bifida/ anencephaly or any congenital abnormality, (2) born in 45 states (that registered congenital anomalies on the certificate). Study population: N= 39,434,211. Baseline characteristics: not provided. Loss to follow-up: Not applicable. Setting: 45 states of the U.S.A.	Outcomes: Comparison of pre- and post-fortification spina bifida and anencephaly prevalence rates. Results: Decline in total neural tube defects post-fortification compared to pre-fortification: 19% (PR= 0.81; 95 CI 0.75-0.87).	II-2
Persad 2002[48]	Aim: To assess changes in annual incidence of open neural tube defects, in Nova Scotia after the introduction of folic acid fortification. Intervention: Folic acid fortification of grain is mandatory as of 1998.	Design: Cohort study. Recruitment: Population based retrospectively from 1991 to 2000 from the Nova Scotia Atlee Perinatal Database and from the Fetal Anomaly Database. Patient sampling: pre-fortification selected all open neural tube defects registered in 1991-1997 vs. post-fortification selected all open neural tube defects registered in 1998-2000. Data collection/ Follow-up: Collection of annual incidence rates pre- and post-fortification.	In-exclusion criteria: All live births, stillbirths and terminated pregnancies with open neural tube defects over a 10-year period registered in the databases. Study population: Total births n=107,851; cases n=239. Baseline characteristics: not reported. Loss to follow-up: Not applicable. Setting: Nova Scotia, Canada.	Outcomes: Annual incidence changes of open neural tube defects, and of the subgroups spina bifida and anencephaly, per 1000 births (live births, stillbirths and terminations) pre- and post-fortification. Results: - The total annual incidence of open neural tube defects fell by 54% after folic acid fortification, from 2.58/1000 births on average during 1991-1997 to 1.17/1000 births during 1998-2000: RR=0.46; 95% CI 0.32-0.66; p<0.001. - Subgroup analysis of spina bifida, the mean annual incidence decreased from 1.51/1000 births before to 0.62/1000 births after fortification: RR=0.40; 95% CI 0.25-0.67; p<0.001. - Subgroup analysis of anencephaly, the mean annual incidence decreased from 0.93/1000 births to 0.38/1000 births after fortification: RR=0.41; 95% CI 0.22-0.77; p=0.0004.	II-2

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
Ray 2002[49]	Aim: To assess the effect of folic acid food fortification before and after on the prevalence of open neural tube defects. Intervention: Folic acid fortification of grain is mandatory as of 1998.	Design: Cohort study. Recruitment: Population based retrospective from 1994 to 2000 from the Ontario MSS database. Patient sampling: pre-fortification selected neural tube defects registered 1994-1997 vs. post-fortification selected neural tube defects registered 1998-2000. Data collection/ follow-up: Antenatal diagnosed open neural tube defects (based on ultrasonography or fetal autopsy after therapeutic termination) and postnatal diagnosed open neural tube defects (based on all live born and stillborn affected infants after 20 weeks' gestation) pre- and post-fortification.	In-exclusion criteria: All antenatal and postnatal diagnosed open neural tube defects among women residing in Ontario and registered in the MSS database were included. Study population: N=218,977 and n=117,986 women were screened for open neural tube defects pre- and after fortification respectively. Cases of open neural tube defects n=248 and n=69 pre- and after fortification respectively. Baseline characteristics pre- vs. after fortification: maternal age mean 30.1 years (SD 0.16) vs. 30.3 years (SD 0.081). Loss to follow-up: Not applicable. Setting: Ontario, Canada.	Outcomes: Decrease in the prevalence of open neural tube defects per 1000 pregnancies after fortification. Results: - The prevalence of open neural tube defects decreased from 1.13/1000 (n=248) pregnancies before fortification to 0.58/1000 (n=69) pregnancies thereafter: PR=0.52; 95% CI 0.40-0.67, p<0.0001. -The prevalence of anencephaly decreased from 0.38/1000 (n=84) pregnancies before fortification to 0.16/1000 (n=19) pregnancies thereafter: PR=0.42; 95% CI 0.26-0.69, p<0.0002. - The prevalence of spina bifida decreased from 0.75/1000 (n=164) pregnancies before fortification to 0.42/1000 (n=50) pregnancies thereafter: PR=0.57; 95% CI 0.41-0.78, p<0.0001.	II-2
Williams 2002[50]	Aim: To assess the effect of folic acid food fortification before and after on the prevalence of spina bifida and anencephaly. Intervention: Folic acid fortification of grain is mandatory as of 1998.	Design: Cohort study. Recruitment: Population based retrospective from 1995 to 1999 from 24 birth defects population-based surveillance systems. Patient sampling: pre-fortification 1995-1996 or during optional fortification 1997-1998 or during mandatory fortification 1998-1999 registered selected neural tube defects. Data collection/ follow-up: Collection of the prevalence of neural tube defects (live births, stillbirths, fetal deaths, and elective terminations) using data from nine surveillance systems with prenatal ascertainment and data from 13 surveillance systems without prenatal ascertainment and electively terminated cases during the three periods.	In-exclusion criteria: All antenatal and postnatal diagnosed open neural tube defects among women residing in Ontario and registered in the MSS database were included. Study population: N=5,630 cases of spina bifida and anencephaly from 1995-1999. Baseline characteristics: not reported. Loss to follow-up: Not applicable. Setting: 24 states in the United states of America.	Outcomes: Decrease in the prevalence of neural tube defects after fortification. Results: Prevalences from the pre- to the mandatory fortification period: - Spina bifida decreased 31%: PR=0.69; 95% CI 0.63-0.74. - Anencephaly decreased 16%: PR=0.84; 95% CI 0.75-0.95. - Spina bifida decreased 40%: PR=0.60; 95% CI 0.51-0.71 among the nine programs with prenatal ascertainment and 28%: PR=0.72; 95% CI 0.65-0.80 among the thirteen programs without prenatal ascertainment.	II-2
CDC 2004[51]	Aim: To assess the effect of folic acid food fortification before and after on the prevalence of neural tube defects. Intervention: Folic acid fortification of grain	Design: Cohort study. Recruitment: Population based retrospective from 1995 to 2000 from 23 population-based surveillance systems. Patient	In-exclusion criteria: All antenatal and postnatal diagnosed neural tube defects among women residing in Ontario and registered in the MSS database were in	Outcomes: Decrease in the prevalence of neural tube defect affected pregnancies after fortification. Results:	II-2

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
	is mandatory as of 1998.	sampling: pre-fortification selected neural tube defects registered 1995-1996 vs. post-fortification selected neural tube defects registered 1999-2000. Data collection/ follow-up: Collection of the prevalence of neural tube defect-affected pregnancies (live births, stillbirths, fetal deaths, and elective terminations) using data from eight surveillance systems with prenatal ascertainment and data from fifteen surveillance systems without prenatal ascertainment pre- and post-fortification.	cluded. Study population: N=6.9 million pregnancies in 1999. Baseline characteristics: not reported. Loss to follow-up: Not applicable. Setting: United States of America.	- Estimated number of neural tube defect-affected pregnancies declined from 4000 in 1995-1996 to 3000 in 1999-2000. Data from systems with prenatal ascertainment showed: - Before fortification the total annual number of neural tube defect-affected pregnancies was 4130: n=2490 spina bifida and n=1640 anencephaly. - After fortification the total annual number of neural tube defect affected pregnancies was 3020: n=1640 spina bifida and n=1380 anencephaly. –> 27% decline. Data from systems without prenatal ascertainment showed: - Before fortification the total annual number of neural tube defect-affected live births, stillbirths, and fetal deaths at >20 weeks' gestation was 2950: n=1980 spina bifida and n=970 anencephaly. - After fortification the total annual number of neural tube defect -affected live births, stillbirths, and fetal deaths at >20 weeks' gestation was 2180: n=1340 spina bifida and n=840 anencephaly. –> 26% decline.	
Liu 2004[55]	Aim: To evaluate the effectiveness of the public health strategy of food fortification with folic acid and to determine possible adverse effects resulting from fortification. Intervention: Folic acid fortification of white flour, pasta, and cornmeal.	Design: Cohort study. Recruitment: Prospectively between 1997 and 1998. Women and seniors were recruited through a random telephone survey prior to folic acid fortification. Follow-up/ data collection: Women and seniors were followed-up to two years after the start of fortification In person interviews recollected vitamin supplement use, a Willet food frequency dietary questionnaire was taken to assess intake over the past year, and blood samples pre- and	In-exclusion criteria: - Women: non-pregnant of childbearing age (19-44 years) not taking folic acid supplements were included. - Seniors: aged 65 years and over without a vitamin B12 deficiency or anaemia, and not taking vitamin B12 or supplements containing folic acid were included. Study population: Pre- fortification n=233 women, n=202 seniors; post-fortification n=204 women, n=186 seniors. Baseline characteristics: not reported.	Outcomes: Neural tube defect prevalence, red blood cell folate and dietary folate intake pre vs. post fortification. Results: - The total annual rate of neural tube defects fell by 78% after the implementation of folic acid fortification (pre fortification: 4.36/1000 births; post fortification 0.96/1000 births; RR=0.22; 95% CI 0.14-0.35; p<0.0001). Neural tube defects amongst terminated pregnancies were stable throughout the pre- and post-forti	II-2

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
		post-fortification were taken.	Loss to follow-up: Not accounted for (women n=29; seniors n= 16). Setting: Rural and urban sites of Newfoundland, Canada.	fication period. - Significant increases in RBC folate levels for women and seniors after mandatory fortification (625 mol/L [SD 601-649] vs. 818 [SD 784-854]; p<0.001). - The proportion of women aged 19-44 years taking a vitamin supplement containing folic acid increased from 17% to 28% (p<0.003).	
Canfield 2005[53]	Aim: To assess changes in birth defect prevalences since folic acid fortification. Intervention: Folic acid food fortification after 1997.	Design: Cohort study. Recruitment: Population based retrospective between 1995 and 2000 from population-based registries. Patient sampling: pre-fortification selected birth defects in 1995-1996 vs. post-fortification selected birth defects in 1999-2000. Data collection/ follow-up: Collection of prevalence rates pre-fortification and post-fortification.	Inclusion criteria: (1) Infants registered in one of the 23 states affiliated to the National Birth Defects Prevention Network, (2) with one of the selected birth defects (anencephaly, spina bifida without anencephaly, common truncus, transposition of the great arteries, tetralogy of Fallot, ventricle septal defects, cleft palate only, cleft lip without cleft palate, pyloric stenosis, renal agenesis, bladder exostrophy, obstructive genitourinary defects, reduction defects of the upper and lower limbs, omphalocele, Down syndrome), (3) live born or born after pregnancy terminations in 8 states. Study population: Total births n=9,729,763; cases n=96,087. Baseline characteristics: not reported. Loss to follow-up: Not applicable. Setting: 23 states in the USA.	Outcomes: Prevalence rate of congenital abnormalities (PR) (N per 10000 live births) pre- and post-fortification. Results: PR combined with availability of prenatal screening: - Anencephaly PR=0.84; 95%CI 0.76 – 0.94. - Spina Bifida PR=0.85; 95%CI 0.69-0.97. - Common truncus PR=0.88; 95% CI 0.72-1.08. - Transposition of the great arteries PR=0.88; 95% CI 0.81-0.96. - Tetralogy of Fallot PR=0.96; 95% CI 0.88-1.04. - Ventricular Septum Defect PR= 0.97; 95%CI 0.94-1.00. - Cleft Palate PR 0.88; 95% CI 0.82-0.95 - Cleft lip and/or palate PR= 0.95; 95% CI 0.90-1.00 - Pyloric stenosis PR= 0.95; 95% CI 0.90-0.99 - Renal agenesis PR= 0.92; 95% CI 0.84-1.01 - Bladder exostrophy PR=1.13; 95% CI 0.82-1.55. - Obstructive genitourinary defects PR =1.12; 95% CI 1.07-1.16. - Upper limb reduction defects PR = 0.89 95% CI 0.80-0.99. - Lower limb reduction defects PR= 0.97 95%CI 0.84-1.11). - Omphalocele PR=0,79; 95%CI 0.66-0.95. - Down syndrome PR=1,06; 95%CI 1,01-1,11.	II-2

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
Botto 2006[52]	Aim: To evaluate international rates and trends of 14 major defects in areas with official recommendations to fortificate or where fortification occurs. Intervention: Folic acid national policy of recommendations or actual food fortification. This varied in type and timing per country.	Design: Multicentre cohort study. Recruitment: Population based retrospective surveillance data through 2003 on major birth defects from 15 population-based registries. Patient sampling: pre-recommendation or fortification selected birth defects vs. post-recommendation or fortification selected birth defects. Data collection/ follow-up: Collection of rates and trends for 14 birth defects.	In-exclusion criteria: Unknown outcomes of pregnancies and subjects with occult spinal dysraphism, including spina bifida occulta, thickened filum terminale, diastematomyelia, caudal regression syndrome, intradural lipoma, lipomeningomyelocele, split notochord, and other forms of myelodysplasia were excluded. Study population: Total births n=1.5 million yearly (from Europe n=1,000,000; from Canada and the USA n=370,000; from Australia n=87,000). Baseline characteristics: not reported. Loss to follow-up: Not applicable. Setting: 15 registries participating in Europe, Australia, Canada and the USA.	Outcomes: Decrease in the prevalence of selected birth defects (live births, terminations), including NTDs, per 1000 births for the time period before and after the year of introduction of national policy of recommendations or fortification. Results: - Significant changes in trends were seen for neural tube defects in areas with fortification but not in areas with supplementation recommendations alone: varying decrease from 10 to 35% in the data of Australia (PPR=0.90; 95% CI 0.82-0.99), Western Australia (PPR=0.70; 95% CI 0.61-0.81); Canada (PPR=0.71; 95% CI 0.53-0.94); and USA (PPR=0.65; 95% CI 0.56-0.76). - For other major birth defects, there was an overall lack of major trend changes after recommendations or fortification.	II-2
Yazdy 2007[56]	Aim: To study the impact of folic acid fortification on orofacial clefts. Intervention: Folic acid fortification of grain is mandatory as of 1998.	Design: Cohort study. Recruitment: Population based retrospective from US birth certificates data. Patient sampling: pre-fortification (1/1990-12/1996) vs. post-fortification (10/1998-12/2002). Follow-up/ data collection: Comparing the prevalence of orofacial clefts among births before and after fortification.	In-exclusion criteria: Infants born with orofacial clefts were included; births between 1997 and 1998 were excluded. Study population: N=38,232. Baseline characteristics: Not specified. Loss to follow-up: Not applicable. Setting: 45 states and the district of Columbia, USA.	Outcomes: Association between folic acid fortification and orofacial clefts. Results: Orofacial clefts declined following folic acid fortification: PR=0.94; 95% CI 0.92-0.96. The decline occurred in non-Hispanic Whites, non-smokers, and women who received prenatal care in the first trimester.	II-2
de Wals 2007[54]	Aim: To assess changes in the prevalence of before and after folic acid fortification. Intervention: Folic acid fortification of grain is mandatory as of 1998.	Design: Cohort study. Recruitment: Population based retrospective from 1993 to 2002 from multiple sources ranging from provincial databases, registry databases and medical records. Patient sampling: pre-fortification selected neural tube defects registered before 1997 vs. post-fortification selected neural tube defects registered after 2000. Data collection/ follow-up: Collection of	In-exclusion criteria: All live births, stillbirths and terminated pregnancies diagnosed with neural tube defects among women residing in seven of the ten Canadian provinces were included. Subjects with occult spinal dysraphism, including spina bififda occulta, thickened filum terminale, diastematomyelia, caudal regression syndrome, intradural lipoma, lipomeningomyelocele, split notochord,	Outcomes: Decrease in the prevalence of neural tube defects per 1,000 births (live/stillborn and terminated pregnancies) after fortification. Results: - The prevalence of neural tube defects decreased from 1.58/1,000 births before fortification to 0.86/1,000 births during the full-fortification period, 46% reduction; 95% CI 40-51.	II-2

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
		annual incidence rates of neural tube defects pre- and post-fortification.	and other forms of myelodysplasia were excluded. Study population: Total births n=1.9 million, cases n=2446. Baseline characteristics: not reported. Loss to follow-up: Not applicable. Setting: Seven provinces in Canada.	- The decrease was greater for spina bifida (53%) than for anencephaly and encephalocele (38% and 31%, respectively).	
V PROGRAMS					
Individual Interventions					
Czeizel 1999[29]	Aim: To evaluate the effect of ten years preconception care. Intervention: A check-up of reproductive health, three months preparation for conception (smoking cessation, alcohol drinking, drug and medication use) and better protection in early pregnancy.	Design: Cohort study. Recruitment: Prospectively during 1984-1994. Women were recruited by physicians, midwives, nurses and social workers. Data collection/ follow-up: Four visits to a preconception care clinic (of which the third and fourth occur during pregnancy) with laboratory testing and data collection of pregnancy outcome by birth certificate.	In- exclusion criteria: Voluntary of non-pregnant and non subfertile women. Study population: N=8,837 of which 6,060 confirmed pregnancies. Age: mean 25.8 years ± 3.4, 85% was primiparous, 60% had the highest class of education. Loss to follow-up: None reported. Setting: Risk screening by qualified nurses in an outpatient clinic in Hungary.	Outcomes: Smoking cessation (verified by urine cotinine). Results: At initial consultation 17.9% was a smoker vs. 12.4% 3 months later.	II-2
Lumley 2006[30]	Aim: Assessment of the effect of pre-pregnancy information, advice and counselling on birth weight on subsequent pregnancy outcomes. Intervention: The intervention group received a home visit with counselling (social health and lifestyle problems/ timing of pregnancy/ family history/ immunization/ referrals for health problems) and a reminder card. The comparison group only received a visit about postpartum experiences.	Design: Randomized controlled trial. Recruitment: Women were recruited at the Maternal and Child Health Centres between 1982 and 1994. Data collection/ follow-up: Data on the subsequent pregnancy outcome was collected by visit, telephone and mail.	In- and exclusion criteria: Postpartum women attending government funded local Maternal and Child Health centres, in a community setting with high risk of poor birth outcomes (due to socioeconomic reasons) Women attending specialist care were excluded. Study population: N= 786 (intervention group n=392; comparison group n=394). The two groups did not differ in baseline characteristics. Loss to follow-up: 392/777 and 394/802 women were analysable. Setting: In Melbourne, Australia in a newly established pre-pregnancy walk-in service and the home of the participants. Counselling by midwives.	Outcomes: Primary outcome: difference in birth weight compared to index pregnancy. Secondary outcomes: gestational age at birth, low birth weight (<2500gram), birth weight <10th percentile, perinatal deaths and birth defects. Results: - Birth weight was significantly 97.4 gram lower among infants in the intervention group. - No significant differences were found for preterm birth (OR 1.44; 95% CI 0.73-2.91), low birth weight (OR 1.85; 95% CI 0.91-3.91) or birth weight <10th percentile (OR 1.14; 95% CI 0.55-2.38). - Compared to the controls, the intervention group had more preterm births <32 weeks (10 vs. 1), more birth weights <2000 g (16 vs. 2), and more perinatal deaths due to birth anomalies (5 vs. 2).	I-A

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
Elsinga 2008[31]	Aim: Assessment of preconceptional health counselling. Intervention: The intervention group received counselling after risk assessment. The control group received standard care as provided their general practitioner.	Design: Randomized controlled trial. Recruitment: Prospectively during 2000-2003. Recruited by annual invitations sent by general practitioners to the eligible sample of patients in their practice. Randomization: At the level of general practices. Data collection/ follow-up: Risk assessment questionnaire was sent at baseline and within two months after delivery.	In- exclusion criteria: Women aged 18-40 contemplating pregnancy within one year; in cases were invitation was undesirable women were not invited. Study population: The intervention group: n=211 women and 150 pregnancies; the control group: n= 422 women and 1,914 pregnancies. Baseline characteristics (intervention vs. comparison group): age 20-30 (26,8% vs. 28,5%), age 30 ->40 (73,2% vs. 71,5%); country of birth in the Netherlands (94,7% vs. 87,8%); educational level high (45,1% vs. 37,6). Loss to follow-up: 82% of the questionnaires obtained after pregnancy in the intervention group were analysable vs. 68% in the control group. Setting: General practitioners practices, the Netherlands.	Outcomes: Smoking**, alcohol consumption*, binge drinking*, start of folic acid use*, adverse pregnancy outcomes (premature birth (<37 weeks); low birth weight (<2500grams), small for gestational age (growth <p2,3) and congenital anomalies. * up to 3 months before the pregnancy ** in or up to 3 months before pregnancy Results: Intervention group vs. comparison group: - Smoking cessation**:18% vs. 10% unadjusted OR=3,04; 95%CI 0,95-9,69. - Folic acid use*: 86% vs. 53%; adjusted OR=4,93; 95%CI 2,81-8,66. - Alcohol consumption: * 32% vs. 45%; adjusted OR=1,79 95%CI 1,08–2,97. - Percentage of adverse outcome: 16,2% vs. 20,2%; OR 0.77; 95%CI 0.48-1.22.	I-a
Ockhuijsen 2011[32]	Aim: To assess efficacy of interventions aimed at altering behavior patterns relating to smoking and obesity in a preconception care service integrated in an IVF programme. Intervention: Consisted of counselling (not specified) during visits and by telephone.	Design: Cohort study. Recruitment: Prospectively from 2007 - 2008. Data collection/ follow-up: Self-reported weight and smoking status and measured weight. Follow-up by telephone call or visit every 4 weeks. The length of follow-up was up to 1 year.	In- exclusion criteria: Couples on the waiting list for an IVF treatment who had visited the preconception clinic and were able to read Dutch. Study population: N=101. Baseline characteristics: 30 women had a BMI >30 kg/m2 (mean value of 33.8; SD 3.6); 23 women smoked. Loss to follow-up: n=25 (obese group n=15; smoking group n=10) and were excluded. Setting: Nurses who were trained for preconception care counselling and had at least 3 months experience at an IVF unit, university hospital, the Netherlands.	Outcomes: Mean weight reduction (self-reported and weighed combined) in kg and smoking cessation. Results: Weight loss: - 15/30 women (50%) lost weight (mean 6.1 kg; SD 3.6); 11 of these 15 women reached the goal of losing 5% or more of their original weight. Smoking cessation: - 7/23 women (30%) quit smoking - 6/23 women (26%) reduced the number of cigarettes.	II-2
Williams 2012[33]	Aim: To assess the effect of preconception care on positive maternal behaviors before and during pregnancy.	Design: Cross-sectional study. Recruitment: Retrospectively during 2004 – 2008. Women were recruited by sampling	In- exclusion criteria: Women that had delivered a live birth 2-6 months ago. Women that reported drinking or smoking during	Outcomes: Prepregnancy daily multivitamin consumption, first trimester entry into prenatal care, smoking cessation (not	II-2

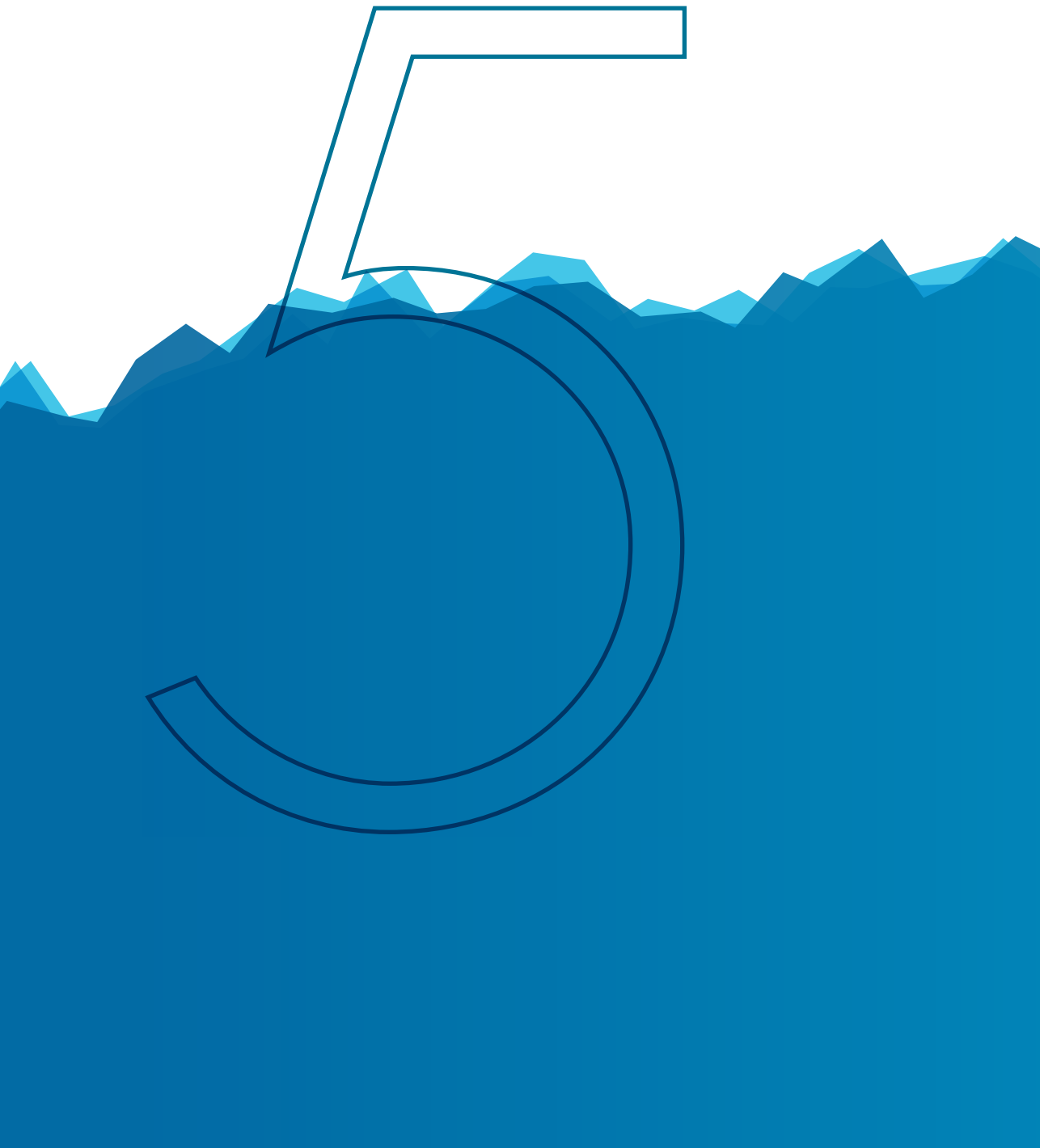
	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
	Intervention: Any form of contact with a health care worker preconceptionally to prepare for a healthy pregnancy and baby compared to no contact with a health care worker to prepare for pregnancy.	of state birth certificates. Data collection/ follow-up: Data from the Pregnancy Risk Assessment Monitoring System (PRAMS) was used; additional data was retrieved by mailed questionnaires. Non-responders were contacted by telephone.	follow-up that did not report this at base line were excluded. Study population: N= 30,481 women of which 9,457 received preconception care. Baseline characteristics: the population that received preconception care contained more women >20 years of age, more non-Hispanic white and black women, years of education ≥12 years, that were married, that were privately insured, have a normal weight, have a prior live birth, have a prior intended pregnancy, have diabetes of a poor prior birth outcome. Loss to follow-up: Response rates ranged from 72 to 89%. Setting: USA (Maine, New Jersey, Utah, Vermont.	smoking on an average day within the prior three months to pregnancy) and cessation of alcohol consumption (not drinking with the last three months prior to pregnancy). Results: Receipt of preconception care was significantly associated with: - Daily consumption of multivitamins one month before pregnancy (AOR 4.35; 95% CI 4.00-4.73). - Cessation of drinking during the three months before pregnancy (AOR 1.34; 95% CI 1.16-1.54).	
Group interventions					
Hillemeier 2008[40]	Aim: To assess the efficacy of a preconceptional health programme. Intervention: The intervention group underwent six 2-hour group sessions spread out over a 12-week period (topics were managing stress, physical activity, nutrition (including folic acid supplementation), preventing gynaecologic infection, tobacco exposure, and alcohol use.) The comparison group did not receive the group sessions.	Design: Randomized controlled trial. Recruitment: Prospectively. Time frame unclear. Women were recruited via triangular community based approach with active (personal communication) and passive recruitment (media, mailings, posters and flyers). Randomization: women were randomized after baseline risk assessment, stratified by site. Data collection/ follow-up: Participants received a baseline and follow-up health risk assessment at 14 weeks (questionnaires, anthropometric measurements, and biomarkers).	In- exclusion criteria: (1) Residence within the 28 county target study region; (2) women aged 18-35; (3) not pregnant at time of enrolment; (4) capable of becoming pregnant; (5) English speaking. Study population: N=692 (intervention group n=473; comparison group n=219). Baseline characteristics intervention vs. comparison group: married or living with partner 59% vs. 48%; mean age 26.52 years (SD 5.02) vs. 24.74 years (SD 4.64); high school education 36% vs. 31%; race White/ non-Hispanic 92% vs. 91%, Other 8% vs. 9%; poor poverty status 27% vs. 29%. Loss to follow-up: 47% in the intervention group and 50% in the comparison group did not attend the follow-up risk assessment. The analytic sample consisted of 362 women (intervention group n=252; comparison group n=110). Setting: Community based; in 15 low-income rural communities, Central Pennsylvania.	Outcomes: Behavioral change related primarily to nutrition and physical activity. Results: Statistically significant behavior changes included greater likelihood of: - Reading food labels to identify nutritional values (OR 2.264; p-value 0.001). - Using a daily multivitamin that contains folic-acid (OR 6.595; p-value <0.001). - Meeting recommended levels of physical activity levels (OR 1.867; p-value 0.019). Significant dose effects were found for: - Reading food labels (OR 1.161; p-value 0.015) - Daily use of multivitamin with folic-acid (OR 1.448; p-value <0.001). - Anthropometric measurements (BMI, waist circumference, and blood pressure) and biomarkers (serum glucose, HDL cholesterol, and total cholesterol) were not significantly different in pre- and post-analysis.	I-a

APPENDIX TABLE 2 (continued)

	Intervention	Methods	Population and setting	Outcomes	Strength of evidence
Weisman 2011[41]	Aim: To assess the long-term effects of the Strong Healthy Women intervention. Intervention: See Hillemeier 2008.	Design: Follow up of the RCT Hillemeier 2008 Data collection/ follow-up: Telephone interviews 6- and 12- months after group sessions in Hillemeier 2008. Birth records from women who gave birth to singletons during the 12-months follow-up period.	In- exclusion criteria: see Hillemeier 2008.40 Study population: The analytic sample n=362 from the original trial were included. Data at 6 months reported on n=315; at 12 months reported on n=302. Data on 45 births were collected. Loss to follow-up: At six-month n=47; at twelve months n=60.These women were excluded.	Outcomes: (1) maintenance of significant pretest-posttest changes; (2) impact on weight, BMI and daily folic acid use, and (3) impact on weight gain during pregnancy. Results: At 12 months follow-up women of the intervention group were more likely: - To use multivitamin with folic acid daily (OR 2.15; 95% CI 1.19-3.88). - To have a lower weight (OR -4.33; 95% CI -8.16- -0.49). - To have a lower BMI (OR -0.75; 95% CI -1.39- -0.11). - Intervention effect on physical activity, consumption of fruit and vegetables was not maintained during the follow-up periods (OR 1.00; 95% CI 0.57-1.76, OR 0.68; 95% CI 0.39-1.21, OR 0.99; 95% CI 0.57-1.71). - Intervention effect on reading food labels for nutritional values decreased between the 6- and 12-month follow-up (OR 1.97; 95% CI 1.07-3.65 and OR 0.70; 95% CI 0.40-1.23).	I-a

PART II

DESIGNING AN INTERVENTION STRATEGY



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 and ABCD studies have contributed to our knowledge of various health problems in pregnancy and childhood and their lasting impact on health in later life.[5,6] 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.[12,13]

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.[14-16] Risks influencing this early pregnancy phase can be modified optimally in the preconception period.[16-18] The Dutch Health Council recommended (2007) to integrate general PCC in the health care system.[19] 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).[20] 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.[20] 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.[4,20-23] 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 effectiveness 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 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.[24] The data are routinely collected by 94% of midwives, 99% of gynaecologists and 68% of paediatricians including 100% of Neonatal Intensive Care Unit paediatricians.[24]

Table 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 1 and 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

Additionally, we compared these outcomes across areas after direct standardisation for population differences by maternal age, parity, ethnicity, and SES.[25] Standardisation 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.

Tables 2 and 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). 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. Based on the sum of the decile scores for the PCC sub-study (table 2), the municipalities have the most adverse outcomes, i.e. 1. The Hague; 2.

TABLE 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 (5 minutes after birth)	3385 (1.4)	14818 (1.1)	18203 (1.1)
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.

FIGURE 1: Absolute prevalence of perinatal mortality per 1000 births.

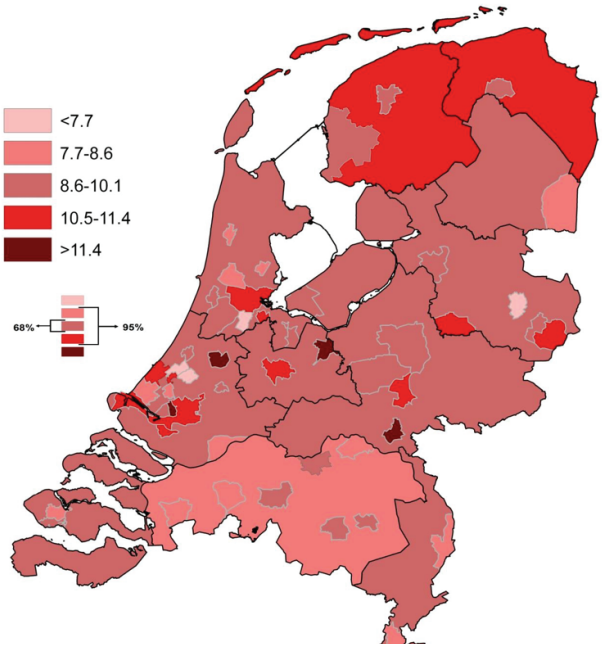


FIGURE 2: Absolute prevalence of 'Big4' morbidities per 1000 births.

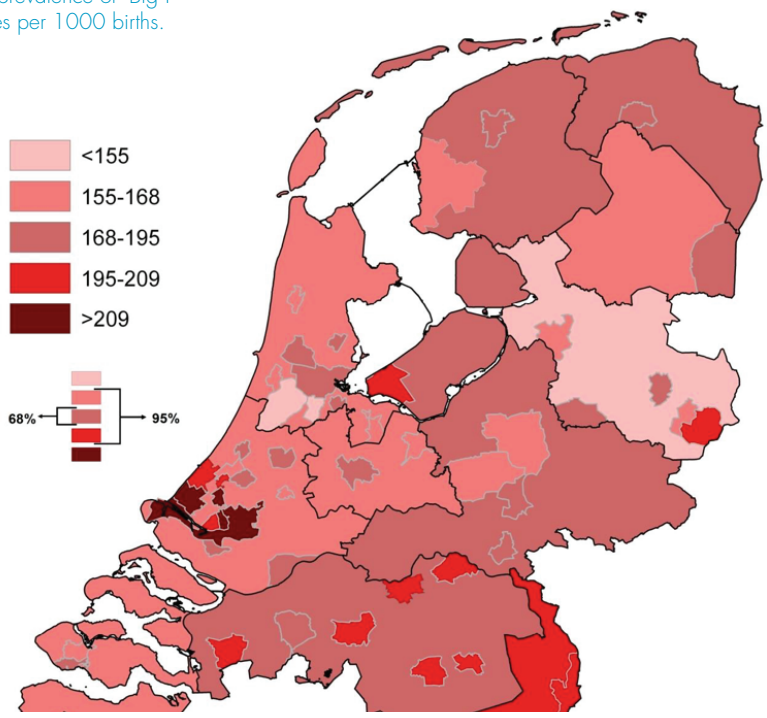


TABLE 2: Selection criteria* for the preconception care experiment with scoring in deciles; the higher deciles represent a more likely qualification for inclusion.

		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

TABLE 2 (continued)

		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	
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

* '% PREG': % Of pregnant women in the general population
* 'AGE <20': % Of teenage pregnancies
* 'NW ETHN': % Of pregnant women with a non-Western ethnicity
* 'LOW SES': % Of 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: 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 city	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

TABLE 3 (continued)

			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	
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

* '% PREG': % Of pregnant women in the general population
* 'AGE <20': % Of teenage pregnancies
* 'PRIMI': % Of primiparous women
* 'NW ETHN': % Of pregnant women with a non-Western ethnicity
* 'LOW SES': % Of 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

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) the following municipalities show the most adverse outcomes: 1. The Hague; 2. Amsterdam; 3. Rotterdam; 4. Arnhem; 5. Tilburg; 6. Nijmegen; 7. Schiedam; 8. Utrecht; 9. Enschede; 10. Spijkenisse; 11. Heerlen; 12. Vlaardingen; 13. Groningen; 14. Leeuwarden[10]. Additional to the identified municipalities, the province of Friesland is best qualified for the PCC sub-study and the province of Groningen for the risk assessment sub-study.

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.

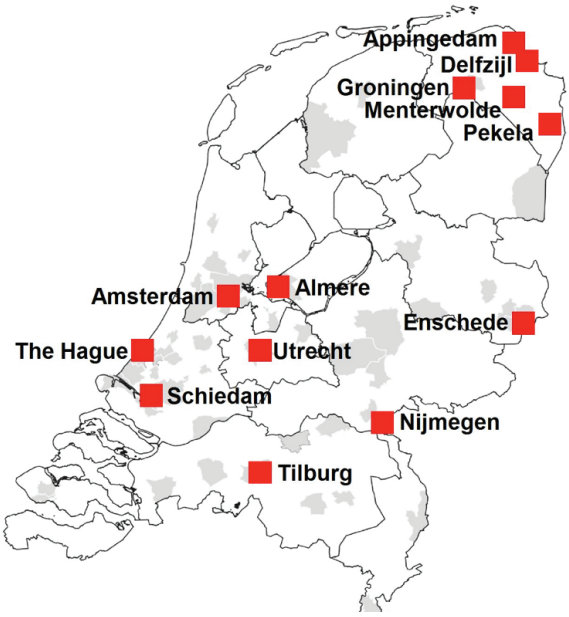
INTRODUCTION TO THE SUB-STUDIES

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 an 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

FIGURE 3: Participating municipalities in the 'Healthy Pregnancy 4 All' project.



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) which lists all conventional (>140) high risk indications (for referral or consultation).[26] 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.

ETHICAL CONSIDERATIONS

The two 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.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHORS' CONTRIBUTIONS

All authors were involved in conception and design of the study. SD, JP, SVV, and AV drafted the manuscript. All authors participated in the design of the study during several meetings. All authors edited the manuscript and read and approved the final manuscript.

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External advisors: J.M.W.M. Merkus MD PhD, [emeritus] professor of Obstetrics and Gynecology and E.W. Steyerberg PhD, professor of medical decision making, Departments of Obstetrics and Gynecology, and Public Health, Erasmus MC, Rotterdam, The Netherlands.

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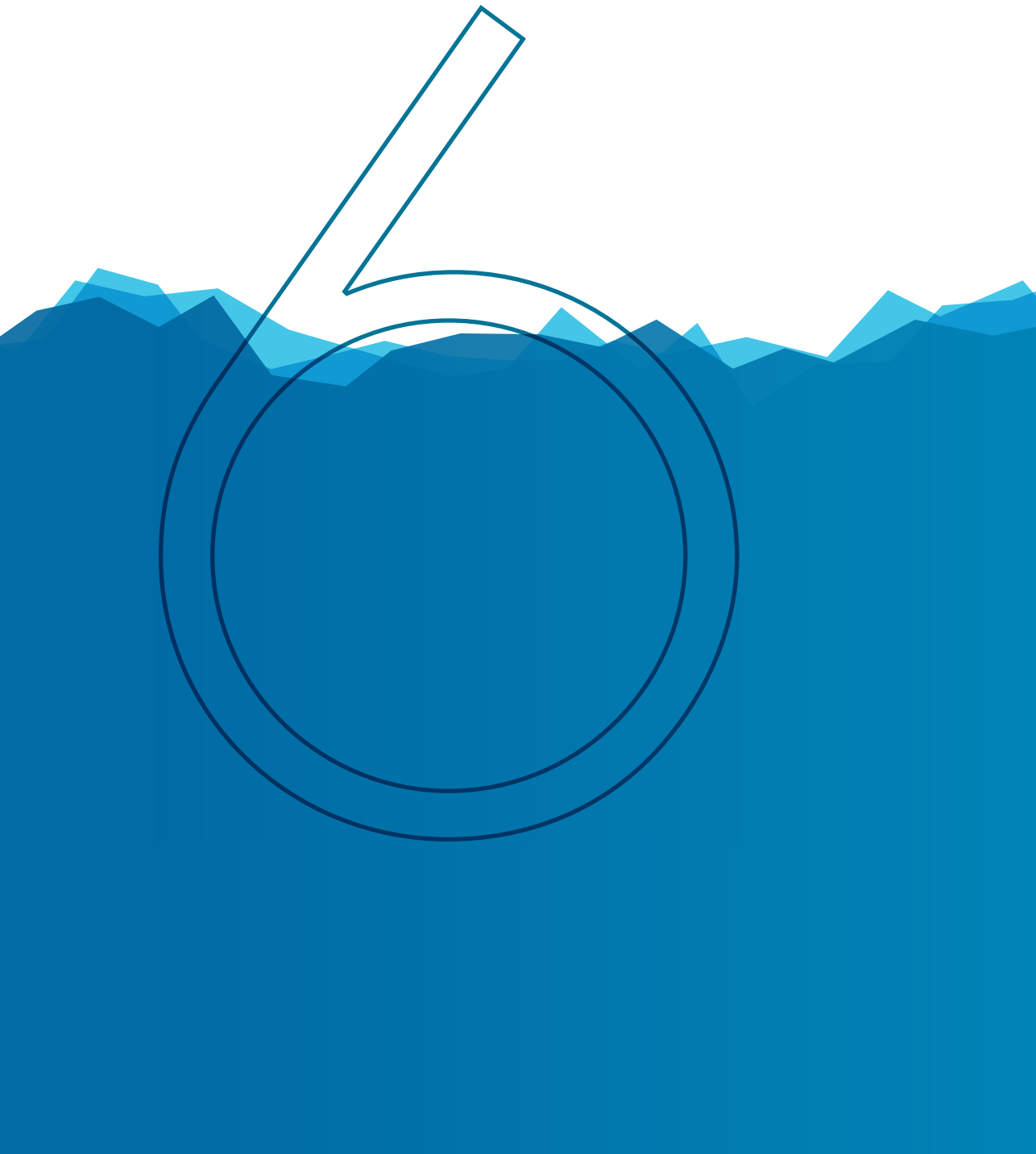

EFFECTIVENESS OF GENERAL PRECONCEPTION CARE ACCOMPANIED BY A RECRUITMENT APPROACH: PROTOCOL OF A COMMUNITY-BASED COHORT STUDY

(THE HEALTHY PREGNANCY 4 ALL STUDY)

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ABSTRACT

Introduction: Promotion of healthy pregnancies has gained high priority in the Netherlands because of the relative unfavourable perinatal outcomes. In response, a nationwide study Healthy Pregnancy 4 All (HP4All) has been initiated. One of the substudies within HP4All focuses on preconception care (PCC). PCC is an opportunity to detect and eliminate risk factors before conception to optimise health before organogenesis and placentation. The main objectives of the PCC substudy are (1) to assess the effectiveness of a recruitment strategy for the PCC health services and (2) to assess the effectiveness of individual PCC consultations.

Methods/analysis: Prospective cohort study in neighbourhoods of 14 municipalities with perinatal mortality and morbidity rates exceeding the nation's average. The theoretical framework of the PCC substudy is based on Andersen's model of healthcare utilisation (a model that evaluates the utilisation of healthcare services from a sociological perspective). Women aged 18 up to and including 41 years are targeted for utilisation of the PCC health service by a four armed recruitment strategy. The PCC health service consists of an individual PCC consultation consisting of (1) initial risk assessment and risk management and (2) a follow-up consultation to assess adherence to the management plan. Primary outcomes regarding the effectiveness of consultations is behavioural change regarding folic acid supplementation, smoking cessation, cessation of alcohol consumption and illicit substance use. The primary outcome regarding the effectiveness of the recruitment strategy is the number of women successfully recruited and the outreach in terms of which population is reached in comparison to the approached population. Data collection consists of registration in the database of women that enrol for a visit to the individual PCC consultations (women successfully recruited), and preconsultation and postconsultation measurements among the included study population (by questionnaires, anthropometric measurements and biomarkers). Sample size calculation resulted in a sample size of n=839 women.

BACKGROUND

The Healthy Pregnancy 4 All (HP4All) study was initiated because of the relatively high perinatal mortality rate of 10 per 1000 births, ranking the Netherlands at an unfavourable position in Europe.[1] A huge concern was the inequality in the perinatal mortality rate within the country: deprived neighbourhoods were found to have an up to four times higher perinatal mortality rate than average.[2] Societal, professional, and political debates about how to improve perinatal health in the Netherlands dominated the policy agenda. One of the results was the launch of the HP4All study - commissioned by the Dutch Ministry of Health and Welfare, in May 2011.[3,4]

The objective of the HP4All study is to develop evidence based strategies to improve perinatal health by interventions in the preconception or the antenatal period, which reduce adverse pregnancy outcomes. Accordingly, HP4All is divided into two sub-studies: the Preconception Care study (PCC) - a prospective cohort study - and the antenatal Rotterdam Risk Assessment (R4U) study – a cluster randomized controlled trial.[5] This paper concentrates on the PCC sub-study.

The rationale of PCC and its delivery approaches

The rationale of preconception care (PCC) originates in the growing recognition that the embryonic development and placentation phase is critical for the outcome of the pregnancy.[6] PCC is a set of interventions that aims to identify and modify biomedical, behavioral, and social risks to a woman's health or pregnancy outcome through prevention and management.[7]

The preconception period can be seen as the earliest link between maternal and newborn health. Therefore it has been recognized as a pivot point which can be utilized to improve perinatal health.[7,8,9] In the Netherlands, 82% of the perinatal mortality cases were preceded by small for gestational age (SGA), premature birth and congenital anomalies.[10] In theory many risk factors for these problems are present and potentially detectable and treatable/ manageable before conception.[6,8] By the time a women enters antenatal care a large part of organogenesis has taken place. PCC should therefore be regarded as a necessary additional component to the obstetric care system, in the improvement of perinatal outcomes.

Organization of PCC

PCC can be organized in three forms: (1) collective PCC consisting of interventions targeted at the general public (e.g. with group education or national campaigns); (2) general individual PCC consisting of individual consultations among couples contemplating pregnancy amongst the general public; (3) specialist individual PCC consisting of individual consultations amongst couples contemplating pregnancy with complex risk factors.[11] These forms can be integrated in different approaches for delivery, dependent on the health system (e.g. primary care, hospital based, PCC clinic) and the targeted audience (e.g high-risk population or general public).[12]

Individual PCC is a unique opportunity for professionally led PCC – which addresses both general risk factors and personal risk factors after systematic screening. Furthermore, individual PCC is an opportunity to deliver PCC in a responsive fashion – so that besides the systematic standard risk factor screening the individual patient's needs or preferences can be met.[13] Thus, individual PCC consultations are seen as the form of PCC to implement in the PCC sub-study.

Recruitment for PCC

The concept of visiting a health care professional for PCC is not common in the Netherlands as well as in many other countries. Firstly, the uptake of PCC requires that a pregnancy is planned. An explanation for low uptake of PCC can be sought in the unfamiliarity of women or couples with the availability and the potential benefits of the health service.[14-16] Women or couples could assume that they are healthy and that it is not necessary to discuss their pregnancy wish with a professional. Women who are aware of risks might believe that nothing can be done to influence the course of a pregnancy in the future. Besides beliefs, actual barriers to attend PCC could also play a role. For instance a woman's or couples willingness to disclose their pregnancy wish to a professional is a known barrier.[16] Simply delivering PCC to women or couples upon request does not seem to be sufficient to provide PCC at a scale to improve perinatal health. An active recruitment approach is necessary. Different active recruitment approaches are described in the literature. Wallace et al., describe that the opportunistic approach of women during daily care is utilised most often by primary caregivers.[17] However, despite the fact that couples in the general public are known to have at least more than one risk factor,[18] many women/couples of reproductive age do not request a PCC consultation from their general practitioner (GP). An opportunistic approach is not feasible for midwives as they rarely see non-pregnant women. One trial employs the approach of inviting women through invitational letters.[19] These approaches, however, require efforts from caregivers in an already stressed system; and the effectiveness is unknown. An evidence-based strategy is necessary to create an outreach for individual PCC consultations in order to improve perinatal health on a larger scale.

The main objective of this study is to implement and evaluate a local recruitment strategy for individual PCC and to promote and evaluate (health) behaviour change by delivery of PCC consultations in primary care. This paper provides an overview of the design and the methodology of the HP4All PCC study.

METHODS/ DESIGN

Key attributes of the study:

The PCC study is designed as a community-based study with a high-risk approach in a primary care setting with tools to improve the uniformity of the health message.

This section describes the key concepts of the study:

- The high-risk approach: The Dutch Ministry of Health, Welfare and Sport, commissioned the HP4All study to target high-risk populations. After ranking the municipalities with the highest

perinatal mortality and morbidity in the country, 14 municipalities were selected as candidates for participation (selection described elsewhere).[4] The key approach of HP4All is to roll out the interventions in high-risk neighborhoods – meaning neighborhoods with rates of adverse perinatal outcomes above the average of the selected municipalities. It is presumed that women in these neighborhoods can benefit the most from interventions in the HP4All study. Prevalence of risky lifestyle behaviors in the preconception phase is not exactly known as there is no surveillance amongst women contemplating pregnancy and risky behaviors tend to be underreported during pregnancy. With regards to folic acid supplementation, a recent Dutch study conducted amongst a multiethnic population reported that 40% of pregnant women to have used folic acid supplements before conception.[20] A different study reported that of 7106 pregnant women, 8% smoked in the first trimester only and 17% continued smoking throughout pregnancy.[21] In total, 35% - 50% of women are estimated to continue their alcohol consumption during pregnancy.[22] The HP4ALL study will provide more information regarding risk behaviors before and in pregnancy in these high-risk neighborhoods.

- The community-based approach: A community-based approach has advantages as it (1) reaches populations which are hard to reach by ensuring trust: collaboration with local health authorities in a community-based approach provides the opportunity that the target population is approached by professionals they know and mostly trust; (2) promotes collaboration and local support as it draws the sectors together necessary for optimal outreach.[23]
- A primary care approach: GP's and midwives practicing in the high-risk neighborhoods are recruited to deliver individual PCC consultations. They were selected because they can deliver the intervention in a responsive fashion, because they are familiar with the target population and by arranging them to provide the PCC consultations, accessibility of PCC is ensured.
- Tools for the consistency of health messages: PCC for the general population necessitates a thorough risk factor screening. Therefore GP's and midwives are facilitated with tools and training to ensure consistency, which is important as different health messages reduce the effectiveness of interventions.[13]

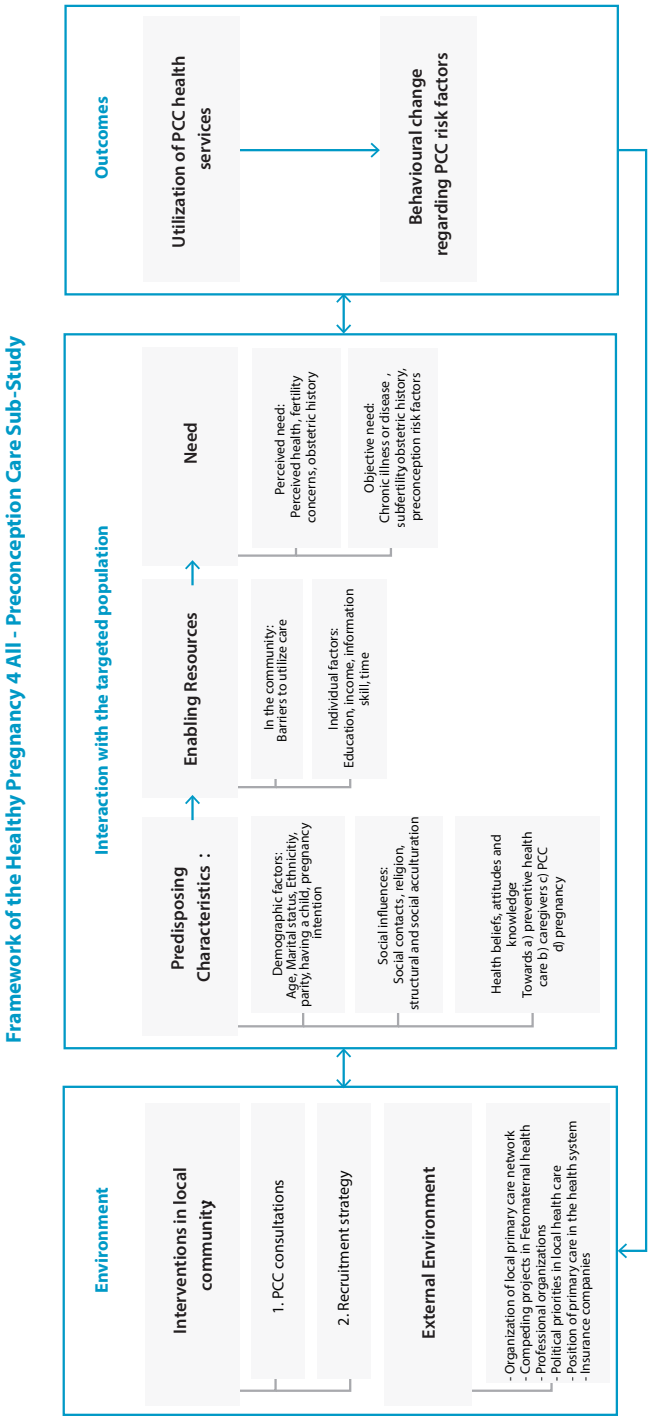
Theoretical framework of the HP4All PCC sub-study

The delivery of PCC in the PCC sub-study is based on the Andersen's model of healthcare Utilization.[24] Andersen defines the utilization of a health service and other personal health behaviors as an outcome. These outcomes are a function of the predisposition (to utilize the health care service) and enabling or impeding factors (to utilize the health care service) and perceived and objective need (to utilize the health care service). These factors originate in the individual which interacts with his/her context. This model has been used to understand utilization of PCC services and other health care services (oral health services, mental health services, primary care).[25,26]

Figure 1 should be read from left to right: The PCC sub-study intervenes in the environment in order to target the population to achieve the outcomes on the right.

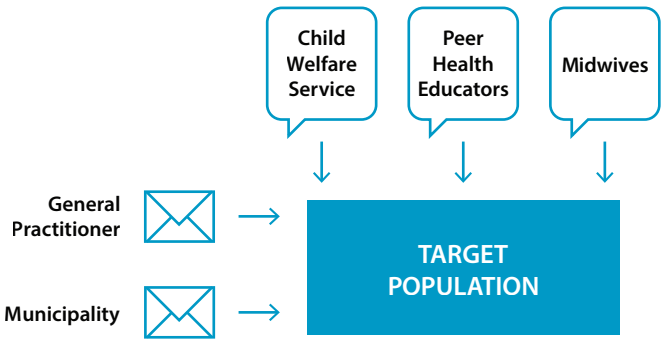
- The environment: The study entails two organizational changes in the environment: Firstly, individual PCC consultations are made available. Secondly, a strategy to recruit eligible women to utilize the PCC services is employed (see Figure 2).

FIGURE 1: The framework for the Healthy Pregnancy 4 All – Preconception care substudy



- The population: The study aims to target women of reproductive age (defined as 18 up to and including 41 years) living in municipalities with high perinatal mortality and morbidity rates with a specified recruitment strategy. Women will however decide individually, within their own context, whether they will use the health care service and/or change their health behaviours. We hypothesize this decision to be a function of:
  - Predisposing factors: In accordance with Andersen's model of health care utilization we contemplate that a woman's decision to utilize PCC will depend on a function of her health beliefs and attitude towards the preconception health service and a healthy pregnancy, social influences and demographic factors.
  - Enabling factors: The targeted woman can be stimulated to visit (or impeded from visiting) the PCC health service by community factors (e.g. a good infrastructure to attend a PCC consultation) or by individual factors (e.g. speaking a different language than the PCC care provider can be a barrier to attending the PCC consultations).
  - Need: The targeted woman needs to feel a need to utilize the service. There are two kinds of need: (1) an objective need (the service is necessary in terms of medical risks) and (2) a perceived need (the service is perceived as necessary by the woman herself). Perceived need can be related to the objective need, but this is not necessarily the case. Factors from the literature or those of which we hypothesized to influence the objective and/or perceived need for a PCC consultation are mentioned in Figure 1. Need, as a resultant of a perceived need and objective need is thought to be influenced by predisposing characteristics (e.g. knowledge regarding risks, social network to point out the relevance of PCC for the individual).
- The outcomes: The primary outcomes of the PCC sub-study are reduction of preconception risks by (1) the utilization of PCC health services and (2) behavioural change regarding preconception risk behaviours. Reduction of preconception risk factors is thought to subsequently reduce (the risk for) perinatal morbidity and mortality.

FIGURE 2: The recruitment strategy of the Healthy Pregnancy 4 All—Preconception Care substudy



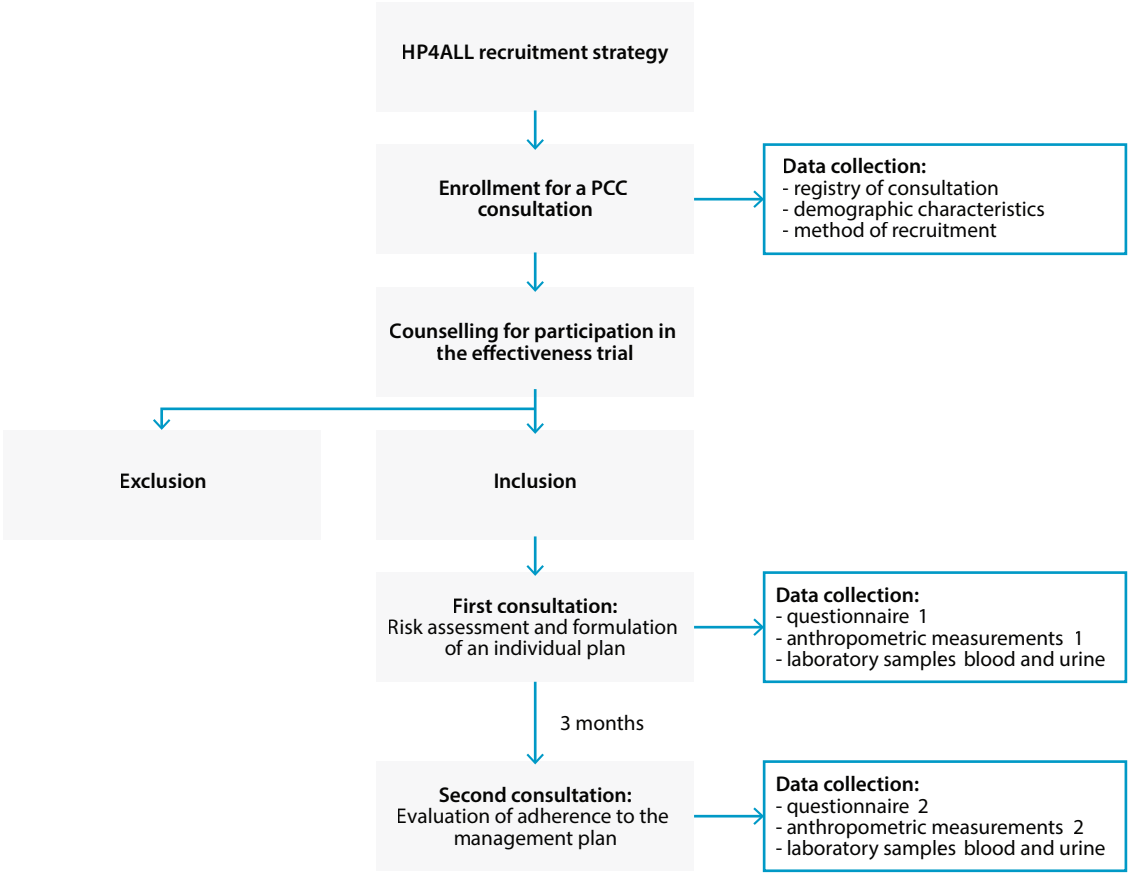
The intervention

As displayed in Figure 3, the Preconception Care Consultation consists of 2 visits to a participating General Practitioner or midwife in the course of 3 months. During the first consultation systematic risk assessment is performed and a tailored management plan to address risk factors. Caregivers evaluate whether goals are reached or whether additional measures are necessary. Consultations are supported and archived with PCC tools (see Box 1).[27,28] The tool for risk assessment (ZwangerWijzer in Dutch) is a validated tool.[29] When women participate in the cohort study as study participants extra data are collected to assess the effectiveness of the provided care (see section on data collection).

Study population

All women aged 18 up to and including 41 years (the adult reproductive life span) who make an appointment at the PCC health service are enrolled (registered in the database) to assess the effectiveness of the recruitment strategy. The additional criteria for inclusion in the cohort study

FIGURE 3: Flowchart for enrollment and intervention and data collection



to assess the effectiveness of PCC are: (1) a pregnancy wish (regardless of in which phase) and (2) voluntary participation. Exclusion criteria are: (1) no permission to be encountered about participation in the study (2) non-response to approach for inclusion (3) not speaking one of the following languages (Dutch, English, Turkish, Polish or Arabic) (4) cancellation/ no-show at the appointment.

Recruitment and enrollment

The recruitment strategy consists of four components (see Figure 2):

(1) an invitational letter from the municipal public health service;

(2) an invitational letter from participating General Practices to their own patients;

(3) Youth Health Care Physicians or nurses inform parents who visit the routine check-ups at the youth health care center for their child with an information leaflet containing the names of the participating practices;

(4) Referral by a preconception health educator after PCC education sessions. (A preconception health educator is a person from the peer group (the local community) who has completed a certified training in health communication skills/ preconception health).

All female applicants for the PCC health care services are registered. These women are sent an information letter followed by a telephone call for individual counselling about participation in the study by the research team. Participants who agreed to take part in the study signed an informed consent form. Women receive the same PCC regardless of participation in the study; participation requires the participant to partake in data collection (questionnaires and laboratory tests) parallel to the care she receives.

Outcomes

The primary outcome regarding the effectiveness of the individual PCC consultations is behavioral change. Behavioral change is assessed for folic acid supplementation, smoking, alcohol consumption and illicit substance use. These four preconception health behaviors were chosen as primary outcomes due to their prevalence, their impact on the fetus and modifiability.[30-35] Differences in these behaviors are assessed by premeasurement and post-measurement by questionnaires (self-reported changes) and biomarkers (biochemical assessment of behavioral change). Biomarkers are used, as it is known that self-reported outcomes can show socially desirable answers. For example in case of the use of folic acid supplements a Dutch study found an over-report of 22% for self-reported folic acid supplement use.[20]

The primary outcome regarding the effectiveness of the recruitment strategy is the utilization of the preconception care services of the program. This is measured quantitatively by the number of women that utilized the preconception care program (women successfully recruited) in relation to the number of women approached by the recruitment strategy. Secondly, the effectiveness of the recruitment strategy is assessed in terms of outreach: by assessing characteristics of women reached. This includes basic demographics of women that were successfully recruited and

identification of predisposing factors, need, and enabling factors according to Andersen's' model of health care utilization amongst women included in study. Data regarding the target group (all women aged 18 up to and including 41 years in the geographically targeted area) is obtained from municipal administrative records.

Outcomes, measures and data sources are presented in Table 1.

Data collection and measurement

BOX 1: Tools for delivery of PCC in the Healthy Pregnancy 4 All - PCC sub-study

Standardised risk assessment instruments improve delivery of PCC; unify risk assessment and facilitate documentation needs. The Healthy Pregnancy 4 All programme uses two tools:

The ZwangerWijzer Tool:

ZwangerWijzer is a self-administered questionnaire for couples designed to be filled in prior to consultation.

The questionnaire is freely accessible on the internet or on paper.[28] The webbased survey has additional features: (1) additional information is provided when a risk factor is present (2) a list of risk factors is generated; listing what should be discussed during the PCC consultation. This list can be emailed to the PCC caregiver.

The questionnaire is adopted from The Preconception Health Assessment Form[47] and a Family History Survey. It covers the following risk domains and risk factors:

Background	Lifestyle	Medical history	Obstetric and Gynecologic history	Family	Work
Maternal age BMI Ethnicity	Exposure to radiation Smoking Alcohol Drugs Eating disorders Nutrition Folic acid supplement use Vitamin A Toxoplasmosis Listeria	STD's HIV Rubella vaccination (Chronic) illness Prescribed medication Over-the-counter drugs	Prior pregnancies Pregnancy complications Uterine anomalies Prior gynecologic surgeries	Family history consanguinity	Chemical exposure Other exposure Infectious agents Shifts/ irregular hours Physically demanding work Stress

The Preconceptiewijzer Tool:

Preconceptiewijzer is a web based PCC archive system complementary to the ZwangerWijzer questionnaire.[27] Providers can create a PCC file for their patients in which the questionnaire can be archived and the consultation(s) can be documented. The tool provides an overview sheet in which present risk factors (identified in ZwangerWijzer) are linked to digital patient information leaflets and protocols for the caregiver about these risk factors. The latter is a measure to improve the uniformity of health messages and interventions. Preconceptiewijzer is available online; providers have an own account which is secured for own use. This account and technical support is freely available.

The process of data collection is illustrated in Figure 3.

All women who make an appointment are registered in the Gemstracker (Generic Medical Survey Tracking system) database.[36] The Gemstracker system firstly helps keep a log of all consultations. Furthermore, the system assists in keeping a log of the inclusion process after which it organizes data collection within a specific time track, by activating fields or questionnaires for respondents or PCC providers.

Data collection consists of a questionnaire (questionnaire 1 and 2 respectively), anthropometric measurements and laboratory tests, performed as a baseline measurement (before the first consultation) and follow-up measurement (around the second consultation).

- Questionnaires: Questionnaire 1 is filled in prior to the first PCC visit. This questionnaire assesses the characteristics of the study participant and health behaviors regarding the primary outcomes and other preconception risk factors. Questionnaire 2 is filled in after three months to assess changes in health behavior regarding preconception risk factors. Questionnaires are filled in on paper or via internet. Participants were reminded up to two times to fill in the questionnaire. The questionnaires were available in Dutch, English, Arabic, Turkish and Polish.
- Anthropometric measurements: PCC providers measure the following anthropometric measurements at both PCC visits: blood pressure (mmHg), length (cm's), weight (kg), hip and waist circumference (cm). These measurements were performed according to a predefined protocol.
- Laboratory tests: Data from the questionnaires regarding the primary outcomes of behavioral change are verified with biomarkers. Folic acid supplementation is assessed by measuring red cell folate in the serum.[32] Smoking cessation is assessed by serum cotinine levels.[37,38] Applying biomarkers for alcohol consumption is challenging because diagnostic accuracy is generally moderate and diagnostic properties differ over different alcohol consumption quantities and patterns. Ideally one would match a biomarker to the presumed alcohol consumption (quantitatively in time) of the study population. However, the prevalence of alcohol consumption is difficult to predict as there is a lack of consensus regarding the classification of alcohol consumption.[39] Numbers in the general population and in cohorts of pregnant women vary.[34] As there is no consensus regarding safety of alcohol consumption in the preconception phase the recommendation is to not consume alcohol in the preconception phase. Thus, we will be interested in biomarkers for any level of alcohol consumption. To detect alcohol drinking in the heavy end of the spectrum we chose to use Carbohydrate deficient transferrin (CDT%).[40] As a biomarker to assess the mild to moderate drinking spectrum we will explore the availability of ethylgluconeride (EtG) or a serum test of phosphatidylethanol (PEth) for the mild-moderate drinking spectrum.[41] Illicit substance use will be tested with conventional urinary drug tests (assessing amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, methadone, opioids (codeine, morphine, heroin, oxycodone etc.), phencyclidine, propoxyphene, synthetic cannabinoids). Providers are blinded to data from questionnaires and from the mentioned biomarkers.

In case of no-show at either consultation, PCC providers are encouraged to provide a new appointment for the consultation. If the woman does not attend the first PCC consultation she will be included for the analysis of the recruitment strategy. However, she will be excluded from the PCC cohort. If a woman does not attend the second PCC consultation she will be asked to complete her second questionnaire and where it is logistically opportune she will be asked to undergo a second laboratory assessment. She will be included in the outcome assessment of the effectiveness trial in that case.

Data analysis

Characteristics of the study population and preconception health behaviors at baseline will be described continuously (mean or median, SD or IQR range) or descriptively (percentages and CI's).

Changes in preconception health behaviors will be analyzed paired. Preconsultation and post consultation differences will be expressed with mean differences and SD's in continuous variables (in case of normality) or with median and IQR (in case of skewed data). Students T tests (in case of normality) or Wilcoxon Matched Pairs Test (in case of skewed data) will be performed for hypothesis testing. Dichotomous variables will be tested with the exact binomial test. Significance testing will be performed two sided with an α of 0.05. Regarding change in folic acid supplementation and smoking cessation one-sided testing will be performed with an α of 0.025 (in line with the hypothesis used for sample size calculation).

TABLE 1: Outcome assessment listed per study aim.

RESEARCH AIM		Outcome measure	Data source
EFFECTIVENESS OF INDIVIDUAL PCC CONSULTATIONS			
Primary Outcomes	Folic acid suppletion	Self-reported folic acid use. Biomarker (erythrocyte folate) confirmed folic acid suppletion.	Questionnaire and blood analysis at first consultation and 3 months after first consultation.
	Smoking	Self-reported smoking cessation. Biomarker (serum cotinine) confirmed smoking cessation.	Questionnaire and blood analysis at first consultation and 3 months after first consultation.
	Alcohol	Self-reported cessation of alcohol consumption. Self-reported reduction of alcohol consumption. Biomarker (serum %CDT; urinary EtG or PeTH) confirmed reduction or cessation of alcohol consumption.	Questionnaire and blood / urine analysis at first consultation and 3 months after first consultation.
	Illicit substance use	Self-reported cessation of illicit substance use. Biomarker (drug assessment in urine) confirmed cessation of illicit substance use.	Questionnaire and urine analysis at first consultation and 3 months after first consultation.

TABLE 1 continued

RESEARCH AIM		Outcome measure	Data source
EFFECTIVENESS OF RECRUITMENT STRATEGY			
Primary Outcomes	Characteristics of the cohort measured by Andersen's' model	Characteristics of women who utilized the PCC health service according to the framework of the sub-study (figure 1).	Questionnaire at first consultation.
	Outreach of the municipal letter	Proportion of women successfully recruited through the letter from the municipality in relation to the number of women approached by the municipal health service/ municipality. Characteristics of women successfully recruited after receiving the letter from the municipality in relation to characteristics of women residing in the selected neighborhood(s).	Data on women successfully recruited (the Gemstracker database) and data from women included in the study (questionnaire 1). (Anonymous) municipal administrative records provide characteristics of the target population: all women aged 18-42 residing in the high risk neighborhood.
	Outreach of the GP letter	Proportion of women successfully recruited in relation to the number of women approached by a letter from their general practice. Characteristics of these women in relation to characteristics of women residing in the selected neighborhood(s).	Data on women successfully recruited (the Gemstracker database) and data from women included in the study (questionnaire 1). (Anonymous) register of women who were sent a letter by general practices. (Anonymous) municipal administrative records provide characteristics of the target population: all women aged 18-42 residing in the high risk neighborhood.
	Outreach of the Preconception health educators	Proportion of women successfully recruited for individual PCC consultation after being approached about the service during a peer health education session. Characteristics of these women in relation to characteristics of women residing in the selected neighborhood(s).	Data on women successfully recruited (Gemstracker database) and data from women included in the study (questionnaire 1). Questionnaires of participants of preconception health education sessions. (Anonymous) municipal administrative records provide characteristics of the target population: all women aged 18-42 residing in the high risk neighborhood.
	Outreach of the Child welfare service	Proportion of women successfully recruited after being approached about the service during a visit at the Child Welfare services. Characteristics of these women in relation to characteristics of women residing in the selected neighborhood(s).	Data on women successfully recruited (Gemstracker database) and data from women included in the study (questionnaire 1). (Anonymous) municipal administrative records provide characteristics of the target population: all women aged 18-42 residing in the high risk neighborhood.

Regarding the effectiveness of the recruitment strategy utilization of the PCC health service will be expressed in percentages in relation to the number of women approached by the recruitment strategy. Characteristics of women who visit the PCC health service will be assessed according to the framework for utilization of the PCC service (see Figure 1).

Sample size calculation

Sample size calculation was performed for the two most important primary outcomes: folic acid supplementation and smoking cessation. Regarding folic acid supplementation, 839 women are needed in order to reject the null hypothesis (H0) that the PCC service will lead to a 20% increase of folic acid users in women who were not already using folic acid supplements at baseline (assumptions for this power calculation were (1) the smallest clinically relevant difference ('Δ') is a 20% increase of folic acid in non-users at baseline, (2) the proportion of women using folic acid at baseline is 30% ($\pi 0=30\%$)[42], (3) a select drop-out rate of 10%, (4) pairwise analysis of results, (5) a statistical significance level of $\alpha<0.025$ (one-sided correction for multiple testing due to primary outcome measures) and (6) a power (1-β) of 0,80). Regarding smoking cessation, 687 women are needed to reject the null hypothesis (Ho) that the PCC service will lead to a <5% decrease of smoking cessation, amongst women who smoked at baseline. (Assumptions for the power calculation were (1) the smallest clinically relevant difference ('Δ') is a 5% decrease in smoking compared to baseline, (2) the proportion of women smoking at baseline is 30% ($\pi 0=30\%$)[43,44] (3) the a- select drop-out rate of 10%, (4) pairwise analysis of results, (5) a statistical significance level of $\alpha<0.025$ (one-sided correction for multiple testing due to primary outcome measures) and (6) a power (1-β) of 0.80.) Thus, the cohort study should comprise 839 women to meet the needs of both primary outcomes.

Organization and time schedule

Municipalities were encountered for participation from June - November 2011. General Practices and midwife practices were encountered for participation from November 2011 to July 2013.

Practices were prepared to deliver PCC in the PCC sub-study after a one-on-one training to deliver PCC according to the study protocol. They received a self-study e-learning course and study material about preconception care in general and about risk factors. Practices were provided with information leaflets, posters and kits to hand out for the laboratory tests. Recruitment strategies were rolled out when practices were ready to receive participants for the study. Data collection is performed in close collaboration with the practices by means of the Gemstracker system. In order to promote the readiness of study participants to provide blood and urine samples and to ensure timely handling of the samples, all laboratory sampling and processing is done at neighborhood health centers or local laboratories in the participating municipalities. Finally, to reduce bias, the non-time critical laboratory tests are performed at one central laboratory (the trial laboratory of the Erasmus Medical Center of Rotterdam, the Netherlands).

After each PCC consultation study participants receive a preassembled laboratory kit form their PCC provider. This kit includes 1mL freezer capsules, a urine container and an application form to process the material according to the standard operating procedure of our study. All local

laboratories were accredited by CCKL (in Dutch: Coördinatie Commissie ter bevordering van de Kwaliteitsbeheersing op het gebied van Laboratoriumonderzoek in de Gezondheidszorg or the organization that audits laboratories in the health care system in the Netherlands).[45] Blood samples are collected in EDTA, SST or sodium fluoride vacutainers (in size and numbers as routine to the local laboratories). Local laboratories perform tests which have to be performed within 1 hour (e.g. glucose) or before refrigeration (hemoglobin, hematocrit, mean corpuscular volume, red blood cell count) directly after blood sampling. Two ml of whole blood is then pipetted and stored and the remainder is centrifuged (depending in local equipment: ±2000g/ 10 minutes). Approximately 2ml of plasma and 7ml of serum is pipetted into 1ml freezer capsules. Urine is centrifuged (depending in local equipment: ±2000g/ 10 minutes) after which 4 ml is stored. Whole blood is stored at -20°C; plasma/serum fraction and urine at -70 or 80°C (depending on local equipment). All laboratories closely monitor their storing protocol and are able to provide a report of the storing conditions at request. At set times all samples are distributed to the central trial laboratory.

The first municipality started enrollment in February 2013 and the last municipality started inclusion in February 2014. Enrollment is ongoing until time period: April 2014 or until the calculated sample size of included participants has been reached to meet current research goals. As the sample size has not been reached as yet, the inclusion period is currently planned until December 2014.

Ethical considerations

The HP4All PCC sub-study has been approved by the Medical Ethical Committee of the Erasmus Medical Center of Rotterdam (MEC 2012-425). In line with regulations an independent physician is available for consultation by the (eligible) study population.

DISCUSSION

The Healthy Pregnancy 4 All – Preconception Care sub-study aims to provide evidence for comprehensive and systematic delivery of PCC to the general public that contemplates pregnancy and to identify effective ways to reach women to promote utilization of the PCC health services. The study is rolled out in municipalities with disadvantaged perinatal health. Outcome measures of the study are the effectiveness of the employed recruitment strategy and the effectiveness of the PCC service in achieving behavioral change regarding preconception risk behaviors. In doing so, we acknowledge that merely providing PCC is insufficient and we aim to develop an integrated approach in which recruitment is combined with delivery of PCC – ultimately to improve perinatal health care by PCC.

Internationally PCC is implemented in various ways and within different settings. This study will place PCC in a cross-domain perspective in the Netherlands for the first time as multidisciplinary collaborations are initiated amongst municipalities, public health services and the curative care setting. Although this can be a strength, it might also be challenging to motivate different partners with different points of departure in the health system. Prior to this program for instance the role

of public health in fetal-maternal health care was very limited. Furthermore, PCC has been brought under attention within general practice and midwifery. However the experience seems to be that PCC is at best, only delivered at a small scale within these echelons. By implementing PCC in these echelons in the context of the current study, more can be learnt about what is necessary to upscale delivery of PCC, if effective.

A limitation in our approach to improve perinatal health outcome with PCC is that we target the group that plans pregnancy, as this is a precondition for PCC. Although the Netherlands has a high planned pregnancy rate and excellent access to contraceptives,[11,46] planned pregnancy rates and the access to contraceptive care could be lower within a population with lower socio-economic status. Initially, we aim to optimize outcomes of planned pregnancies. If this is effective, it would be the time to assess where PCC and family planning could be integrated to increase further effectiveness.

A limitation in the assessment of the effectiveness of PCC consultations will be that the sampled population could be prone to a participation bias. First, since the eligible population will rely on the extent to which the recruitment strategy is able to recruit a study population that is representative of the community. Second, because eligible high-risk women might be more difficult to include in the effectiveness study. However, we believe that we will have the data to explore the representativeness of the included population in relation to the population that did not want to participate in the cohort study and in relation to the targeted population in the community.

This is one of the first cohort studies in the Netherlands that assesses effectiveness of a PCC approach in a high-risk area in a general practitioner and midwifery setting. We have future aspirations to do further research within the context of the current study.

AUTHORS' CONTRIBUTIONS

SVV, AV, LDJ, AW, ES, SD were involved in conception and design of the study. SVV drafted the manuscript. SVV, AV, LDJ, AW, ES, SD revised the manuscripts critically for intellectual content and read and approved the final manuscript. SVV, AV, LDJ, AW, ES, SD agree to be accountable for the contents and integrity of this manuscript.

CONFLICTS OF INTEREST

None declared.

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PART III

IMPLEMENTATION & EVALUATION

CURRENT PRACTICES OF PRECONCEPTION CARE BY PRIMARY CAREGIVERS IN THE NETHERLANDS

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ABSTRACT

Objectives: Over the past decade the value of preconception care (PCC) consultations has been acknowledged. Investments have been made to promote delivery and uptake of PCC consultations in the Dutch primary care setting. We assessed current activities, perceptions and prerequisites for delivery of PCC in primary care.

Methods: A questionnaire was compiled and distributed by mail or e-mail among 1682 general practitioners (GPs) and 746 midwives in the Netherlands between 2013 and 2014.

Results: The questionnaire was completed by 449 GPs and 250 midwives. While GPs and midwives were frequently asked about preconception risks, explicit requests by patients for a PCC consultation were less frequent. Although caregivers gave information on preconception risk factors, only a minority recommended PCC in the form of a dedicated consultation. Such consultations occurred infrequently. Risk factor assessment varied between GPs and midwives. Respondents' perceptions of PCC consultations, however, were generally positive. A small proportion believed that PCC medicalised pregnancy, and recognised barriers in actively raising the topic of patients' pregnancy wishes. More training, staff, promotion of PCC and adequate reimbursement were prerequisites for future delivery. GPs differed in their opinion of whether they or midwives were primarily responsible for PCC consultations. Midwives, however, saw themselves as responsible for providing PCC consultations.

Conclusions: Primary care is underserving prospective parents with regards to PCC consultations. Targets to increase delivery of systematic PCC are: (1) promotion during routine care; (2) increased use of tools; (3) increased collaboration among primary caregivers; (4) reduction of caregivers' negative perceptions; and (5) tailoring PCC consultations to suit women's preferences.

INTRODUCTION

Preconception care (PCC) is care for all women or couples contemplating pregnancy that aims to identify and modify biomedical, behavioural and (psycho)social risks to parental health and the health of the future child through counselling, prevention and management.[1] The number of PCC risk factors is abundant.[1,2] An example of a PCC measure applicable to every woman is folic acid supplementation. PCC measures depend on the risk profile of the woman or couple. An example is strict glycaemic control in the case of diabetes. Intervention before conception gives time to tailor a PCC health plan to individual needs in order to optimally reduce risks before the critical phase of placentation and organogenesis. This phase is crucial to the course of pregnancy and perinatal health outcome. PCC has therefore been internationally recognised as a method to improve perinatal health.

In the Netherlands, improvement of perinatal health is highly relevant. The perinatal mortality rate in the Netherlands is high and has declined more slowly than in other European countries over the past decade.[3] PCC is regarded as a feasible measure with great potential to improve perinatal health, because couples in the general Dutch population are known to have a high prevalence of preconception risk factors but generally plan a pregnancy.[4]

PCC can be delivered in many ways: the ideal approach depends on the local health system.[5] In the Netherlands, delivery of PCC in the form of an individual PCC consultation is advocated.[6] Individual consultations provide the opportunity for professional-led broad risk assessment to ensure that risk factors are not overlooked. Furthermore, it encourages the delivery of interventions in a tailored fashion and monitoring of improvement in PCC health by a professional.

The effectiveness of PCC is debated. Evidence for PCC is mostly based on association studies of preconception risks and the occurrence of adverse pregnancy outcomes. Theoretically, eliminating risk factors should lead to improvement of preconception health (e.g., risk of maternal smoking is avoided after smoking cessation). Although evidence has been established for many single preconception interventions (e.g., folic acid supplementation), the effectiveness of an integrated approach in which interventions are delivered as a set or programme has not yet been established.[7] The introduction of individual PCC consultations has been advocated in the Netherlands since 2007, based on the available evidence for risk factors and evidence for single preconception interventions.

As in other countries with strongly developed primary care settings, in the Netherlands general practitioners (GPs) and midwives are seen as responsible for delivering individual PCC consultations to the general public. Several prerequisites for delivery of PCC by GPs and midwives have been met over the past decade in order to enable this. First, guidelines for individual PCC have been developed.[8] Second, different standardised risk assessment tools have been developed.[9,10] Third, different pilot projects in the GP and midwife settings have taken place which show positive attitudes of Dutch women towards PCC consultations.[11–13] Lastly, prior audits show positive ambitions of GPs and midwives to deliver PCC. Despite the aforementioned developments, PCC consultations remain scarce.[14–16] No studies have, however, assessed what primary caregivers actually do with regard to PCC consultations. This study therefore aimed to establish to what extent

Dutch GPs and midwives currently promoted and provided individual PCC consultations. The study also aimed to evaluate caregivers' perceptions about PCC and their prerequisites for future delivery. These perceptions and prerequisites are potential targets to increase the delivery of individual, standardised PCC consultations in primary care.

METHODS

Design and setting

A cross-sectional audit was conducted as a pre-intervention study prior to the implementation of PCC consultations within the Healthy Pregnancy 4 All (HP4All) PCC substudy.[17] The central aim of the HP4All PCC substudy is to develop a standardised approach to PCC consultations. This standardised approach requires GPs and midwives to perform PCC using a validated questionnaire and according to protocols. The present study designed a survey to address current activities, perceptions and prerequisites regarding delivery of PCC and was carried out among primary caregivers within the 50 municipalities identified at the launch of the HP4All PCC substudy. These municipalities were identified because they have the highest perinatal mortality and morbidity rates in the country. The municipality selection process is described elsewhere.[18] The municipalities were categorised into 14 intervention municipalities and 36 non-intervention municipalities. The survey was carried out as described below.

All midwife practices within the 50 municipalities were located through the midwives' professional organisation. Practices were contacted and asked for individual contact information of affiliated midwives. If provided, midwives were personally invited to participate; otherwise, the contact person was asked to distribute the surveys among all midwives in the practice.

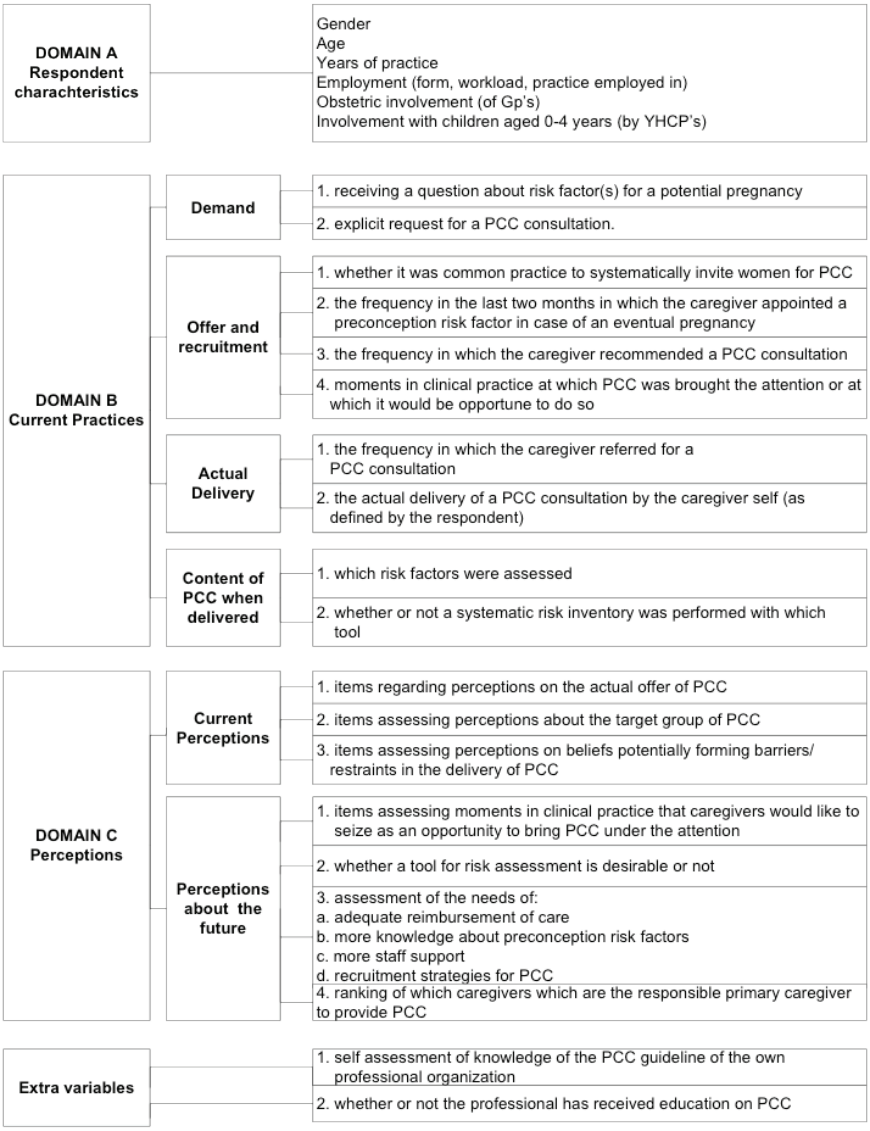
All GP practices were located within the 14 intervention municipalities and in a random sample of 50% of the postcodes in the 36 non-intervention municipalities. This sample was drawn because it was estimated that 50% of the postcodes would provide a sufficient number of respondents to fulfil the aims of the study. Second, the sample was drawn for feasibility reasons: in the absence of an up-to-date list of GP practices per postcode, locating practices would have involved a time-consuming internet search. It would have been too onerous to perform an online search for all postcodes. Similar to the procedure to recruit midwives, GP practices in the selected areas were contacted and asked for individual contact information of affiliated GPs. If provided, GPs were personally invited to participate; otherwise, the contact person was asked to distribute the questionnaires among all affiliated GPs in the practice.

Data collection

The authoring team compiled a questionnaire of 23 open-ended or closed questions within three domains: (1) respondents' characteristics; (2) current practices assessed over the two months prior to filling in the questionnaire; and (3) perceptions. The questionnaire was piloted to assess whether it was understandable and covered all potential answer categories. This was done by asking two GPs, a midwife and an obstetrician to fill in the questionnaire. Adjustments were

made accordingly. A summary of the questionnaire is presented in Figure 1; the full questionnaire is available on request. The questionnaire was available on paper and via an internet link sent by e-mail. Respondents were invited to participate by phone or by letter. In the case of non-response a reminder was sent. Data collection was performed between February 2013 and February 2014. The questionnaire was distributed prior to implementation of PCC in the intervention municipalities of the HP4All PCC substudy.

FIGURE 1: Domains, constructs and items of the questionnaire.



Analysis

Results were analysed using SPSS 20.0 software (Statistical Package for Social Sciences, Chicago, IL, USA) and descriptive statistics, and $\chi 2$ or Fischer's exact test where applicable to test for significant differences in proportions. Significance was defined as a p-value <0.05.

RESULTS

Respondents

Of the 1682 GPs, 449 filled in the questionnaire (individual response rate 27%). These responses accounted for 268 of 763 GP practices (practice response rate 35%). Of 746 midwives, 250 filled in the questionnaire (34%), accounting for 108 of 187 approached midwife practices (practice response rate 58%). Table 1 presents the characteristics of the respondents. Respondents were representative of Dutch GPs and midwives, except for a slight overrepresentation of female GPs, part-time employed GPs, and self-employed midwives. PCC training was reported by 15% of GPs and 63% of midwives; 20% of the GPs and 67% of the midwives rated their knowledge of the PCC guideline as good (rather than moderate or not at all).

TABLE 1: Characteristics of the respondents.

Characteristic	GPs (n=449)			Midwives (n=250)		
	No.	%	Ref.	No.	%	Ref.
Sex						
Male	205	45.7	57.4	4	1.6	1.6
Female	236	52.6	42.6	244	97.6	98.4
Age in years, median (range)	47 (24-66)	-	49 (27-87)	35 (21-65)	-	36 (21-65)
Type of employment						
Self-employed	376	83.7	89.9	182	72.8	51.2
Employed by another self-employed GP/midwife	45	10.0	11.1	20	8.0	6.2
Employed by a primary care practice or organisation	NA	NA	NA	24	9.6	2.3
Employed by a hospital	NA	NA	NA	6	2.4	27.7
Locum/temporary	NA	NA	NA	14	5.6	12.7
Employment						
Part time	343	76.4	57.4	143	57.2	53
Full time*	102	22.3	42.6	105	42.0	47.1
Type of practice						
Solo	114	25.4	25	8	3.2	5.4
Duo	110	24.5	37.9	23	9.2	15.0
Group	212	47.2	36.4	208	83.2	79.6
Other	0	0	0	3	1.2	0

Percentages do not always add up to 100%, due to missing values.
Ref., reference characteristics of GPs and midwives in the Netherlands in 2012, provided by the Netherlands Institute for Health Services Research (Nivel); NA., not applicable.*Full time is defined as 40 h per week.

Current PCC practices

Table 2 shows the current demand, offer and delivery of PCC consultations.

TABLE 2: Demand for and offer and delivery of PCC.

Variable	GPs (n=449)		Midwives (n=250)		p-value*
	No.	%	No.	%	
Demand for PCC					
Received a question about risk factors for potential pregnancy**	257	57.2	101	40.4	<0.005
Received an explicit request for a PCC consultation**	104	23.2	69	27.6	0.183
Offer of PCC					
Pointed out a risk factor in a future pregnancy**	299	66.6	107	42.8	<0.005
Policy to bring a PCC consultation to patient's attention at an appropriate moment	379	84.4	204	81.6	0.338
Explicitly recommended a PCC consultation**	74	16.5	54	21.6	0.086
Systematically invited patients for a PCC consultation (e.g. by direct mailing)	2	0.7	4	1.6	0.193

*$\chi 2$ test was applied; when data in cells were <5, Fischer's exact test was applied.
**In the past 2 months.

Demand

Both GPs and midwives had been asked questions about preconception risks in the previous two months: GPs more often than midwives (57% vs. 40%; p<0.005). There were fewer specific requests for a PCC consultation (23% of GPs and 28% of midwives).

Offer

In the previous two months, 67% of GPs and 43% of midwives reported that they had mentioned to patients risk factors for a future pregnancy. GPs did this significantly more often than midwives (p<0.005). The majority of GPs (82%) and midwives (84%) routinely mentioned the availability of PCC consultations during their clinical practice. Opportunities that both caregivers took to mention the availability of PCC were if women mentioned a desire to become pregnant (66% of GPs and 66% of midwives), during care after a miscarriage (45% of GPs and 54% of midwives), and when adverse pregnancy outcomes were apparent (36% of GPs and 48% of midwives). Fifty percent of midwives mentioned PCC consultations (or interconception care) during the routine postnatal check-up a few weeks after delivery. Among activities in the daily practice of GPs, a majority reported the availability of PCC during consultations about hereditary conditions (57%). Opportunities in general practice that were reported to be taken by a minority of GPs were: prescription of a medication (25%), when contraception was discussed (14%), and during routine follow-up of chronic medical conditions (16%). A few GPs (52%) reported that they mentioned the availability of PCC if their patient was getting married, feared encountering problems during pregnancy, requested travel vaccination,

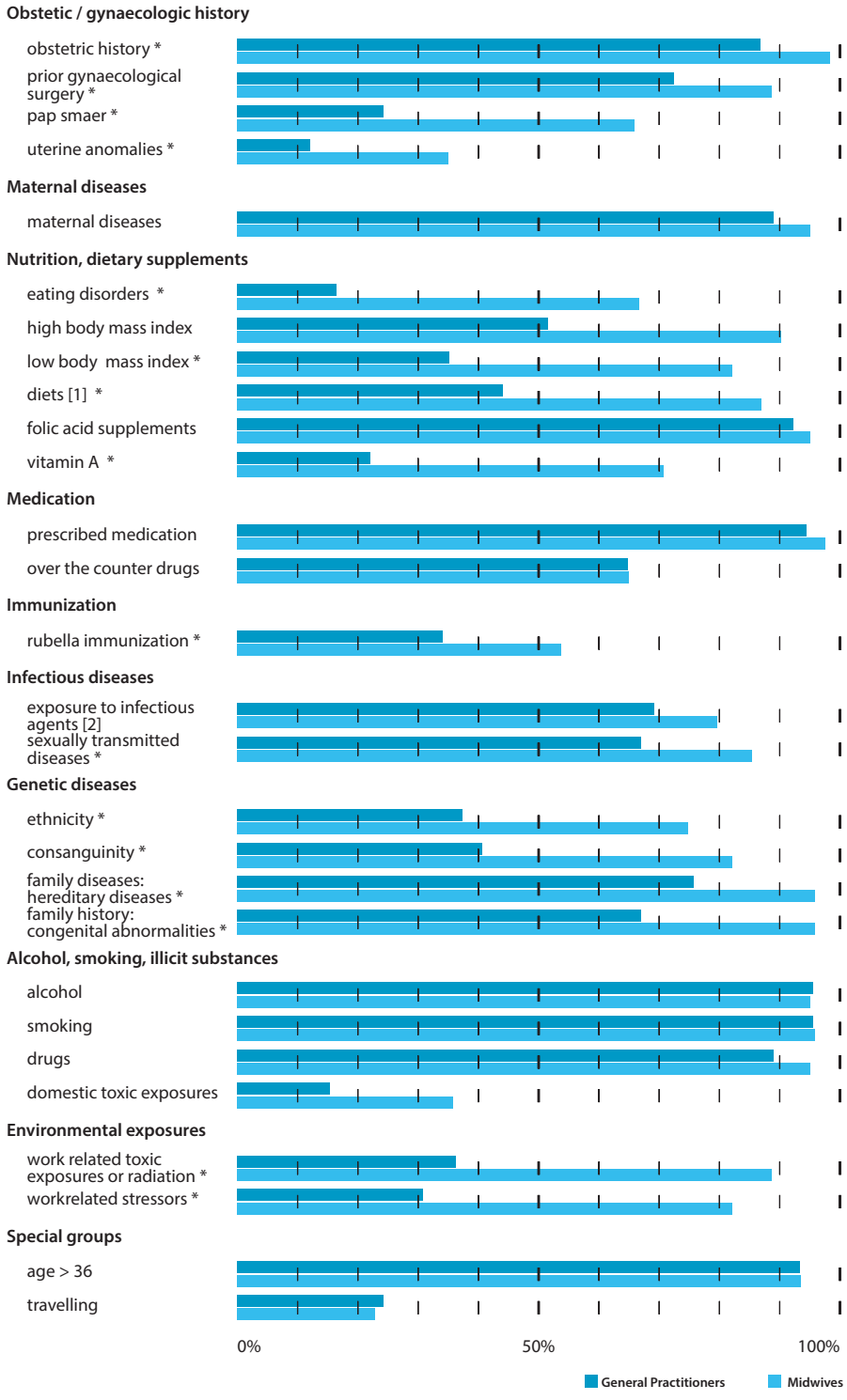
was undergoing evaluation of chronic medication use or a Pap smear, and if sexually transmitted infections or sexual matters were addressed. However, explicit invitation for a PCC consultation had occurred less frequently in the two months prior to the questionnaire (by 17% of GPs and 22% of midwives). Very few GPs and midwives systematically sent out invitations for PCC consultations to women in their patient record system.

Delivery

A small proportion of GPs and midwives had carried out PCC consultations in the two months prior the questionnaire (27% of GPs and 20% of midwives). The proportion of GPs who performed a PCC consultation was significantly higher compared with the proportion of midwives.

Respondents were asked how they organised the delivery of PCC. Twenty percent of GPs (n = 91) and 49% (n = 123) of midwives reported providing PCC consultations themselves according to their professional guideline (i.e., their PCC constituted a risk assessment across the domains presented in Figure 2). We restricted our analysis to the content of PCC reported by these respondents. Figure 2 presents the PCC risks that are routinely assessed by respondents who reported carrying out PCC consultations themselves. Pap smears, eating disorders, vitamin A, low body mass index, rubella immunisation, work exposures and stressors were assessed by <40% of GPs. Domestic exposures, presence of uterine anomalies, and risks due to travel received less attention from both GPs and midwives. For the majority of risk factors, a significantly larger proportion of midwives reported assessing them compared with GPs. This could be inherent to the fact that GPs are the medical file keepers within the system. Content of delivered PCC is also influenced by the use of tools such as screening question- naires, as recommended in guidelines. Of those included in the analysis shown in Figure 2, 25% of GPs and 94% of midwives reported using a tool for delivery of PCC consultations. The tools they reported using were the web-based questionnaire ZwangerWijzer[19] (12% of GPs and 83% of midwives), its complementary archive software programme, PreconceptieWijzer[9] (12% of GPs and 11% of midwives), the questionnaire provided by the professional organisation of midwives (39% of midwives), a self-assembled intake form (1% of GPs and 3% of midwives), or a questionnaire integrated into the patient record system (2% of midwives).

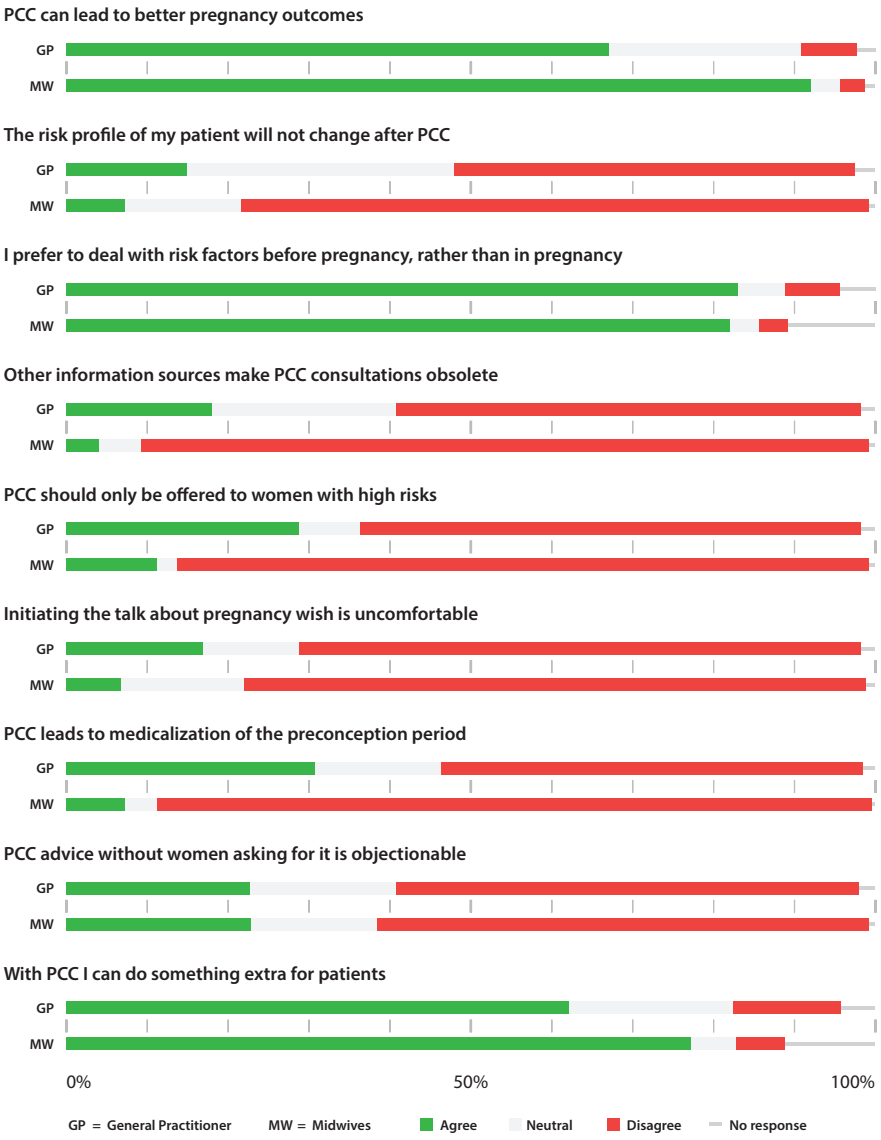
FIGURE 2: Elements of PCC and proportion (%) of GPs (n=91) and midwives (n=123) who included these risk factors in their standardised PCC consultation.



Current perceptions about PCC

Figure 3 presents the agreement of respondents with statements about PCC. It shows that the majority of respondents had a positive attitude towards PCC. Potential views that could be a barrier to the delivery of PCC by GPs were that PCC consultations should only be offered to women with high risks (30%), that PCC medicalised the preconception period (31%) and that offering PCC without women asking for it was objectionable (23%). Twenty-three percent of midwives also agreed with the last statement.

FIGURE 3: Views regarding PCC among GPs and midwives (MW).

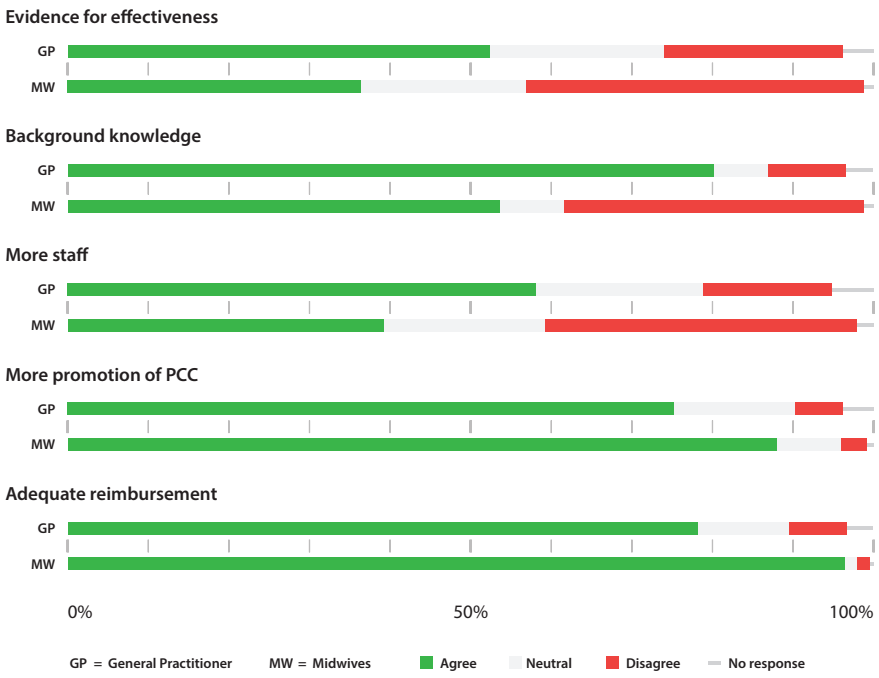


Perceptions about PCC in the future

Respondents said they were willing to mention the availability of PCC during routine care, if they did not already do so. They did not, however, favour discussing PCC during contraception counselling. The majority of caregivers who did not use a tool would be willing to use one in the future (90% of GPs and 71% of midwives).

Figure 4 shows the prerequisites for PCC delivery in the future. All items were prerequisites for a substantial proportion of GPs and midwives. Respondents especially agreed that adequate reimbursement and more promotion of PCC were prerequisites. Respondents were asked which caregivers (GPs, midwives, gynaecologists or adolescent health care physicians) should be primarily responsible for systematic delivery of PCC consultations. Among midwives, the majority (67%) thought that midwives were primarily responsible. There was disagreement among GPs, as 42% thought that midwives should be primarily responsible for delivery of PCC and 40% thought that GPs should be responsible for its delivery. The remaining GPs and midwives thought that adolescent health care professionals and gynaecologists were primarily responsible for the delivery of PCC.

FIGURE 4: Prerequisites for delivering PCC in the future among GPs and midwives (MW).



DISCUSSION

This audit shows that activities of GPs and midwives in PCC delivery mostly revolve around answering questions and pointing out risk factors when asked by a patient. The step to a dedicated, standardised PCC consultation is made less frequently. Approximately one in four GPs, and one in five midwives, had given a PCC consultation in the two months prior to the survey. Given the total number of pregnancies in the Dutch perinatal registry within the selected regions in 2013 (72,591 births in the postcodes of invited midwife respondents, 35,186 births in the postcodes of invited GP respondents), the potential population for PCC in the two months could have been 13 women per midwife or 3.5 women per GP (assuming a planned pregnancy rate of 80% and an equal distribution of conceptions throughout the year). In practice, however, the potential number of PCC consultations in the GP setting is likely to be higher, as GPs have more contact with non-pregnant women and opportunities in daily practice to address PCC compared with midwives. Half the midwives and approximately 20% of GPs performed PCC in a standardised manner. We conclude that only a minority of couples contemplating pregnancy are currently being offered PCC consultations.

We believe that the strength of this study lies in the assessment of performed activities during a set time period. These activities may be viewed in light of the demand caregivers receive and how they promote PCC. A difficulty in assessing PCC activities is that caregivers have different understandings of the content of PCC. Therefore, we first chose to assess the extent to which PCC activities were performed according to caregivers' own definition of PCC. We then chose to assess the proportion of caregivers who conducted PCC systematically as stated in the guidelines. Applying this definition in an earlier phase would have underestimated PCC activities. On the other hand, we regret that we could not assess the actual performance of systematic PCC consultations and the content of PCC delivered by caregivers that did not adhere to the guidelines. Other recurring reasons for non-response were personal factors, a policy not to participate in studies in general or from a non-affiliated centre.

We cannot exclude the presence of a selection bias, as it is feasible that caregivers with a higher affinity for PCC were more motivated to participate in the survey. Caregivers' interest might have been influenced by simultaneous conversations about participation in the HP4All PCC substudy that took place in 14 of the municipalities.[17] These municipalities provided 36% of the GP respondents and 53% of the midwife respondents, respectively. Response rates were 35% among GPs and 56% among midwives in the HP4All municipalities vs. 23% of GPs and 21% of midwives in the remaining municipalities. Subgroup analysis was performed to ensure that the design did not affect the results. There were no significant differences in actual activities regarding PCC.

A limitation in our design was that we relied on self-reported delivery of PCC consultations. Research in medical files would have been more reliable but was not feasible.

Previous studies in the Netherlands regarding delivery of PCC have been conducted before the advocacy of individual, standardised PCC by the Dutch health board in 2007.[6] The aim of these studies was mainly to assess perceptions and attitudes about delivery of PCC among GPs and midwives. The results showed that GPs and midwives occasionally provided a recommendation

about a single PCC risk.[14–16] The studies, however, do not provide data about the frequency of PCC activities and the extent to which PCC consultations were systematic. Therefore, we cannot reflect on whether delivery of standardised PCC consultations has changed over time.

Comparison of activities of primary caregivers in other countries is limited to a few studies.[20–23] Again, PCC in these studies seems to be limited to provision of one or more single pieces of advice rather than a standardised, dedicated and systematic consultation. PCC should be seen in light of countries' policies. The Netherlands might be unique in its clear advocacy of standardised PCC consultations in primary care by the Dutch health board and in professional guidelines for GPs and midwives.[6,8,24] This possibility is supported by a recent review of PCC policy in six European countries.[25]

Other studies report the number of pregnancies exposed to PCC.[26–28] In our opinion, this number does not reflect implementation of PCC by caregivers because this number only reflects a part of the actual delivery of PCC. It does not include PCC received by couples who did not conceive or whom were offered PCC but did not utilize the service. In order to assess overall PCC activities we advocate evaluation from the point of view of both delivery and receipt.

We recommend increasing PCC activities. With regard to everyday practice, GPs and midwives should be more proactive and explicit about the availability of PCC consultations during appropriate moments in routine care. As midwives have fewer opportunities in daily practice to inform non-pregnant women about PCC than GPs, we recommend that GPs and midwives collaborate. This could also be a solution for GPs who do not deliver PCC themselves. Increasing the use of tools can promote uniformity of PCC consultations.

Training, reimbursement, more staff resources and recruitment strategies are prerequisites that should be met. Among prerequisites, more evidence for the effectiveness of PCC was mentioned. This perception is in contrast with the abundant amount of evidence for preconception risk factors, which prompted the Dutch health board to decide that individual PCC should be delivered. Another perspective could be that it is unethical not to inform prospective parents about preventive measures. Training, guidelines and advocacy to deliver PCC by a professional organisation may reduce negative perceptions about the effectiveness of PCC.

Future research

The difficulty of making changes in everyday practice should not be underestimated. We recommend monitoring the implementation of standardised PCC as it finds its way to common practice. This implementation research should aim to identify facilitators for and barriers to the delivery of standardised PCC in the context of the health care system. Additionally, research is necessary to align caregivers' approaches to standardised PCC to the preferences and needs of women. This could promote its uptake and therefore reward caregivers' efforts, providing a positive feedback loop.

This study was confined to PCC in the form of individual PCC consultations. Individual PCC consultations have the advantage that thorough risk assessment across all risk domains can be performed for a couple contemplating pregnancy. Yet, there is a trend internationally to integrate

PCC into well-women's health care services. Although this is outside the scope of the current study, we recommend that future research addresses how PCC can be integrated into preventive health care services for women. This will require increased collaboration between the health care prevention and primary care sectors.

CONCLUSIONS

Delivery of PCC to couples in the general population has been advocated since 2007. This study, however, confirms that delivery of PCC only occurs for a minority of women contemplating pregnancy. Targets to extend delivery of PCC are: (1) explicit promotion of comprehensive PCC consultations at appropriate moments in everyday clinical practice; (2) promotion of standardised content of PCC by increasing the use of tools; (3) collaboration between GPs and midwives to promote and deliver PCC; (4) changing negative perceptions about PCC among GPs and midwives; (5) improving uptake by tailoring PCC consultations to meet the needs of women.

CONFLICTS OF INTEREST

No funding was received for this study. The authors have no conflicts of interest to declare.

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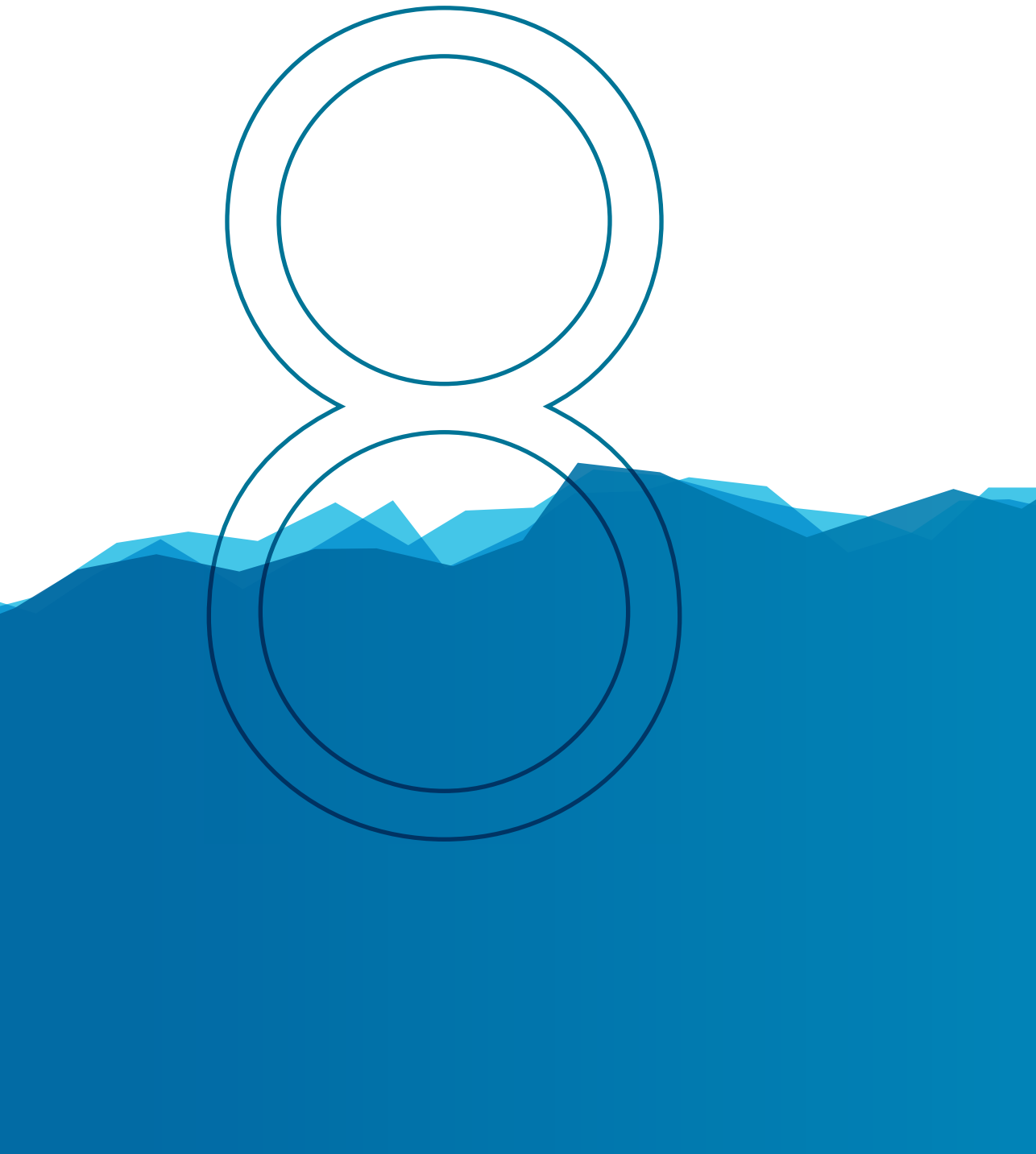

DEVELOPING SOCIAL MARKETED INDIVIDUAL PRECONCEPTION CARE CONSULTATIONS: WHICH CONSUMER PREFERENCES SHOULD IT MEET?

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ABSTRACT

Aims: Preconception Care (PCC) is care that aims to improve the health of offspring by addressing risk factors in the pre-pregnancy period. Consultations are recognized as a method to promote perinatal health. However, prospective parents underutilize PCC services. Uptake can improve if delivery approaches satisfy consumer preferences. Aim of this study is to identify preferences of women (consumers) as a first step to social marketed individual PCC consultations.

Methods: In depth, semi-structured interviews were performed to identify women's views regarding the 4 components of the social marketing model: product (individual PCC consultation), place (setting), promotion (how women are made aware of the product) and price (costs). Participants were recruited from General Practices and a midwife's practice. Content analysis was performed by systematic coding with NVIVO software.

Results: The 39 participants reflected a multiethnic intermediately educated population. Product: Many participants had little knowledge of the need and the benefits of the product. Regarding the content of PCC, they wish to address fertility concerns and social aspects of parenthood. PCC was seen as an informing and coaching service with a predominant role for health care professionals. Place: The General Practitioner and midwife setting was the most mentioned setting. Promotion: A professional led promotion approach was preferred. Price: Introduction of a fee for PCC consultations will make people reconsider their need for a consultation and could exclude vulnerable patients from utilization.

Conclusion: This study provides consumer orientated data to design a social marketed delivery approach for individual PCC consultations.

INTRODUCTION

Preconception care (PCC) includes all measures taken before conception to increase the health of the prospective mother (parents) and child. It addresses risks associated with adverse pregnancy outcomes. The large number of acknowledged preconceptional risk factors can be categorized into 13 domains: health promotion, immunizations, infectious diseases, chronic medical conditions, psychiatric conditions, maternal exposures, genetic risks, medication, nutrition, environmental risks, psychosocial stressors, reproductive history and special groups.[1,2] Whilst some risks and interventions are applicable to all couples (e.g. lifestyle recommendations, folic acid supplementation), some risks are only present amongst some individuals (e.g. a positive family history for hereditary diseases).

PCC has been acknowledged as a valuable addition to perinatal health care, to improve and reduce inequalities in perinatal health and women's health.[3,4] Many countries are facing challenges regarding which approach for the delivery of PCC is best suited to their health care setting. In the Netherlands, the Dutch Health Council advocates PCC for the general public in the form of individual consultations.[3] Rationale is that the majority of couples in the general population is known to have at least one risk factor for which PCC would be useful.[4] Furthermore a consultation with a health care professional provides the opportunity for individual risk assessment and intervention. However, despite availability of tools and guidelines, PCC consultations are only offered at a small scale.[5] When offered, uptake is low due to hesitancy amongst people to utilize PCC.[6,7] In order to increase the utilization of individual PCC consultations we need to address the question of how this service should be delivered in order to meet demands and preferences of prospective parents. Using a consumer-oriented approach to change behavior of a target group (namely uptake of PCC services) is the basis of social marketing. Social marketing is defined as "the application of commercial marketing technologies to the analysis, planning, execution, and evaluation of programs designed to influence voluntary adoption of recommended behaviors by a targeted audience in order to improve their personal welfare and that of society."[8] One of the steps is applying a marketing mix in which 'product', 'price', 'place', and 'promotion' characteristics are blended in a marketing plan that reflects the appropriate mix of these 4 'P's. The right 'product' has to be backed by the right 'promotion' and put in the right 'place' at the right 'price'.[9]

Social marketing has been suggested to develop approaches for the delivery of preconception care.[10,11] As the Dutch health system advocates delivery of PCC in the form of individual PCC consultations, this study is confined to the 'product' of individual PCC consultations. Goal of the product is primarily to promote a healthy pregnancy and to reduce the chances of adverse pregnancy outcomes. A consultation constitutes a thorough risk assessment to identify risks that warrant intervention or counselling in the preconception phase. 'Promotion' concentrates on the promotion of individual preconception care. The 3rd P, 'place' addresses characteristics of the setting. The 4th P, 'pricing', includes the costs for patients for this product.

Aim of this study is to identify consumers' preferences regarding these marketing components as a first step in designing a socially marketed delivery approach for individual preconception care.

METHODS

This study is a prospective, community based, qualitative study.

Participants were enrolled via purposive sampling from waiting rooms at 2 general practices (GP) and 1 midwife practice participating in the Healthy Pregnancy 4 All study.[12] Staff of the practice asked women if they would allow for a medical student to explain a study in which they could participate. These women attended their respective practices for a scheduled appointment for other health issues. If women were open to talk about participation in a study, a medical student (CtK) explained the study and assessed the participants' eligibility. Women in the reproductive age range (18-42 years) who did not exclude a future pregnancy were eligible (see supplementary file for script). Insufficient proficiency of the Dutch or English language was defined as an exclusion criterion. If women agreed to participate they filled in a questionnaire on baseline characteristics and the interview was scheduled at a convenient time at the respective practice. Sample size was set at 40 interviews. Fewer interviews were deemed sufficient if theoretical saturation would be reached at an earlier point.

Data collection consisted of individual semi-structured interviews. The topic list was designed to address each 'P' of the marketing mix. Questions were formulated to identify aspects of the 4'ps which authors had brainstormed to be important and which are known to be of importance in literature. As the interviews proceeded the interview strategy was adapted slightly, to ensure that participants understood the questions. The topic list contained 27 open-ended questions - with scripted sub questions when relevant – (Supplementary file 1). In order to ensure successful discussion about individual PCC, we provided a definition of our product: individual PCC consultations. All interviews were recorded and transcribed verbatim. Participants filled in a questionnaire on baseline characteristics. The ethics committee approved the study (MEC 2013-586). All participants provided informed consent for the recording and the use of data.

The interview transcripts were analyzed to identify elements of the social marketing model. Analyses were done with NVIVO software for qualitative analysis of data.[13] After the data was imported, a basic coding scheme was made according to each P of the social marketing model. This coding scheme was piloted. Two researchers independently applied the coding scheme to 10 interviews, and discussed discrepancies and modification of the nodes to optimally fit the content of the interviews. This led to a definitive codebook. The remainder of the interviews were coded by one researcher and checked by the other researcher. With the matrix coding function and query function of NVIVO, contents could be analyzed to identify contents (perceptions of respondents) and patterns in contents (consistency, frequency). Quotes were extracted to illustrate findings. The quotes were translated from Dutch to English (by a native speaker) and back again (by a second translator) to verify consistency of the translation.

RESULTS

40 women were recruited. One interview was discontinued because the candidate did not speak Dutch or English sufficiently to understand and answer the questions. After the 36th interview, no new information was provided and it was decided to stop data collection after 39 interviews. 23 participants were recruited from the midwifery setting, 16 participants were recruited from the GP setting. Mean interview time was 22 minutes. Table 1 presents the characteristics of the study participants. Participants were between 21 and 38 years old and reflect a multiethnic, intermediately educated population. At the time of the interview 56% of the participants were pregnant. Most non-pregnant participants did not contemplate pregnancy within the next 6 months.

Product

TABLE 1: Characteristics of participants.

Baseline characteristics of participants		**N (%) Total = 39**
Age	Median age (years)	27.97 (21-38)
Obstetric history	Nulliparous	19 (48.7)
	Multiparous	20 (51.3)
Maternity	0 children	25 (64.1)
	1 child	10 (25.6)
	2 children	3 (7.7)
	3 children	1 (2.6)
Current pregnancy wish	pregnant at the moment	22 (56.4)
	planning pregnancy <3 months	1 (2.6)
	planning pregnancy 3-6 months	0
	planning pregnancy >6 months	16 (41.0)
Marital status	Married	22 (56.4)
	Cohabiting	9 (23.1)
	In a non-cohabiting relationship	5 (12.8)
	Single	3 (7.7)
Ethnicity[1]	Dutch	26 (66.7)
	Surinamese	2 (5.1)
	Turkish	1 (2.6)
	Moroccan	3 (7.7)
	Other	7 (17.9)
Educational attainment level[2]	Low	4 (10.3)
	Intermediate	17 (43.7)
	High	16 (41.0)
	Other	2 (5.0)

Numbers reflect number of participants (N) unless specified differently. (1) Ethnicity is defined as the social or cultural group that the participant considered themselves to be part of; (2) Educational attainment level was classified according to the International Standard Classification of Education (ISCED).[33]

Knowledge about the purpose and the contents of PCC consultations was low amongst participants. The majority presumed PCC to be fertility related care. Its aim was 'to help women get pregnant', hastened by many participants with 'as fast as possible' or 'within the desired time frame'. Participants also thought its goal would be to help women with decisions about parenthood. In line with these presumed goals, participants mentioned that the target group would consist of women in the prepregnancy period ranging from women considering having a child to subfertile women. In line with this, presumed content would be education about fertility and diagnostic work-up and treatment of subfertility.

After participants were informed about what PCC actually was, intentions to utilize PCC varied. Reported reasons to utilize PCC were mostly to be informed on their questions about perceived risks and fertility. Participants reported they would be more likely to utilize PCC consultations after trying to become pregnant for a longer period or when they are becoming pregnant for the first time. Multiparity was reported as a reason not to utilize PCC, because most participants thought they would know enough after prior pregnancy experiences. Lack of perceived need or benefit of a PCC consultation was the most recurrent theme, as one respondent said illustratively:

> *"I still believe my body protects the fetus against harmful exposures during the first three months. Secondly, it has been going fine without the existence of PCC services in the past, so it will be fine regardless."*

Practical considerations (e.g. having to take time off from work), having other information sources or feelings about interference in the privacy and spontaneity of conception were other reasons not to utilize PCC consultations.

Regarding the contents of PCC, participants preferred PCC to address fertility, questions about their perceived risks and about parenthood. In line with this the most mentioned approach for the consultation was the provision of information. A few participants mentioned a preference for a coaching approach:

> *"You can stop with contraception; however it would be better if you were coached in the course of becoming pregnant instead of – 'well ok I'm just going to stop with contraceptives, and just see what happens."*

Although contact with peers and the use of tools (apps, internet, questionnaires) were valued positively, participants valued them as an addition to professional lead PCC consultations rather than a replacement. The personal approach, the authority and the credibility of a health care professional were the most important advantages of a PCC consultation by a professional. Participants mentioned the lack of credibility of the information and privacy issues, as the main disadvantage of forementioned tools. A hallmark for tools with trustworthy information sources and a function in tools where questions could be placed for answering by a health care professional were suggested improvements.

Expertise, trust and involvement in care for pregnant women were mentioned as the most important prerequisites of PCC providers. Based on these attributes GP's, midwives and gynecologists were most frequently suggested as PCC providers. Delegation of care to a nurse/ nurse practitioner/ medical assistant within general practices was deemed appropriate.

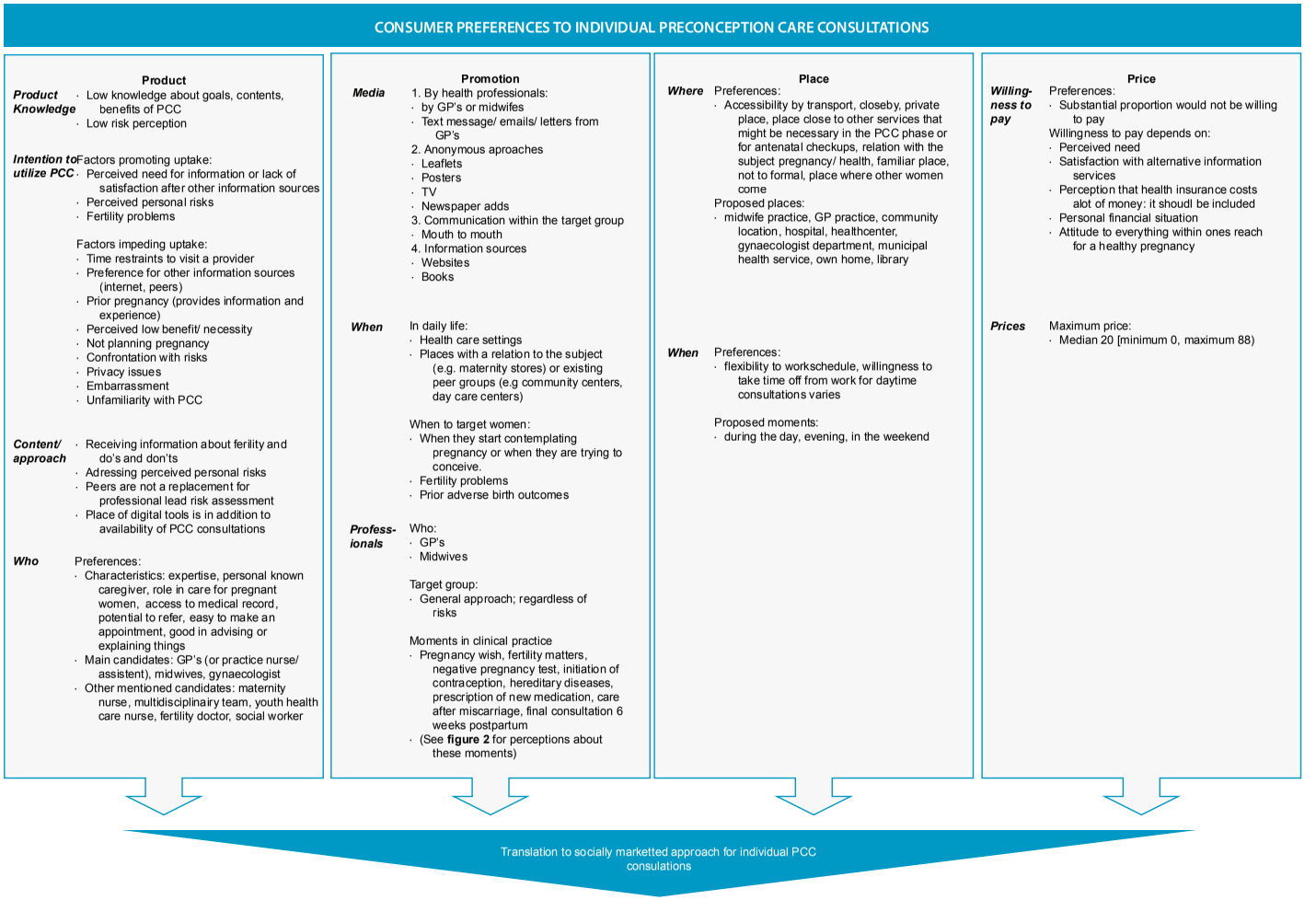

FIGURE 1: Perceptions and preferences of women regarding the four components of social marketing model: Product, Promotion, Place and Price. Items are listed according to the frequency they were mentioned.

Promotion:

Four communication approaches to make women aware of PCC were mentioned by participants (see Figure 1). The most preferred way to be informed about PCC was through a professional, mostly directly or indirectly via an email, text message or a letter. GP's were seen as the most suitable professionals to do so as they are the starting point for health care in the Dutch Health system and everybody has a GP. Midwives were also seen as suitable professionals to promote PCC. However, participants mentioned that people generally associate midwives to care during pregnancy. Figure 2 displays perceptions about the suitability of contact moments with GP's and midwives to be informed about PCC.

In the promotion of PCC, participants preferred a general approach in which professionals promote PCC to all women so everybody would be enabled to make an informed decision whether or not they would utilize PCC. Suitable places for the promotion of PCC were all related to either pregnancy or the target group. Participants preferred to be made aware of PCC when they start thinking about becoming pregnant or when they are trying to become pregnant. They mentioned that this is most likely when they have a stable life, being married or having finished education. There is understanding that these factors differ per person and that early promotion of PCC is necessary to reach women in time. Participants realized that caregivers generally do not know whether women are planning a pregnancy or not.

Place

Accessibility, in terms of distance and convenience with public transport, was the most important prerequisite. Other recurrent preferences of the location were privacy, location close to other services related to PCC (e.g. access to midwifery care or dietician if needed), familiar places or places where other women would come. These attributes caused participants to mention primary care places (midwifery practices, GP practices, health centers) or hospitals (where gynecologist/ specialist care takes place) as suitable settings for a PCC consultation. At home, municipal health centers and community centers were also mentioned.

Flexibility to consumers' working schedules was the most mentioned prerequisite regarding time. With differences in willingness to take time-off from work between participants, consultations in the evening or even in the weekend were mentioned to be preferred or even essential to some.

FIGURE 2: Suitability of moments for health care providers to promote a preconception care consultation – according to participants. Participants were asked to rate (grades 1- 10) the suitability of moments in routine care for a health provider to point out the opportunity to have a PCC consultation. Based on these grades, moments were ranked from being most suitable (top, green) to being least suitable (bottom, red).

Pregnancy wish	+	Ideal moment to be informed	"At that moment you are disclosing that you have a pregnancy wish, that is the moment when you need the information"
Fertility matters	+	It is likely that there is a pregnancy wish, which is the ideal moment to be informed about PCC consultations	"I wouldn't be bringing it up if I would not be interested in having a child"
Negative pregnancy test	+	It is likely that there is a pregnancy wish, which is the ideal moment to be informed about PCC consultations	"It depends on if that person has a pregnancy wish. But if that person does want to become pregnant, then they can get advice."
Initation of contraception	+	Contraception has to do with pregnancy/ contraception has a direct relationship with a pregnancy wish in the future	"Suitable because there is a relation between having children and contraception"; "When you stop some types of contraception, you can get pregnant immediately. With other types it takes a while before you become pregnant. It's good to know this on forehand, for the future."; "If you stop, chances are big you want to become pregnant."
	–	Might not be open for PCC	"When you discuss contraception you want to talk about not becoming pregnant."
Hereditary diseases	+	Relevant topic for future offspring	"It is relevant for pregnancy and for your future child"
	–	Confronting and scary	"No, that doesn't feel good. No I would get extra worried then."
Prescription of new medication	±	Acceptable if the specific drug influences future pregnancy or the health of the child, yet risk perception regarding drug varies	"If the medication has low risks, for example in case of Astma, then it's not necessary. I would find it weird if my GP would mention it. However I would want to be informed if medication would have more risks."
	±	Less suitable if there is no pregnancy wish	"Ok if I would be wanting to become pregnant at that moment, however if I wouldn't I wouldn't find it acceptable."
	–	Mentioning safety of the drug before/ during pregnancy on the box or the insert of the drug is sufficient	"It is not necessary because it says so on the box or the insert of the prescription."
	–	Drugs are needed to improve the women's health first, which is less important than the pregnancy at that moment	"If you are sick, you need something to get better first"
Care after a miscarriage	+	Information about becoming pregnant or preventing a miscarriage is likely to be welcome	"Because I have had a miscarriage myself. At that time I thought: how will I become pregnant again and which advices should I be following? So that would be a rational moment."
	–	Time is needed before parents have an open mind about the next pregnancy	"It took me a long time before I was open to talking about the miscarriage"
6 weeks post-partum	+	You can be informed if you did not know about PCC before the respective pregnancy.	
	+	If you mention PCC it can be related to risks that became apparent in the respective pregnancy/ delivery.	"Because if you didn't have a PCC consultation before the respective pregnancy, you can be told about it so you now about it in case you want to become pregnancy again."; "You may have questions related to you prior pregnancy"
	±	Suitable in case of problems during pregnancy and labour; might be less suitable because women are not thinking about the next pregnancy at that moment	"If it would be relevant. But if everything went well during the pregnancy and labour, I don't see the need of pointing out PCC"; "I don't think that would be what is on you mind then"

Price

Willingness to pay is mostly related to own financial situations and perceptions about reimbursement of health care in the Dutch system - where health insurance is mandatory and perceived as expensive. The requirement to pay for PCC would make a substantial proportion of participants seek other (free) alternatives for a PCC consultation or to reevaluate their need for a PCC consultation. This could provide a dilemma, for instance to women on social benefits.

> *"Just financially speaking, if it is not reimbursed, it would not be convenient, because I am on social welfare, I have fixed expenses, and sometimes at the end of the month it's difficult to pay them and I have to stick it out. My children are always my priority."*

According to participants, PCC should be reimbursed because it is preventive care. If they had to pay, the majority would be willing to pay a fee below 25 euro.

DISCUSSION

Summary of findings

This manuscript presents consumer research to drive socially marketed strategies for delivery of individual PCC consultations. The most profound finding was the lack of knowledge about the content and potential benefits of the product. Fertility and psychosocial aspects of parenthood are components which should be added to PCC. This study points out a key role for health professionals to promote PCC during moments in routine care with an explainable link to relevance of PCC. Participants find the community based primary care setting (GP's and midwives) to be the most suitable place for PCC. Regarding price, a fee will influence who is reached with the PCC service.

Comparison to the literature

This is not the first study to employ a social marketing approach within the field of PCC; however, studies define their product differently. Lewis and co-authors define their product as preconception health and performed a formative inquiry regarding women's preferences regarding preconception health.[11] Quinn and co-authors confined their product to a single preconception measure: preconception folic acid supplements. Their intervention approach was a collective campaign.[14] To our knowledge this is the first study in which the product is confined to a specific approach for PCC, namely individual comprehensive PCC consultations.

To our knowledge there are no studies assessing the effectiveness of social marketing approaches for preconception care in terms of uptake of services or behavioral change.

Perceptions about preconception care have been assessed in numerous studies. Regarding the 'product', the general misconception of the need and perceived benefits of preparing for a healthy pregnancy, has been acknowledged as the primary challenge to overcome in the delivery of preconception care.[4,15-17] The need to address fertility and psychosocial aspects of parenting during PCC is in line with reported low knowledge about fertility (e.g. fertile days) and timing of parenthood.[18] Regarding 'place', prior studies underline the preference of women for GP's and midwives to be the primary providers of PCC.[7,15,19,20] Regarding 'promotion', it has been

recommended that health care professionals point out PCC in the event of a negative pregnancy test, when birth control is discussed and in the check-up following delivery of a baby. [15,21,22] This study supports that the proposed moments are in line with women's preferences. To our knowledge there are no studies that assess the effectiveness of pointing out PCC during routine daily care in terms of promotion of the uptake of PCC.

Strengths and limitations

We believe one of the strengths of this study is that the product is confined to a specific approach: individual comprehensive preconception care. Firstly, findings over the remaining P's are valid as respondents are all talking about the same approach to PCC. Secondly, this way the social marketed intervention plan is in line with recommendations of the Dutch health board and guidelines of GP's and midwives.[3,23,24] By taking these points into account, results are close to the situation in practice, which is important for feasibility of implementation of the approaches which derive from our findings.

Ideally studies about PCC are performed with a study population that is trying to conceive. However, these women are not detectable within the general population. Therefore, we employed a second best approach: women were included if they did not exclude having a pregnancy wish in the future. This caused the study population to include women throughout various stages of their reproductive life. We believe our study population to be a representative study sample of planners and non-planners and nulliparous and multiparous women. We explored patterns regarding planners/ non-planners; nulliparous/ multiparous and women with prior adverse pregnancy outcomes. However, preferences regarding components of the social marketing plan were not consistent within these groups, due to the small size of these subgroups. A limitation due to the recruitment in GP and midwifery practices is that results only apply to women that utilize health care. We recommend effectiveness of approaches that derive from our findings to be evaluated for subgroups to fine-tune intervention strategies.

This study presents findings in the Netherlands, where individual comprehensive PCC consultations in primary care are advocated in policy and guidelines. Many countries explore roles of GP's and midwives in the delivery of PCC.[24,25-30] Findings of this study could be valuable to such countries or countries with a strongly developed primary care system seeking an individual approach to preconception care. Furthermore, the methods of consumer research employed in this study could be illustrative to other countries with other preferred approaches to PCC.

CONCLUSION

Preferences of women are largely in line with how PCC is intended to be delivered by primary care givers. Explicit matters that need rethinking are (1) product: adding fertility matters and psychosocial aspects of parenthood to the contents of PCC, (2) place: how PCC can be made accessible to subgroups such as the working population and the low health literate population (3) price: PCC is currently not reimbursed within basic health insurance whilst a substantial proportion of women is not willing to pay for individual PCC.

The most profound finding in this study was the low knowledge about contents, benefits and availability of individual PCC consultations. This emphasizes the importance of promotion. Participants point out a central role for GP's and midwives in promoting PCC. They should feel empowered to promote PCC during the proposed moments. Furthermore, they should point out PCC regardless of the presence of risk factors; participants prefer to know about availability of PCC so they can decide whether they want to utilize PCC. However, the low knowledge about PCC and the fact that midwives generally do not see non-pregnant women provide rationale for a campaign within the public health sector additional to efforts of PCC providers. This would reach women that do not visit health care providers and it could sensitize the public to messages about PCC from health care providers

Our consumer research provides the foundation for a socially marketed programmatic approach to individual PCC care. An approach needs to be designed in which the identified preferences are met. The low knowledge and perceived need for PCC entails that there is a need for a continuous promotion strategy parallel to delivery of PCC. A promotion campaign needs to be developed and evaluated regarding their comprehensiveness and appeal to different target groups. Feasibility of meeting women's preferences needs to be evaluated with PCC providers and policy makers. The designed program needs to be delivered iteratively, with continuous monitoring and adaption to specific target audiences.

CONFLICTS OF INTERESTS

None declared.

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☐ Brief introduction to the study:
"Purpose of this interview study is to learn how individual preconception care consultations could best be offered, according to women."
☐ Check if participant complies with inclusion criteria.
"Therefore we ask women between 18 and 41 years old, that wish to have a child in the near future, later in life or are sure not to have a completed family yet, to participate. Does this apply to you?"
☐ The participant has filled in the base-line questionnaire.

Product

A. Preknowledge Firstly assess what people know about the product.

1. What is a PCC consultation? (**Preknowledge)**
2. What do you think is the goal of PCC consultation? (**Preknowledge)**
3. Would you utilize the possibility of a PCC consultation if you had a child wish? (**Preknowledge)**
4. Why would or wouldn't you make use of a PCC consultation? (**Preknowledge)**

B. Presentation with our product
Assure that from now on the interview is about the product.

○ *I'll now explain our vision on preconception care, so we are sure we are talking about the same thing for the rest of the interview. It is possible to visit a preconception care service if you are thinking about becoming pregnant. During the consultation you can ask questions about fertility, getting pregnant,* your *health and you will receive advice about what you can do to be optimally prepared for a healthy pregnancy. In the first months the baby is very vulnerable: for example important organs such as heart and lungs are formed. During the PCC consultation advice is given about your personal health (e.g. regarding medication use because they can give deformities to the fetus, or regarding hereditary diseases) and general advice is given (for example folic acid supplementation). Preconception care consultations are for everybody in any stage of pregnancy contemplation. Furthermore it includes a thorough risk analysis after which individual advice is provided."*
5. After this explanation, would you utilize the possibility of a Preconception Care Consultation if you had a child wish? Why or why not? **(Utilization of product)**
6. What would be important reasons for you to utilize an individual preconception care consultation service? **(Utilization of product)**
7. What would be barriers to utilize an individual preconception care consultation service? **(Utilization of product)**
8. What would you like to address during a preconception care consultation regarding your pregnancy wish? (**Content of consultation)**?
9. Who should deliver individual PCC to you? **(Delivery by who)**
10. What makes this person the most appropriate provider of individual PCC to you? **(Delivery by who)**
11. Should individual PCC always be delivered by a health care professional? Yes/ no and why? **(Alternatives)**
12. Which alternatives for delivery by a health care professional would you find suitable? **(Alternatives)**
13. What is your opinion about digital media to provide you with preconception information (for example an app or website)? (**Alternatives)**
14. Could this replace an individual consultation with a health care professional? **(Alternatives)**

Promotion

15. How would you prefer to be informed about the possibility to visit a health care professional for a PCC consultation? **(How)**
16. Which moments in daily life would you find suitable to be informed about a PCC consultation? **(When)**
17. During which phase in your life would you like to be appointed the possibility to visit a health care professional for a PCC consultation? **(When)**
18. Which health care professional would you prefer to inform you about the opportunity to visit a health care professional for a PCC consultation (by this professional or by a different professional)? **(Who)**
19. During the next few questions I will mention moments during which you might visit a health care professionals. How suitable are these moments for health care professionals to point out the possibility of a preconception care consultation? Please tell us why moments are or aren't suitable and provide a grade between 1 -10 for their suitability (1 being absolutely unsuitable and 10 being very suitable). **(When)**
    a. When I mention my pregnancy wish
    b. During regular follow-up of a chronic disease (e.g. check-up for Diabetes)
    c. When hereditary diseases are discussed
    d. When a medication is prescribed to me, which hasn't been prescribed to me before
    e. When contraception is discussed
    f. When a pregnancy test is done and turns out to be negative
    g. When I have questions about fertility
    h. In the care after a miscarriage
    i. During a consultation after I had a baby
    j. When there are/ were health problems with my baby/child
20. a. What do you think about a more anonymous approach to inform you about the possibility of an individual PCC consultation?
    b. Would you prefer an anonymous approach or an approach by a professional or somebody else? **(How)**
21. Would you only prefer to be informed when you have risks or always (regardless of your health)? **(When)**

Place

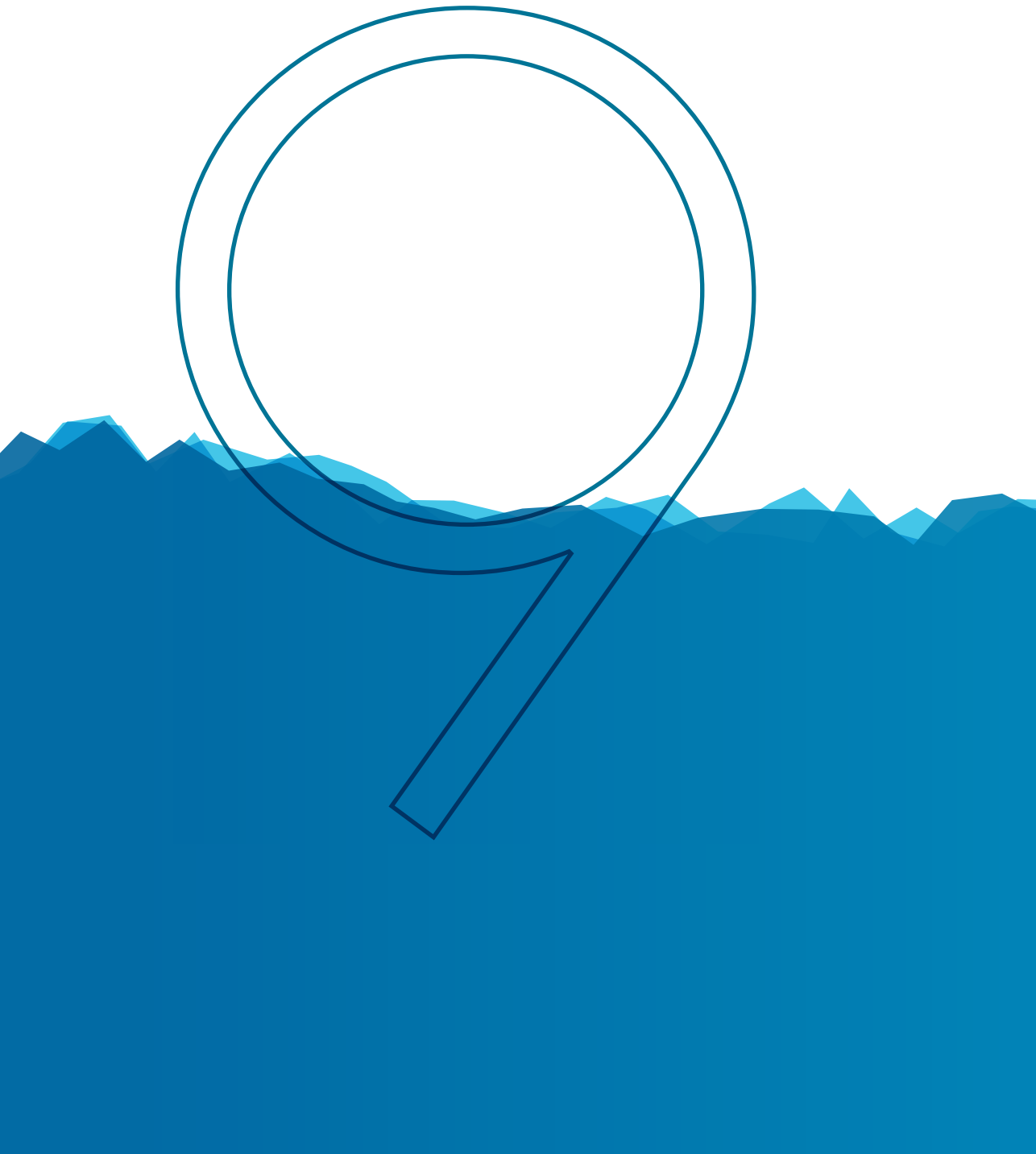
22. What do you find important regarding the place where the individual PCC consultations are provided? **(Where)**
23. Where would you like the PCC consultation to be provided? **(Where)**
24. Which moment would you find suitable for a PCC consultation to take place? **(When)**
25. What is important regarding the moment at which PCC is offered? **(When)**

Price

26. Would you be willing to pay for a PCC consultation? Why or why not? **(Acceptance)**
27. How much would you maximally be willing to pay for a PCC consultation? **(Amount)**

☐ *Do you have any remaining remarks or questions?*

We thank you for your participation.



IMPLEMENTATION OF A COMMUNITY-BASED PEER HEALTH EDUCATION STRATEGY FOR PRECONCEPTION CARE

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Manuscript submitted

ABSTRACT

Objective: To evaluate the implementation of peer education as a strategy to a) reach underserved women of reproductive age with preconception peer education and to b) refer them to preconception care (PCC) consultations in primary care (the Healthy Pregnancy 4 All – Preconception care substudy) in fourteen Dutch municipalities.

Methods: Process evaluation was performed according to Saunders Guideline for Process Evaluation. Implementation criteria were applied to assess the extent to which process measures regarding dose delivered, dose received, fidelity and outreach, were achieved.

Results: The intervention was adopted in seven out of ten municipalities. Overall implementation rates for items regarding dose delivered was 100% and 81% regarding dose received. Implementation fidelity was 62% and led to low outreach amongst the target population (49%). The strategy led to uptake of individual PCC by one woman. We identified several explanations for the insufficient implementation.

Conclusion: The implementation strategy is feasible, yet needs improvement before conclusions can be drawn regarding the effectiveness of the strategy.

Practical implications: Improved strategy should invest in 1) developing working relationships between peer educators and PCC providers; 2) consensus amongst stakeholders regarding the target group and 3) developing recruitment strategies for peer education sessions.

INTRODUCTION

Peer health education, or 'the teaching and sharing of information, values and behaviours, between individuals with similar characteristics', is a popular approach in the field of health promotion.[1] This form of education – referred to as 'peer education' from now on, has been successfully employed to increase women's knowledge about preconception health.[2-4] However, education alone is not sufficient to reduce preconception risks. Peer education provides general information to participants, while the majority of couples have one or more risk factors for which a visit to a general practitioner (GP) is indicated.[5, 6]

Preconception care (PCC) aims to optimize the health of (future) parents and their babies by reducing risks amongst prospective parents before pregnancy. The contents of care ranges from interventions which are applicable to all future parents (e.g. folic acid supplementation) to interventions applicable to specific risks amongst parents (e.g. optimizing glycaemic control in case of diabetes).[7, 8] A study estimated that up to 35% of perinatal complications could be prevented by addressing risk factors with PCC.[9]

Recent studies suggests that peer education is an effective strategy for reaching participants that are from disadvantaged neighbourhoods and typically "underserved" by PCC services.[4, 10] The intervention described in this article aims to a) reach underserved women of reproductive age

BACKGROUND

The intervention

During this peer education intervention, trained peer health educators (called peer educators onwards) delivered education sessions about preconception health to women from disadvantaged neighborhoods. The aim of the sessions was to cover behavioral risks (e.g. intake of folic acid supplements or illicit substance use) and medical risks (e.g chronic diseases, prior obstetric complications) associated with adverse pregnancy outcomes. Peer educators were to refer participants to a preconception consultation services at GP's and midwifery practices that participated in the Healthy Pregnancy 4 All program (HP4All). The sessions aimed to be interactive and informal, and to take place within local and familiar settings (e.g. a community center or participants' home).

Setting and context of the intervention

The peer education approach presented in this article is part of the preconception care sub-study within the Healthy Pregnancy 4 All program (HP4All).[11] This sub-study is a cohort study conducted between 2011 and 2014. Its aim was to improve perinatal health in disadvantaged neighborhoods of 14 municipalities with perinatal mortality rates that exceeded the national average of 10:1000 births.[12, 13] The sub-study had two organizational goals: (1) delivery of PCC consultations in primary care (by GP's and midwives in the community) and (2) develop a recruitment strategy to target women aged 18 – 41 to utilize these PCC consultations. The peer-education intervention described in this article was one of these recruitment strategies.

Similar to other countries, PCC in Dutch primary care is fairly new and – before the intervention - only offered at a small scale.[14] Therefore, we set up dedicated PCC centers, where providers were trained and assisted in their delivery of PCC. The HP4All program achieved that a median of 88% (50-100%) of the midwife practices in the municipalities and a median of 17% (12-75%) of the GP practices in the municipalities participated as PCC delivery centers. Preconception peer educators were not present in the municipalities before.

THE IMPLEMENTATION STRATEGY

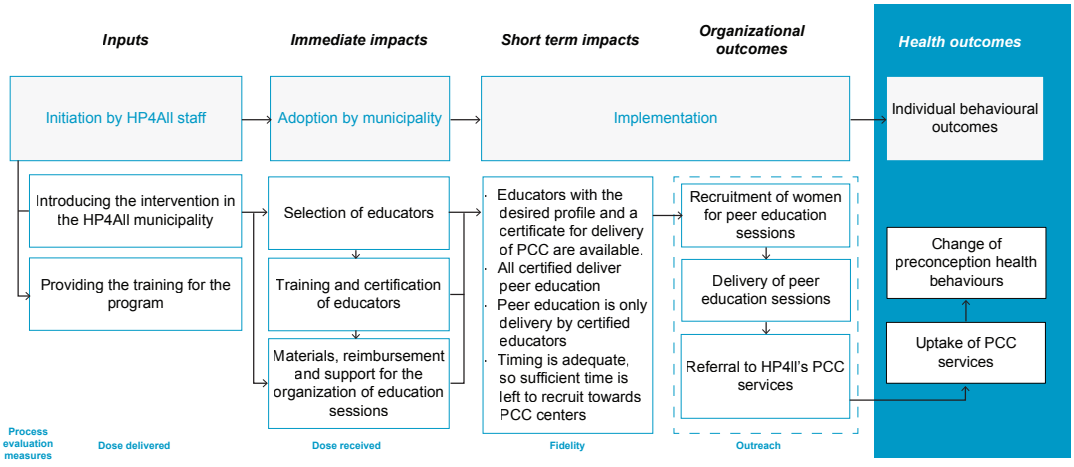
Figure 1 depicts our implementation strategy, or the chain of events that should eventually lead to improved preconception health.

Inputs consist of tasks performed by HP4All staff to initiate the intervention. HP4All staff consisted of staff at the national level and a program manager for each municipality. Two members of the HP4All staff were responsible for the roll out and the evaluation of the peer education approach. The HP4All program aimed to achieve adoption of the peer education strategy by bringing the program on the municipal health agenda via the local program manager. Local program managers were either attached to the municipal health service or the municipal department of public health. They were responsible for the local roll out of the intervention. Local program managers were seen as crucial to provide adaptation to the local setting, access to existing networks with health care professionals and knowledge of ways to reach the target group.

Immediate impacts

Once the municipality agreed to adopt peer education, the local program manager was responsible for the recruitment of the peer educators. The selection criteria for the recruitment of peer educators were (1) completion of at least upper secondary level education, (2) adequate

FIGURE 1: The implementation approach for peer health education intervention.



proficiency of the Dutch language and preferably of a second language, (3) knowledge and access to the hard to reach groups in the community, (4) cultural sensitivity and (5) access to organizations through which participants for peer education sessions could be reached (e.g. a maternity care organization). Local program managers were responsible for the allocation of budget for actual delivery of peer education sessions and for supplying educational materials suitable for the local setting.

Development and delivery of the training was delegated to one training bureau that facilitated training in each municipality. The training was designed as a post-secondary course. It consisted of eight modules ranging from practical skills (communication, presenting, organization of sessions) to theory (general health and common diseases, reproductive health, preconception health, parenting and perinatal health care in the Netherlands).[4] The educators-in-training were assessed with assignments and a practical exam and rewarded with a certification. The training was scheduled to take a maximum of six months.

Short term outcomes and organizational outcomes

The prior mentioned efforts were expected to result in certified educators that were ready to deliver peer health sessions as soon as the GP's and midwives were ready to receive referred participants for PCC consultations. Peer educators and program managers were tasked to develop a recruitment approach based on their knowledge of the local target group and the available networks to reach them.

The efforts of trained peer educators were expected to result in outreach. We define outreach as: 1) recruitment of women of reproductive age to participate in peer education sessions 2) delivery of peer education sessions to this target group and 3) referral to HP4All PCC consultation services.

Health outcomes

Peer education sessions were expected to result in the uptake of HP4All's PCC consultations. Results of the effectiveness of PCC consultations services and the recruitment strategy will be described elsewhere (see van Voorst et al 2015 for the study protocol).[11] with preconception peer education sessions and to b) have peer health educators refer these women to local preconception care consultation services, therefore promoting their uptake of PCC.

This article provides the process evaluation of the implementation strategy to in seven municipalities in the Netherlands. The performed process evaluation is important for formative purposes to understand the extent to which an evaluation of the effectiveness of the intervention is warranted, as well as for summative purposes to improve implementation strategies of future interventions. To our knowledge, this is the first study reporting a process evaluation for peer education for preconception health. Likewise, it is the first study outlining an approach to using peer education for referral to local health care services.

TABLE 1: Process evaluation items, criteria for implementation and results of process evaluation per municipality.

	Process evaluation measures	Data Source	Rating Scale / Coding	Implementation criteria per municipality	A	B	C	D	E	F	G	Met implementation criterium **
	Dose delivered											
1	Did the HP4All team discuss the peer education strategy with the municipal program manager?	Logbook	1 = yes (1/1) 0 = no (0/1)	Score = 3 (100%)	1	1	1	1	1	1	1	7/7
2	Did the HP4All staff provide the training material?	Logbook	1 = yes (1/1) 0 = no (0/1)		1	1	1	1	1	1	1	
3	Was funding delivered to execute the planned training program?	Logbook	1 = yes (1/1) 0 = no (0/1)		1	1	1	1	1	1	1	
	Dose received											
4	Was there an agreement between to adopt the peer education strategy?	Logbook	1 = yes (1/1) 0 = no (0/1)	Score ≥8 (≥60%)	1	1	1	1	1	1	1	7/7
5	How many peer educators were selected for the training?	Logbook	3 = ≥ 4 2 = 2 to 4 1 = 1 0 = 0		3	2	3	3	3	2	3	
6	What was the proportion of peer educators that completed the training?	Logbook	4 = 80 - 100% 3 = 60 - 80% 2 = 40 - 60% 1= 20 - 40% 0 = >20 %		2	4	4	2	4	2	2	
7	Did HP4All provide material for the peer education sessions to the municipalities?	Logbook End of program interview (program manager and peer educators	1 = yes (1/1) 0 = no (0/1)		1	1	1	1	1	1	1	
8	Did the municipal program manager ensure peer educators with material for the sessions?	Logbook End of program interview (program manager and peer educators	1 = yes (1/1) 0 = no (0/1)		1	1	1	1	1	1	1	
9	Did the municipal program ensure reimbursement of costs of the sessions?	Logbook End of program interview (program manager and peer educators	1 = yes (1/1) 0 = no (0/1)		1	1	1	1	1	1	1	
10	Did the municipal program manager provide support to peer educators in developing the recruitment strategy for the target group?	Logbook End of program interview (program manager and peer educators	1 = yes (1/1) 0 = no (0/1)		1	1	1	0	1	0	1	
11	Did municipal program managers bring peer educators in contact with PCC health centers?	Logbook End of program interview (program manager and peer educators	1 = yes (1/1) 0 = no (0/1)		0	0	1	0	1	0	0	

	Fidelity												
12	Were peer educators ready to deliver group sessions as of the moment that PCC services were available?	Logbook End of program interview (program manager and PHE)	1 = yes (1/1) 0 = no (0/1)		0	1	0	0	1	0	1		
13	Was the intended course executed as intended?	Logbook End of program interview (program manager and peer educators	1 = yes (1/1) 0 = no (0/1)		0	0	0	0	1	0	0		
14	Did the candidates have the intended profiles?	Logbook	1 = yes (1/1) 0 = no (0/1)	Score ≥4 (≥60%)	1	1	1	1	1	1	1		4/7
15	Were all the sessions provided by peer educators certified by the program?	Logbook	1 = yes (1/1) 0 = no (0/1)		1	1	1	1	1	0	0		
16	Which proportion of the certified peer educators organized sessions?	Logbook	2 = 100% 1 = 50 -100% 0 = < 50		2	2	2	1	2	0	0		
	Outreach												
17	How many peer education sessions were there organized?	Peer education registration forms	4 = ≥ 15 3 = 10 to 15 2 = 5 to 10 1 = 1 to 5 0 = 0		2	1	3	2	4	0	4		
18	How many participants attended the peer education sessions?	Peer education registration forms	4 = ≥ 150 3 = 100 to 150 2 = 50 to 100 1 = 10 to 50 0 = 0	Score ≥6 (≥60%)	3	1	2	1	4	0	4		4/7
19	To what extent did the educators refer to the HP4All PCC services?	End of program interview (program manager and peer educators	3= generally always and when women have risk factors; 2= always; 1= during some of the sessions; 0= did no		1	2	2	0	2	0	1		

METHODS

The steps of our process evaluation are described below and were based on Saunders Guideline for process evaluation of health promotion strategies.[15]

Development of process evaluation measures

We drafted a chain of events model, as displayed in Figure 1, to break down each event into single actions that have to happen for the given event to take place. We then formulated process evaluation measures and scoring criteria for each action, as shown in Table I. For example, one of the actions was that only certified peer educators should provide peer education. Adherence to this principle was evaluated with process measure 15: "Were all the sessions provided by peer educators certified by the program?" If our data indicated that all sessions were provided by a certified educator, one point was given, if not, zero points were given.

In a next step, we clustered our process evaluation measures into implementation components: dose delivered, dose received, fidelity, and "outreach". Dose delivered (labelled 'input' in figure 1) describes to what extent the HP4All team delivered the specified actions to initiate the implementation strategy. Dose received ('immediate impacts') explains to what extent municipalities responded to the dose delivered. Fidelity ('short term impacts') explains to what extent the intervention was implemented as originally planned. In turn, this was expected to result in outreach ('organizational outcomes'). We defined outreach as the scale at which the population was reached by peer education and referred to PCC consultations. Table I presents the process measures and scoring criteria per implementation component.

Data collection

We collected implementation data from the start of the intervention (September 2014) until its completion (July 2014). Data collection consisted of:

- Logs and program administration files about the training and selection of peer educators. This data was collected by the national HP4All staff.
- End of program interviews held with one purposively selected peer educator from each municipality and all program managers. During these interviews we went through the process evaluation measures of Table I and cross-checked the data from our other sources with the respondent's accounts. Additionally, we asked respondents about constraints and facilitating elements in the implementation process to identify factors that may have influenced the implementation. These answers were transcribed and organized per topic in a spread-sheet.
- Questionnaires for educators were filled in by educators after each education session throughout the entire intervention. This included data about the location and date of the given session, the number of participants and how the participants were recruited.
- Questionnaires for participants were handed out to all participants of the group sessions. These questionnaires collected data on participants' characteristics, such as age, education and whether or not they were planning to conceive.
- The HP4All database of the PCC sub-study: All women who applied for preconception services

participating in the HP4All study were registered in the HP4All database as of September 2011 – December 2014.[11] The participating practices registered whether the women were referred by a peer educator.

Data analysis and applying criteria to assess levels of implementation

Triangulation of the collected data was performed to score the process evaluation measures in Table I. The first author (SVV) discussed the attributed scores with DVV, and in case of disagreement, a third scorer (SD) was approached for consensus. We organized data into tables and calculated sum scores. The overall aim was to achieve adoption of PHE in at least six of the ten participating municipalities.

We set the implementation criteria at 100% for dose delivered as these items concerned our own activities and at 60% for the other process evaluation components (dose received, fidelity and outreach). This means that if 100% of the maximum points within dose delivered, and 60% within the other implementation components were achieved, we regarded the component to be implemented sufficiently. Our decision to apply a 60% criterion was based on a review by Durlac and Dupre.[16] They state that program implementation rates above 80% are rare and that a rate of 60% tends to produce an effective program.

Our process evaluation showed which steps were implemented insufficiently and helped understand why steps did or did not go as planned. Based on these findings, we developed an improved implementation strategy (supplementary file 1).

RESULTS

Adoption

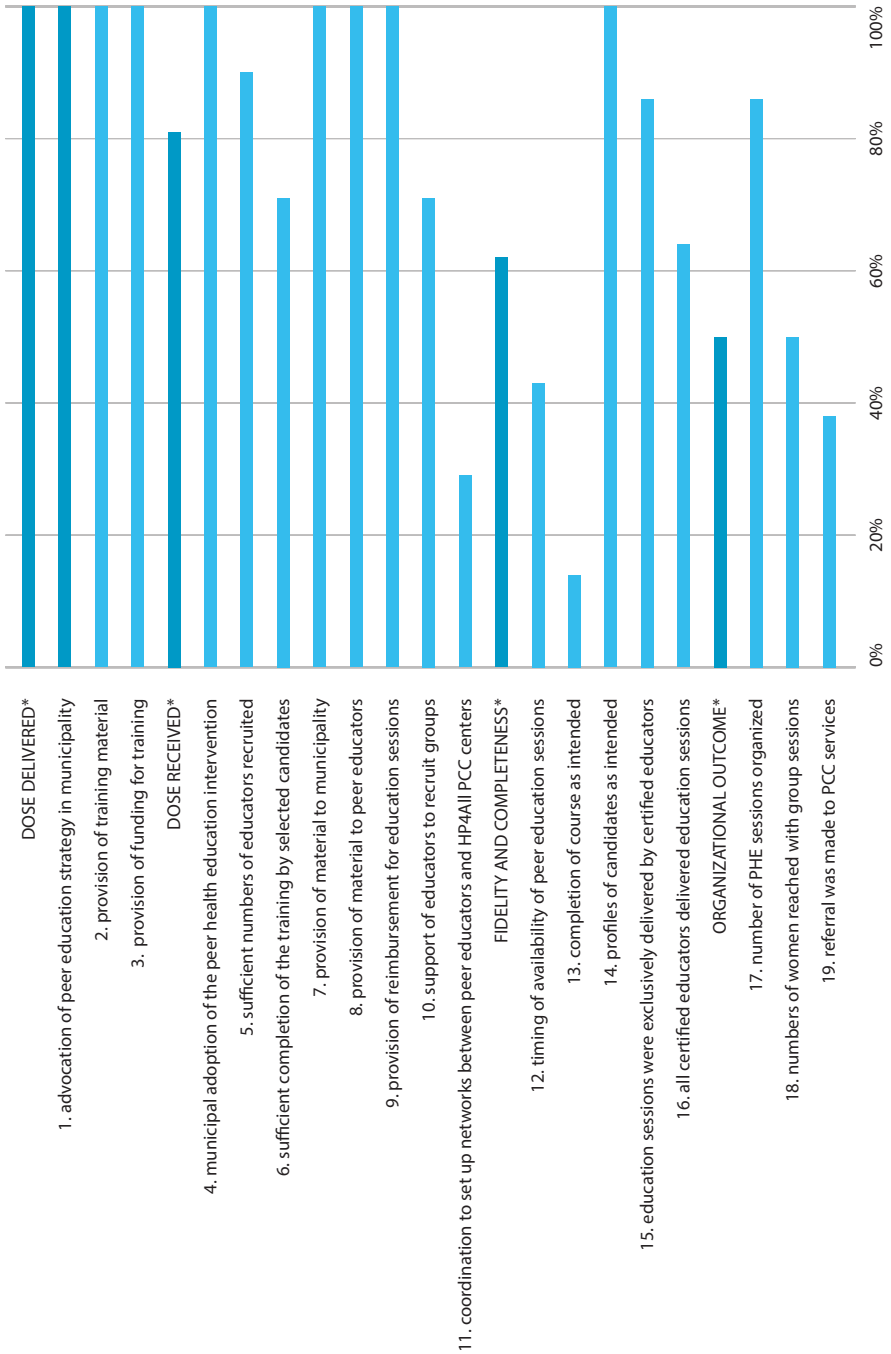
Pear education was adopted by seven municipalities (the Hague, Enschede, Groningen, Nijmegen, Schiedam, Tilburg and Utrecht). Reasons for other municipalities not to adopt the intervention were lack of governmental funding and concerns regarding the feasibility of implementation within the timeframe of three years. In this study we evaluate the implementation process of the seven municipalities that adopted the strategy.

Implementation

Figure 2 shows how well the municipalities scored per process evaluation measure. These results were computed by aggregating the scores of the seven municipalities per process measure. Table I provides the scores per municipality.

We will discuss the highlights of our process evaluation based on items in Figure 2 and the scores in Table I. We provide additional data extracted from the data sources specified in the methods section to add contextual information to our evaluation.

FIGURE 2: Assessment of the overall implementation of the peer health education strategy. These scores were computed by aggregating the scores for the seven municipalities that adopted the peer education intervention Numbers correspond with process measures in Table I.



Dosage

All participating municipalities reached 100% for dose delivered. The HP4All program succeeded in advocating the strategy in the municipality (measure 1). This was enabled by the partnership between the national HP4All staff and the municipal program manager. Furthermore, HP4All succeeded in providing budget and material for the training (measure 2, 3). The training material was largely adapted from a previous Dutch peer education health program that included preconception health.[4]

Overall, the municipalities scored well on dose received (81%). The municipalities recruited the desired number of peer educators (measure 5) and the drop-out rate of the peer education training was within the anticipated range (measure 6; drop-out rate of 15% amongst 41 selected candidates). Low satisfaction with the training was the main reason for drop-out. Peer educator candidates indicated that they experienced low satisfaction as there was not enough practice in actual delivery of education sessions and the training required much more time than anticipated. Moreover, candidates who were already active as peer educators in other health topics felt that the training was redundant.

There were no problems with the distribution of material (measure 7, 8) and the financing of the education sessions (measure 9). Municipalities adhered to the recommended material. Peer educators and program managers indicated that the materials were versatile and could be used in different ways to meet the different knowledge levels of the participants. Moreover, municipalities provided adequate support in the recruitment of participants in five of the seven municipalities (measure 10). Educators from two municipalities had to rely on their own network to the target population which they perceived to be low.

Within the dose received component, one item that was not achieved sufficiently: peer educators and participating PCC centers in the municipalities were not brought into contact with each other by program managers in five of the seven municipalities (measure 11). This is problematic, as this step was seen as essential so that educators could form a dedicated network for referral. In end of program interviews, program managers stated that they did not connect educators with PCC providers due to time restraints. They were more focused on the completion of the training, setting up recruitment strategies and the organization of the peer education sessions. The program managers indicated that developing relationships with primary caregivers would have needed more time and multiple contacts rather than a single effort just to get acquainted. They foresaw that there was not sufficient time for this within the program. With the exception of two municipalities, peer educators did not approach the caregivers that delivered PCC within the program themselves. They joined existing meetings of GP's and/ or midwives and sent letters to GP's and midwives. Despite enthusiasm of these primary caregivers, these efforts did not result in a working relationship.

Fidelity

The overall score for fidelity, or the extent to which the intervention was implemented by program members as planned, was 62%. Lower scores on fidelity in all municipalities were due to the adjustment of the training (measure 13) and the late initiation of peer education sessions (measure 12).

The training for peer educators was not delivered as intended (measure 13). Program managers requested to shorten the training as many educators had ample pre-training knowledge. The course was restricted to the contents of preconception health and only briefly addressed practical aspects of recruiting participants and the delivery of peer education sessions (i.e. presentation training). Retrospectively, some peer educators reported that more practical training would have been better.

Fidelity was mostly compromised because peer education sessions were delivered later than planned (measure 12). It was planned that peer educators would deliver peer education as soon as preconception consultation services were available at participating GP and midwifery practices. Program managers and educators explained that late delivery of peer education sessions was due to a late completion of the training and that the strategy did not provide enough time to develop strategies to recruit women to participate in the educational sessions. To resolve lack of time to recruit women, PCC was integrated into existing events in the community (e.g. coffee sessions amongst parents at schools or information meetings about other health conditions) rather than setting up specific recruitment strategies for preconception peer education. Our analysis provided that most participants (46%) were reached because the peer education sessions were integrated into a group event for which participants were already recruited. This approach was applied in three municipalities. Furthermore, fidelity was reduced in three municipalities, because educators provided peer education whilst they were not certified or because certified educators did not come around to provision of peer education time wise.

Outreach

The overall score for outreach of the peer education strategy was insufficient (50%). Although the overall number of organized peer education sessions was sufficient (86%, item 17), the extent to which the desired of participants was reached was insufficient (50%; measure 18). A total of 1796 participants attended the group sessions, but many sessions only hosted a small number of participants (<8).

Table II shows the characteristics of the participants that attended peer education sessions. The participants were mainly non-Western ethnic minorities, predominantly first generation immigrants, low to intermediately educated women with low Dutch language proficiency and low knowledge about PCC. These characteristics are typical for people from disadvantaged neighbourhoods, who are typically underserved by PCC. Interestingly, 43% of the participants were beyond the targeted age range (18 up to and including 41 years). Only nine percent of the participants intended to become pregnant. The fact that peer education was often integrated into existing group events explains the lack of adherence to the target population and the low number of participants that

wished to conceive. Additionally, program managers stated that the developed recruitment strategy was deliberately not restricted to women of reproductive age. They felt that improving women's health literacy and motivation to attend PCC would require talking about preconception health with teenagers but also with the social network of prospective mothers. Furthermore, addressing a broader age range about reproductive health was their primary aim rather than the short term aim of promoting the potential uptake of PCC, within the HP4All program.

Lastly, the extent to which educators referred women to PCC services was insufficient (adherence to the concept of referral was 38%; measure 19). Peer educators in three municipalities reported always mentioning the availability of preconception services at GP's and midwifery practices. This was only done occasionally in two municipalities, and was never done in the two remaining municipalities. The educators mentioned the following reasons for not referring to preconception consultations within the HP4All program were (1) thinking that a participants' risk factor required referral to the women's GP which happened not participate as a PCC delivery center within HP4ALl, (2) sessions were sometimes delivered outside of areas with participating PCC centers; so people were referred to their own caregiver (who did not participate in the HP4All program) (3) not knowing to which GP and midwifery practices they could refer women to.

Health Outcome

Within the course of the project one of 587 applications for a PCC consultation at the GP and midwife practices was registered.

DISCUSSION

This study provides a new approach to integrate different preconception approaches: a classic approach from the public health care field (peer education) and one within the primary care setting (individual PCC consultations). Our evaluation shows that seven out of ten municipalities adopted the intervention strategy. The implementation strategy resulted in 147 peer education sessions, with a total of 1796 participants. Overall dosage was sufficient; fidelity was marginally sufficient (62%) and outreach of the program was insufficient (overall score 49.4%). Four of the seven municipalities satisfied our implementation criteria. However, only one of the 1796 participants of the peer education sessions visited a PCC service of the HP4All program, although it is possible that more participants made use of non HP4All PCC services.

Our process evaluation helped us to identify explanations for low outreach: 1) deviation from the intended target group (women of reproductive age) 2) insufficient dedication and time allocated to the development of the referral network between educators and PCC caregivers 3) referral was not performed consistently or beyond the desired network of PCC providers within the project.

Peer education has been implemented in the field of PCC before.[2-4, 10, 17, 18] These studies were mostly conducted amongst underserved populations. These studies show that peer education can reach underserved women. However, none of the studies referred women to individual PCC

TABLE 2: Background characteristics of participants of the preconception peer education sessions per municipality..

Municipality		A N= 20 (resp. rate = 18.5%)	B N= 37 (resp. rate = 90.2%)	C N= 45 (resp. rate = 81.8%)	D N= 13 (resp. rate = 26.0%)	E N= 856 (resp. rate = 100%)9	F N= 156 (resp. rate = 22.8%)	Total N=1127 resp. rate 63%
Age	Years (median (range))	38 (26-71)	48 (32-68)	30 (19-59)	44 (28-67)	27 (13-76)	40 (19-66)	31 (13-76)
Ethnicity[1]	Native Dutch:	0 (0)	0 (0)	30 (66.7)	5 (38.5)	174 (20.3)	4 (2.6)	213 (18.9)
	Surinamese	2 (10.0)	0 (0)	0 (0)	0 (0)	50 (5.9)	1 (0.6)	53 (4.0)
	Antillean/Aruban:	0 (0)	0 (0)	1 (2.2)	2 (15.4)	36 (4.2)	0 (0)	39 (3.5)
	Indonesian/Moluccan:	0 (0)	0 (0)	1 (2.2)	0 (0)	15 (1.8)	0 (0)	16 (1.4)
	Turkish	5 (25.0)	36 (97.3)	0 (0)	4 (30.8)	233 (27.2)	76 (48.7)	354 (31.4)
	Kurdish	3 (15.0)	0 (0)	0 (0)	0 (0)	6 (0.7)	0 (0)	9 (0.8)
	Moroccan	7 (35.0)	0 (0)	8 (17.8)	1 (7.7)	134 (15.7)	69 (44.2)	219 (19.4)
	Polish	0 (0)	0 (0)	0 (0)	0 (0)	23 (2.7)	0 (0)	23 (2.0)
	Other	3 (15.0)	0 (0)	5 (11.1)	1 (7.7)	171 (20.0)	3 (1.9)	183 (16.2)
Immigrant status[2]	First generation	20 (100)	34 (91.9)	9 (20.0)	9 (69.2)	413 (48.2)	124(79.5)	609(54.0)
	Second generation	0 (0)	2 (5.4)	9 (20.0)	1 (7.7)	273 (31.9)	26 (16.7)	311 (27.5)
	Native Dutch:	0 (0)	0 (0)	27 (60.0)	3 (23.1)	139 (16.2)	4 (2.5)	173 (15.4)
Civil status	Married or living together	17 (85,0)	31 (83,8)	24 (53,3)	8 (69,2)	77 (72.6)	118 (75,5)	276 (63)
	In a relationship, not living together	0 (0)	0 (0)	6 (13.3)	0 (0)	8 (7.5)	4 (2.6)	18 (4.8)
	Not in a relationship	3 (15.0)	6 (16.2)	15 (33.3)	4 (30.8)	18 (17.0)	29 (18.6)	75 (19.9)
Residence[3]	Non-deprived neighbourhood	1 (5.0)	29 (78.4)	42 (93.3)	9 (69.1)	557 (65.1)	56 (35.9)	694 (61.6)
	Deprived neighbourhood	18 (90.0)	6 (16.2)	1 (2.2)	3 (23.1)	293 (34.2)	93 (59.6)	414 (36.7)
Educational attainment level[4]	Low	13 (65)	27 (73)	12 (73)	5 (38.5)	481 (56.2)	68 (60.5)	625 (53.8)
	Intermediate	3 (15.0)	6 (16.2)	22 (48.9)	5 (38.5)	191 (22.3)	42 (26.9)	269 (23.9)
	High	1 (5.0)	0 (0.0)	8 (17.7)	2 (15.4)	110 (12.8)	21 (13.5)	142 (12.6)
	Other	2 (10.0)	1 (2.7)	2 (4.4)	0 (0)	26 (3.0)	4 (2.6)	35 (3.1)
Occupational status[5]	Unemployment	14 (93.3)	29 (80.6)	27 (62.8)	7 (53.8)	24 (27.6)	106 (72.1)	

Language Proficiency[6]	Excellent	1 (5.0)	5 (13.5)	36 (80.0)	9 (69.2)	43 (49.4)	51 (32.7)	145 (40.5)
	Sufficient	7(35.0)	15 (40.5)	6 (13.3)	2 (15.4)	23 (26.4)	42 (26.9)	95 (26.5)
	Moderate	5 (25.0)	6 (16.2)	2 (4.4)	0 (0)	7 (8.0)	21 (13.5)	41 (11.5)
	Insufficient	6 (30.0)	10 (27.0)	36 (80.0)	9 (69.2)	43 (49.4)	51 (32.7)	145 (40.5)
Knowledge about PCC[7]	Mean score, (SD)	4.94 (3.33)	4.14 (1.86)	7.55 (2.00)	7.10 (2.80)	4.63 (2.49)	5.40(2.49)	5.46 (2.64)
Pregnancy intention[8]	Yes	6 (30.0)	1 (2.7)	6 (13.3)	0 (0)	6 (6.9)	14 (9.0)	33 (9.2)

- These numbers reflect data from the respondents that agreed to fill in the questionnaire (overall response rate 67.7%)
- Numbers reflect number of participants (N) unless specified differently.
- Percentages do not always count up to 100% due to missing data or rounding.

1. Ethnicity is defined as the social or cultural group that the participant considered themselves to be part of.
2. First generation immigrant is defined as somebody that is not born in the Netherlands; a second generation immigrant is defined as somebody that is born in the Netherlands but either of her parents was born in a foreign country.
3. Classification of living in deprived neighbourhood was performed with zip-codes according to classification of the Central Bureau of Statistics (CBS) in the Netherlands in 2008.
4. Educational attainment level was defined as the highest completed educational level classified according to the International Standard Classification of Education (ISCED) i.e. low (level 0-2: early childhood; primary education; lower secondary education); intermediate (level 3-5: upper secondary; post-secondary; short cycle tertiary); and high (level 6-8: bachelor; master; doctoral) Unesco institute for statitstics 2014.
5. Employment was defined as having a paid job.
6. Language proficiency was self rated and based on an average score for comprehension, reading, writing and speaking.
7. Knowledge about PCC was assessed with 10 questions concerning preconception health, each correct answer is rewarded with 1 point resulting in a maximum score of 10 points; these questions were assessed prior to the peer education session.
8. Pregnancy intention was assessed by asking whether or not women were currently trying to conceive or not.
9. Number of participants was not registered; however PHE reported that all participants filled in the questionnaire. Therefore the response rate is assumed to be approximately 100%.

consultations after they attended peer education sessions.

This article is an illustration of how effectiveness data alone would provide an incomplete picture of outcomes.[19] An effectiveness study would have indicated that peer education is not effective to improve uptake of individual PCC. With a process evaluation, however, we can show that potential lack of effectiveness might not be because the program does not work, but because it was not implemented as intended. Lack of implementation evaluation could result in a "type III" error, where a program is rejected while it was not implemented as intended.[20]

Potential limitations of our study are inherent to our program monitoring strategy and the data sources. The monitoring mostly relied on data that was analyzed or collected at the end of the program. This was partly due to time constraints.[11] Interim evaluations could have flagged barriers to implementation at an earlier stage. Regarding data sources, one peer educator per municipality was asked to participate in the end of program interviews and the response rate of the participant questionnaires varied per municipality between 18.5% and 100%. This could give rise to selective process evaluation data. Lastly, the way uptake of PCC services was registered might have led to an underestimate of the actual number of PCC consultations after referral by peer educators. Firstly because we experienced that PCC consultations were not always registered. Secondly, how women had heard of the PCC service was not registered amongst 10% of the admissions. Furthermore, the low percentage of participating GP's (median 17% (12-75%) might have played a role in referral to non-participating GP's. We were unable to collect data regarding referrals for PCC from these practices.

CONCLUSION

Peer health education can be implemented in community-based health care. This study showed the potential of peer health education to reach underserved women, however referral to PCC consultations in primary care was performed inadequately. Therefore, an evaluation of the effectiveness of the referral strategy on uptake of PCC consultations is not warranted yet. There is however sufficient ground to adjust the implementation strategy for the purpose of improving future implementation of (similar) interventions.

PRACTICE IMPLICATIONS

- We recommend introducing a municipal field coordinator dedicated to 1) making and maintaining contact with PCC providers in primary care, 2) designing and managing recruitment strategies to recruit the target group for the peer education sessions and 3) monitoring the skills and training levels of peer educators.
- As not all primary caregivers provide PCC, educators should adhere to the dedicated referral network developed within the strategy, because preconception care is only offered by a minority of caregivers.[14]
- The training of the peer educators should be tailored to individual needs. It should include

practical training and observation of a PCC consultation to increase educator's familiarity and appreciation of such services.

- Decisions should be made regarding the target group. Within this study municipalities targeted potential social influencers of prospective mothers (e.g grandmothers).There is a rationale for this approach however it may also take longer before such an approach sorts effectiveness because target groups are reached indirectly.
- Future research should tailor preconception health messages to fit the needs of the potential sub-groups amongst participants. Social marketing strategies could provide a framework for this.[21] Peer educators could include an individualized approach in their peer education sessions - by applying a generic risk assessment tool.[22-24] Identification of one or more risks might motivate women to visit preconception consultations.

Supplementary figure 1 provides a renewed organizational model.

ETHICAL CONSIDERATIONS

The HP4ALL PCC sub-study has been approved by the Medical Ethical Committee of the Erasmus Medical Center of Rotterdam (MEC 2012-425).

CONFLICTS OF INTERESTS

Danielle van Veen is associated to 'the foundation of peer educators' as an advisor. This foundation is the foundation that effectuated the preconception health education in one of the 6 participating municipalities. Sabine van Voorst, Vera Schölmerich, Carissah Stewarts, Eric Steegers and Semiha Denktaş have no conflicts of interest to declare.

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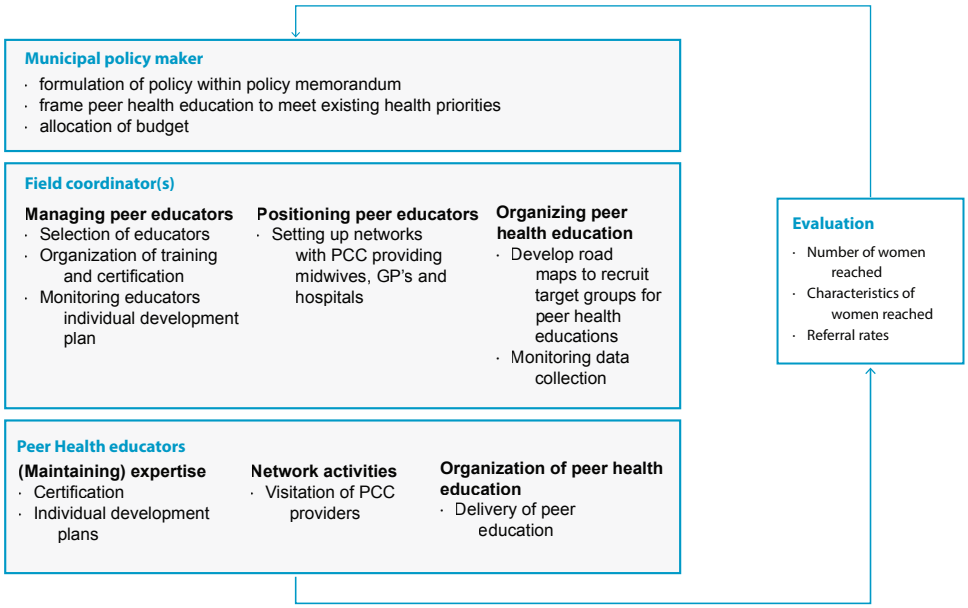
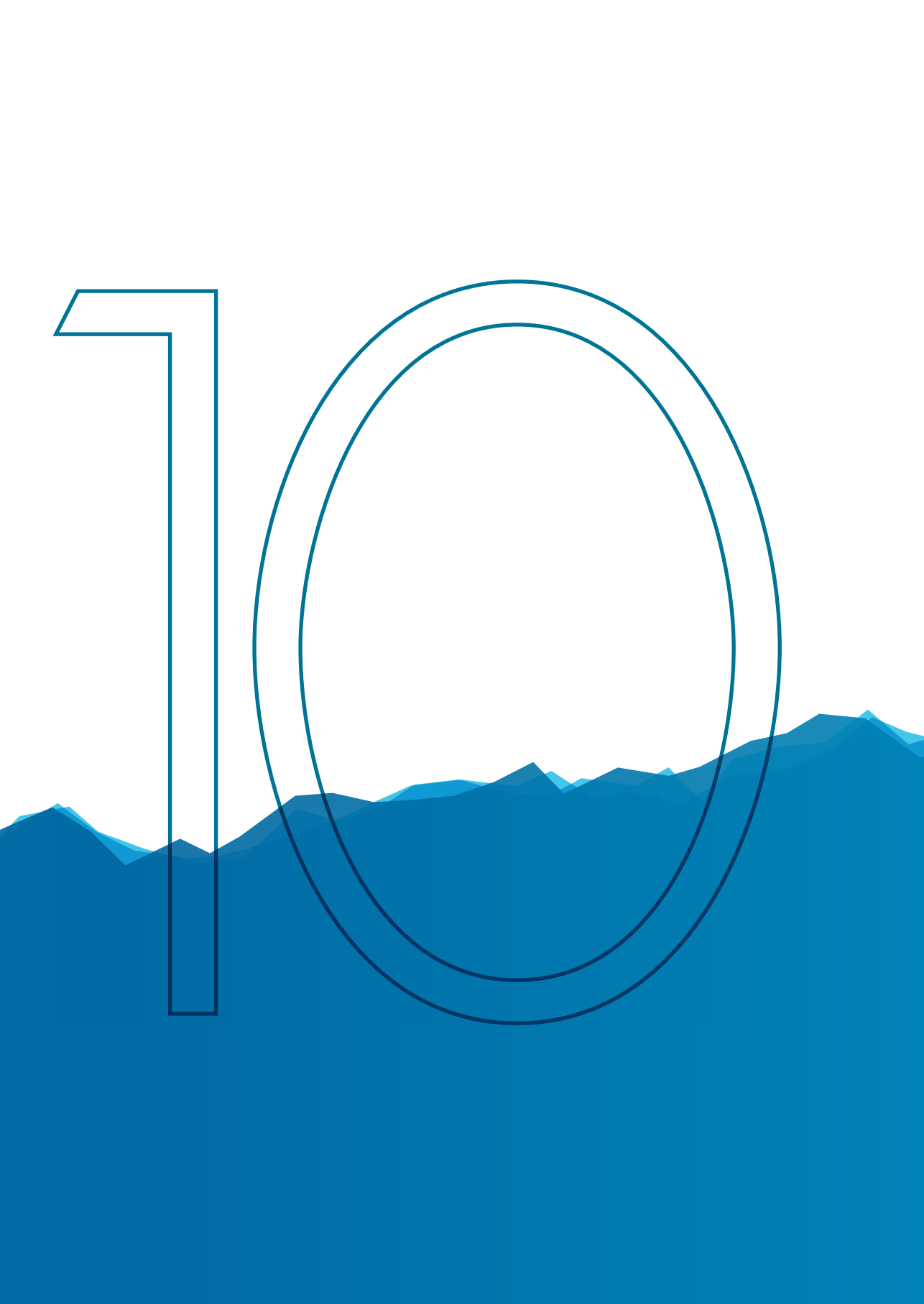
SUPPLEMENTARY FIGURE 1: An improved organizational model for preconception health education.



PART IV

BACK TO POLICY & PRACTICE



GENERAL DISCUSSION

This thesis looks back upon the emergence of PCC in the Netherlands over the past decade – from policy to practice and back. This chapter reflects upon principle findings and methodological considerations. Recommendations are provided for translations of findings to policy and practice.

PART I – AGENDA SETTING AND EVIDENCE TO SELECT PCC AS AN INTERVENTION

Aim of this part was to evaluate the policy process and to review the evidence which led to selecting PCC as an intervention to reduce perinatal mortality. Key conclusions are summarized in Box 1.

Emergence of PCC as a standard component of perinatal care

Quantification of perinatal mortality and morbidity in European context and in national context led to a debate about the organization of perinatal health care in the Netherlands. This perinatal mortality debate led to a sense of urgency to innovate in the organization of perinatal health care. Various measures were formulated from the preconception period to early childhood. The key finding of our policy analysis in **Chapter 2** was that the preconception period was acknowledged as a standard care component in perinatal healthcare policy.

BOX 1: Key features in policy regarding PCC(Part I)

- After the emergence of the concept of preconception care in the 1980's, preconception care was taken up in the Netherlands as a standard component of perinatal health care policy as of 2009.
- The perinatal mortality debate promoted adoption of preconception care.
- Preconception care is largely based on evidence for risk factors and expert opinions.
- Implementation of preconception care requires a 'leap of faith' from involved practitioners and policy makers, whilst activities in the preconception field continue to emerge and are evaluated iteratively.

Before the perinatal mortality debate, decisions regarding introduction of PCC had been stalled by policy makers. PCC was mostly initiated for single preconception health issues (e.g. genetic testing for autosomal recessive disorders) or for health issues amongst specific populations. Reason to decline the implementation of PCC was that the infrastructure for PCC was lacking. The Ministry of Health commissioned the Health Council of the Netherlands and the Steering group to evaluate the effectiveness and outreach of PCC before decisions regarding implementation of PCC were made.[1,2] Where prior agenda setting had failed to reach adoption of PCC, the perinatal mortality debate succeeded to. This is striking given that the concept of PCC already took flight in the 1980's.[3,4] Thus, it took three decades before introduction of PCC was agreed upon a national policy level.

Internationally, PCC has often been introduced in response to unfavorable perinatal mortality and or morbidity rates. The primary aim of programs is often to reduce perinatal mortality and morbidity.[5-11] However, literature regarding the extent to which these preconception research initiatives are taken up into national perinatal health policy of developed countries is scarce. To my knowledge, the largest body of literature derives from the United States. Here, perinatal mortality

rates led to a 'prenatal care crisis.' Prenatal care had been promoted as the answer to infant mortality in the beginning of the twentieth century. Yet, by the end of the twentieth century US prenatal care was not doing what obstetricians had promised it would do. This led to the questioning of the ability of prenatal care to combat adverse pregnancy outcomes. This fed the idea that there were certain drivers for adverse pregnancy outcomes that were resistant to antenatal care. This led to theorizing about innovative ways to improve birth outcomes.4 One of the consequences was the launch of 'the National Preconception Health and Health Care Initiative (PCHHC) of the Centers of Disease Control and prevention (CDC).[12-14] This initiative has achieved that PCC was integrated into three subsequent editions of the 'Healthy People' blue prints, as of 1980. These documents of the United States Department of Health and Human Services outline the ten year objective for improving health in the United States.[15-17] This approach illustrates a life course approach for improving population based health. In the Netherlands, such a research frame and consequent performance indicators for preconception health are lacking.

Implementation of PCC in the light of its evidence: a leap of faith?

Chapter 2 and 3 shows that evidence for PCC mostly relies on association studies showing the association between (single) risk factors and adverse pregnancy outcomes. Available evidence for interventions mostly focusses on single preconception interventions rather than comprehensive intervention programs. Intervention studies mostly report self-reported behavioural change as the outcome, rather than the effect on perinatal outcome.

Implementing PCC has been referred to by some as taking a 'leap of faith' in the light of the current evidence for the effectiveness of interventions.[4,18] However, there are three strong arguments to implement PCC. Firstly, effectiveness has been established for single preconception risk interventions.[19] Secondly, PCC provides opportunity for reproductive choices (Dutch Definition of PCC, Chapter 3) and secondary beneficial effects on parental health.[20] Lastly, it is unethical to withhold the emerging scientific knowledge about the importance of the periconception phase from prospective parents.

For the time being an authority based approach is acceptable. Having expert meetings, such as the one described in Chapter 3, can generate 'expert approved PCC program' complementary to the available evidence and guidelines. [21,22]

The challenge at hand, is providing a comprehensive delivery approach, as evidence for such approaches is lacking. Delivery approaches need to be implemented and evaluated in real time settings to provide the population with care and to refine care based on the generated evidence for different approaches. The Dutch national government has promoted research by allocating budget for a dedicated research program for PCC (the Netherlands Organisation for Health Research and Development (ZonMW)) as well as for the study that forms the basis of this thesis: the Healthy Pregnancy 4 All - PCC sub-study.

PART II - DESIGNING AN INTERVENTION STRATEGY

The aim of part II was to provide insights in how a programmatic PCC intervention strategy can be developed in high risk municipalities. Key features are summarized in Box 2.

The Healthy Pregnancy 4 All (HP4All) - PCC program is in line with contents of policy (**Chapter 2**), the expert meeting (**Chapter 3**) and the available evidence (**Chapter 3 and 4**). The PCC program is consistent to policy formulated in response to perinatal mortality with respect to the fact that it aims to activate the public health care at municipal level to participate in PCC. The PCC program is in line with the view of the field that dedicated actors are needed to recruit women for PCC, that PCC should be delivered in a comprehensive approach and that available tools should be used (ZwangerWijzer). Lastly, given limitations of the evidence highlighted in **Chapter 4**, the effectiveness of the program is evaluated iteratively.

BOX 2: Key features in the design of intervention approaches (Part II)

- The Healthy Pregnancy 4 All program was a vehicle to move the national policy towards a strategy for municipal implementation of preconception care.
- The PCC sub-study is in accordance with views of the field.
- Given the limitations in the evidence of PCC, the PCC sub-study is evaluated iteratively.
- The creation of a dedicated field for preconception care requires 'multilevel intervention' and 'knowledge brokering.'

To elaborate on the design of the HP4All – PCC sub-study from a broader perspective, I would like to emphasize its 'multilevel intervention' strategy and refer to the method of 'knowledge translation.' These are two emerging concepts in the public health care field.[21-23]

Multilevel interventions: HP4All is designed as a multilevel intervention program. Multilevel interventions can broadly be defined as intervention programs with targets to create change at more than one of the following levels: policy level, community level, organizational level, intra- or interpersonal levels.[21] The HP4All program targets four of these levels (see Table 1). The multilevel intervention strategy is a strength of the HP4All study because it provides vertical integration of PCC interventions. This provides benefits for PCC. Firstly, it allows utilizing socio-environmental resources such as the local health care professionals and local health care facilities. Local health care professionals could promote outreach of the intervention, as they might be trusted more by the target population in the community when it comes to discussing pregnancy contemplation.[24] Utilizing existing services is also important because PCC requires integration with other services. E.g. in case of smoking, a woman can be referred to a local smoking cessation service. Local health care providers may provide such services themselves or are likely to be acquainted with those services within the reach of their patients. This could enlarge the effectiveness of the PCC strategy, not to mention the effectiveness of other existing health care services. Another advantage of the multilevel strategy is that it allows identification of socio-environmental factors if evaluation of context factors is performed. This is important to fine-tune programs or to adopt strategies in different settings. Lastly, perhaps the most important advantage of multilevel intervention strategies is that it overcomes the volatile nature of health promotion programs. The strategy

equips the local setting with expertise and experience which are likely to outlive the duration of the program. This is important for sustainability. Equipping local settings with expertise is an essential part of the cycle towards science based policy.[25]

Knowledge translation: It is commonly acknowledged that there is a gap between 'what is known and what gets done in practice.[26,27] This gap is attributed to the large volume of scientific knowledge findings which is difficult for policy makers and health care professionals to keep up with and may be too complex to understand.[28] It has even been estimated that it takes 17 years to turn 14% of funded research into benefits to patient care.[29] Basic elements for science based practice are knowledge generation, knowledge exchange and knowledge uptake.[28] Knowledge brokering is a knowledge exchange strategy in which intermediaries, or 'brokers' function as mediators between researchers and intended users to help them understand each other's languages and

TABLE 1: HP4All as a multilevel intervention with knowledge brokering at different levels

LEVEL	WORKING DEFINITIONS	HP4ALL TARGET	KNOWLEDGE BROKERS
Policy level	"Larger systems possessing the means to control several aspects of the lives and development of their constituent subsystems."[31]	Municipal Aldermen and health care departments were made aware about their perinatal health situation and the need for PCC.	*HP4All*
Community level	"Collectives of people identified by common values and mutual concern for the development and well-being of their group or geographic area (villages neighbourhoods)."[31]	The programs recruitment strategy targeted the awareness for the need, benefits and availability of PCC services amongst women of reproductive age within the community.	*HP4All, municipal program managers*
Organizational level	"Systems with a formal multi-echelon decision process operating in pursuit of specific targets (schools, companies, professional organisations)" [31]	The availability of PCC was created and the quality of PCC was ensured by means of training of health care professionals and the use of tools.	*HP4All, municipal program managers*
Intrapersonal level	"Persons and small groups with whom the at-risk people associate" (family friends)."[31]	Not applicable	*Not applicable*
Interpersonal level	"Characteristics of the individual such as knowledge, attitudes, behaviour, self-concept, skills, etc."[32]	The recruitment approaches and the preconception consultations targeted improved knowledge and behavioural change regarding the uptake of PCC consultations and behavioural change	*HP4All, municipal program manager, recruitment partners, PCC providers*

Adapted from Scholmerich V.L.N. and Kawachi I, Multilevel interventions: theory and practice.[33]

eliminate barriers to the use of scientific knowledge.[30] In the HP4All program knowledge brokering was an ongoing mechanism to drive the actions of the project at the different levels (see Table 1). Available evidence suggests that knowledge brokering promotes the use of research evidence to inform decision-making while quality of the knowledge used is improved.[30]

PART III – IMPLEMENTATION OF PCC

The aim of part III was to evaluate implementation of PCC with its stakeholders. It provides insights regarding awareness for PCC, existing networks for PCC, the promotion of PCC, the delivery of PCC and context factors.

Awareness of PCC

Low awareness of PCC was a recurring theme throughout the studies of this thesis and during the introduction of the HP4All preconception program in the field.

Firstly, the need for PCC was hardly known amongst most Aldermen, Municipal health care departments and GP's. They were surprised when they were confronted with the high perinatal mortality and morbidity rates as presented in **Chapter 5**. They provided the explanation that they didn't have access to their loco-regional perinatal health statistics. Although prevalence's of perinatal morbidity and mortality was high at municipal levels, experienced prevalence within the whole case load by GP's and midwives was said to be too low to be tangible. Most stakeholders said awareness of local perinatal mortality and morbidity numbers provided the urgency to participate in HP4All.

Secondly, the field was unaware of PCC. Although Aldermen, Municipal health care departments, Youth Health Care (YHC) professionals and GP's were aware of some single preconception risk factors (e.g. folic acid), many were unaware of delivery of PCC. On the other hand, midwives were very aware of comprehensive PCC consultation services. This seems to be because when the midwifery guideline for PCC was made available, training in delivery of PCC was provided and it was integrated into the curriculum of midwives training programs. Other than publication in the

BOX 3: Key features in the implementation of PCC (Part III)

- Awareness about preconception health and PCC was low amongst Aldermen, Municipal health services, youth health services, GP's and high amongst midwives.
- Networks for programmatic PCC are underdeveloped.
- The role of the Dutch public health system in PCC needs to be further explored.
- The private nature of the topic of conception is a barrier for all stakeholders to approach women; yet women are more lenient than we think they are with regards to what is acceptable in the promotion of PCC.
- Individual comprehensive PCC is only delivered at a small scale and tends to be single risk factor focussed rather than comprehensive.
- It is not necessary that all GP's and midwives deliver PCC, however it is necessary that they all recruit for PCC.
- GP's need to utilize the identified moments in routine care to recruit for PCC consultations.
- PCC needs to be delivered in a more uniform way; risk assessment tools and 'blue prints' for risk factors can provide a solution.
- Context factors: Lack of reimbursement for general PCC and fragmentation of care in the Dutch tiered health system impede implementation of PCC.
- Indicators need to be developed to monitor implementation of PCC.

scientific journal of Dutch GP's followed by one temporary e-learning tool there have been no other structural efforts (e.g. training) to inform and train GP's about PCC.[34] In order to achieve delivery of PCC, awareness of the need for PCC and skills to either deliver or refer for PCC are essential.

Awareness of women in the Netherlands regarding the need and the availability of PCC is low. This has been experienced in prior Dutch programs and is a recurring finding in international studies as well.[35-38] This should be an important target point for campaigns and recruitment strategies.

Existing networks for programmatic PCC

Within the HP4All - PCC strategy collaboration was needed between public health care and curative health care. These networks were generally underdeveloped. The peer health education component (**Chapter 9**) illustrated this: women were not referred for PCC consultations to participating GP's and midwives providing PCC despite the program implementation strategy. Some women had been referred beyond the network. However, it is not simply the referral action that counts; it is about referring women to the right professionals that counts.

The commissioners of the HP4All study foresaw that it would be challenging to achieve collaboration between public health care and curative health care. Such collaboration is a generic requirement for the current perinatal health care field and for women's' health services. With regards to PCC it is important that efforts to create networks between public and curative health care are made and/or maintained. The different stakeholders have different expertise and resources and can therefore have a synergistic effect in PCC initiatives. Lastly collaboration is important to embed efforts in the cycle of policy making – intervention design – implementation and evaluation. This increases effectiveness and sustainability.

Promotion of PCC

Manuscripts in this thesis and experiences in setting up the HP4All program provide insights in the recruitment roles of stakeholders.

Prior to the HP4All study, the public health system had a very minimal role in preconception health promotion (**Chapter 2**, figure 1) and no role in recruiting women for PCC. Sending invitational letters was not new for municipalities (e.g. youth vaccination program or cervical cancer screening). Yet, when it came to an active role in inviting women for PCC there were more barriers than foreseen. The main barriers to send the municipal letter was the fears of hurting feelings of sub- or infertile women and to meddle with such a personal topic as conception as a governmental institute. These concerns were taken seriously and the letter was adapted so 11 of the 14 municipalities agreed to send the letter.

Youth Health Care (YHC) practitioners were asked to personally inform women of a PCC consultation by midwives or GP's during consultations for their children. Barriers to implement this strategy was that it would be in contradiction to the trending working approach to deliver care depending on individual risks (a high-risk approach) and demand (a demand driven approach). The 'high-risk approach' conflicts with the scientific finding that no less than 98% of the primary care population has one or more risk factors for which a PCC consultation is indicated.[39] Furthermore

the prevalence of preconception risk factors is likely to be higher in the designated area's (**Chapter 3**). The demand driven approach conflicts with the fact that the demand for PCC and the preconception health literacy are both low (**Chapter 7 and 8**). Consumer research highlights that the high-risk approach is not in line with the preferences of women, who found it acceptable to be told about preconception care regardless of their risks (**Chapter 8**). In other words these approaches are not according to the so called 'every women every time' approach that is necessary for recruitment.40 The program failed in achieving active personal referral by YHC: YHC activities were mainly restricted to providing an information leaflets and posters in waiting rooms.

Where the municipal letter and referral by YHC were not meant to selectively target women with a pregnancy wish, peer health intervention was meant to. However, process evaluation showed that only a minority of women that attended peer health education sessions had a pregnancy wish (**Chapter 9**). Implementation evaluation explained that this was because preconception health was introduced into existing meetings about other health topics, rather than that women were specifically recruited. This was not the programs recruitment strategy. However, perhaps reaching people influential to (future) mothers can indirectly sensitize women to the importance of preconception health and other recruitment activities. Effectiveness of such a strategy would need to be evaluated.

GP's are accustomed to opportunistic approaches in pointing out preventive health care issues.[41] We discovered several moments (e.g. pregnancy wish, fertility matters, negative pregnancy test, hereditary diseases and after miscarriage) during which both GP's and women find suitable to talk about PCC. These moments are currently underutilized by GP's (**Chapter 7 and Chapter 8**). Furthermore, GP's need to be aware of the importance of the availability and the benefit of a comprehensive consultation besides only pointing out risk factors. In other words, they need to abandon their 'single risk factor approach' and translate their activities to the explicit delivery of PCC consultations.

It is not common practice for GP's to send invitational letters for PCC (**Chapter 7**). GP's insisted they could exclude patients from the mailing because of fear to hurt patients' feelings in certain circumstances (again because of subfertility or adverse life-events). The program agreed that exclusion criteria could be applied, if reasons for exclusion were accounted for. This meant we had to deviate from the HP4All protocol as the program intended to send letters to all women aged 18 and up to 41 (**Chapter 6**). 21930 letters were sent in 32 of the 49 general practices. The letter is likely to have missed some women with a pregnancy wish. The Parents to Be Study demonstrated, that GP's simply cannot predict who has a pregnancy wish.[42]

Prior to the program, midwives that delivered PCC have set up recruitment for their own practice (e.g. with leaflets). Furthermore, the professional organization provides a list of midwives that are certified to deliver PCC. Experience was that prior small scale attempts have only yielded small scale uptake of PCC, if at all. This has been experienced as demotivating. Efforts at larger scale are necessary and were welcomed.

Overall, the implementation of the HP4All recruitment interventions was a first step in engaging the field in the recruitment for PCC. More important, it led to discussions about the roles

of the different stakeholders and which target population would be suitable for them to address. A trunk line was the fear that the recruitment approach would be inappropriate. At the same time the number of complaints from recipients was very limited. **Chapter 8** also showed that women find many approaches acceptable if explained adequately. This should encourage stakeholders to participate in recruitment approaches for PCC in the future. The effectiveness of the strategy and process evaluation needs to provide data to further adopt and refine strategies.

Delivery of PCC

Outside the scope of HP4ALL, the delivery of comprehensive preconception care by GP's and midwives only occurs at a very small scale (**Chapter 7**). This could be due to the underlying opinions as to who is responsible for PCC. A substantial number of GP's and midwives believe they are not primarily responsible for delivering PCC (**Chapter 7**). I am convinced that if there is a guideline from a professional organization, the specific topic belongs to its professionals. However, regardless of responsibility, whether a GP or midwife delivers PCC should depend on whether they feel capable to do so. HP4All showed us that it required training and conducting [5-10] PCC consultations to feel capable of delivering PCC. Therefore, it might be a solution to concentrate the actual delivery of PCC consultations to one or two GP's or midwives in a community. This will require more collaboration between professionals. Such collaboration is currently felt to be limited.[43]

Lack of uniformity of the contents of PCC (**Chapter 7**) is problematic. I believe uniformity starts with standardized risk assessment. The utilization of risk assessment tools needs to be increased, especially amongst GP's.

To date, comprehensive PCC has not been implemented within the YHC setting in the Netherlands. During the HP4All PCC study, some YHC professionals indicated they were willing to deliver comprehensive PCC consultations themselves. To explore this, we adapted the questionnaire in **Chapter 7** to investigate Youth Health Care physicians' activities and attitudes towards PCC. A low response rate (8%; n=88/1088) brought us to exclude the results from this chapter. 22% of the YHC physicians found themselves primarily responsible for PCC. Although this result should be interpreted with caution, it highlights that there may be some ambition to deliver PCC. This was confirmed within a recent consensus meeting with YHC professionals, although it also became apparent that YHC professionals foresee barriers in the delivery of PCC.[44] As women said that they prefer to receive PCC from a GP or midwife, preference of women to receive PCC from YHC physicians would need to be evaluated (**Chapter 8**). The role of YHC is currently further investigated in the sequence program of HP4All: "Healthy Pregnancy 4 All 2."[45]

Preconception care is now an isolated care entity within perinatal health care. There is a need to have continuity between preconception care and antenatal care. This is important to ensure women's compliance with the preconception health plan during pregnancy and for efficiency (there is a large overlap in the risk assessment during pregnancy for instance). This requires that a preconception health file is integrated into antenatal files and that communication between professionals improves. Changing the organization of perinatal care was the main point of departure after the societal perinatal mortality debate described in **Chapter 2**. One can also argue

that it could be integrated 'vertically' with other preventive health services. In the US the desire to integrate PCC into 'well women visits', has been expressed.[46] Long-term effectiveness of these visits are unknown, however they are thought to promote delivery of preventive services.[47] Revisiting the preventive health scheme across a woman's lifespan can make delivery of care more efficient.

Context factors

The Dutch tiered health care system provides challenges in the organization of perinatal health care (**Chapter 2**). Preconception care is complex, requires extensive risk assessment and subsequent intervention. In this process, it is likely to come across risk factors that exceed the competence of the respective professional. Therefore, collaboration is necessary across the tiers and there is a need for multidisciplinary care pathways to deliver preconception health interventions. To overcome the challenges of the tiered system during pregnancy, HP4All's other sub-study developed care pathways for risks. Many of these care pathways could be adapted to the preconception phase and hence promote uniformity of care.[48]

Before and during implementation of the HP4All study, PCC consultations were not reimbursed within basic health insurance packages. Consequently, many providers did not deliver PCC or transferred costs into bills for the patients. However, women are generally not willing to pay for PCC (**Chapter 8**). During the HP4All program a temporary reimbursement plan had to be created to achieve delivery of PCC without financial barriers. It is an excellent development that the 4 largest health insurance companies now reimburse PCC.[49]

Up to 2010 the monitoring of perinatal health was mostly seen as a responsibility of the curative field. Public health care partners often had no access to perinatal health statistics. If we want the public health care system to become more involved in perinatal care, university medical centers need to collaborate with municipalities in the evaluation of loco-regional perinatal health. Indicators for the receipt and delivery of PCC need to be formulated and integrated within existing data registries to monitor PCC.

Methodological considerations

There are some overall methodological considerations in this thesis.

Study populations

This thesis is based on data that reflects all stakeholders that have a role in PCC. This is one of the strengths of this thesis, yet we have some considerations regarding the sampling of data from these stakeholders.

The reflection upon the agenda setting of PCC (**Chapter 2**) mostly relies on the document analysis within the database of the Dutch government, which included 'PCC' in its search. Key–informants were selected if they were deemed to have had a significant role in the perinatal mortality debate or if they were mentioned by other key-informants. By applying this selection criterion, we could only identify key–informants for PCC agenda setting if they participated in the agenda setting of PCC in relation to perinatal mortality. Therefore, we may have missed events

which had a specific role in the agenda setting for PCC. This limits the verification of findings regarding the agenda setting of PCC.

A selection bias may be present with regards to sampling of practitioners. Professionals with more affiliation with PCC are probably more inclined to participate in the expert meeting (**Chapter 3**), the inventory about PCC activities (**Chapter 7**) and in the HP4All PCC study (**Chapter 9**). This could have resulted in overinflation of results leading to more positive findings. It is challenging to include women preconceptionally in preconception studies. Women planning to conceive (excluding subfertile women) do not present themselves within networks where it is opportune to enroll women into studies. Thus, we had to broaden the eligibility criteria for participation in our consumer research (**Chapter 8**). Women were eligible if they did not exclude wanting a pregnancy in the future. This might make findings more negative than when opinions about PCC were assessed purely amongst women with an actual pregnancy wish.

Review of evidence for PCC

It is a strength that the literature reviews in **Chapter 2** and **Chapter 3** include observational studies as well as case-control studies. Only including randomized controlled trials (RCT's) is incorrect with regards to PCC. It is not ethical to recruit women in the preconception period and not provide any form of preconception intervention because of the evidence of several single risk factors.

The high risk approach

In the design of the Healthy Pregnancy 4 All program there was a need to roll out interventions in municipalities with highest perinatal mortality and morbidity rates, because effectiveness of the program was believed to be the largest there. This required developing an intervention approach that targets populations which are known to be the most difficult to reach. Retrospectively, one can argue whether this is the most practical approach as hard-to-reach groups require special strategies. As an intervention strategy in general is lacking, it would have also been feasible to develop a strategy for the general population and to consequently fine tune the strategy to target risk areas. This fine-tuning would then require audience segmentation and developing materials together with members of the target population. Practical reasons set aside, it may well be that introducing PCC amongst the general population first may increase acceptability of PCC amongst the hard-to-reach women.

Effectiveness of recruitment strategy and individual PCC

This thesis does not include results regarding the effectiveness of the recruitment strategy and preconception consultations. This is because the program implementation had to be extended to be able to achieve the calculated sample size. This was given in by the fact that time remaining for implementation was less because it took longer than expected to set up the programs. Furthermore, it took more time as the program was rolled out in 14 municipalities instead of 6 municipalities. After extending the inclusion period, it was closed In December 2014 because the target population was not thought to be attainable and there was a lack of funding to further extend the inclusion

period. A total of 587 women had made an appointment for a PCC consultation, of which 259 (44%) women participated in the study. This is below the calculated study size of 839 which means the study is underpowered. Lack of statistic power is likely to be due to short inclusion period (one municipality had an inclusion period of 9 months), insufficient implementation of the peer health education recruitment component, and the youth health care recruitment component and limited effectiveness of the recruitment strategies.

It proved that the by far the most important hampering factor in the HP4All study was related to bringing about change within the health care system itself. Process evaluation is necessary to get grip on to the challenges of implementation in the real time setting and to understand program outcomes.

Process evaluation

A limitation of our approach to process evaluation (**Chapter 9**) is that the process evaluation is conducted by HP4All itself. Evaluation by an external partner which would include evaluation of the role of HP4All itself, would increase validity. Internationally, there is a need for evaluation of implementation strategies so initiatives can learn what works or doesn't work in various settings.

RECOMMENDATIONS

After reflecting upon findings in this thesis, the following recommendations apply to future PCC:

- Implementation and research of PCC need to occur within a continuous cycle of agenda setting, intervention selection (or refinement), implementation and back translation to policy and practice. This requires:
  - Keeping PCC on the policy agenda by providing numbers regarding PCC performance indicators (e.g. % of pregnancies after PCC consultations, number or PCC consultations in relation to women of reproductive age). Data collection could be integrated into the Dutch Perinatal Registry and into the 4 annual municipal health inquiries which municipalities use to identify health and socioenvironmental issues that need to be addressed in preventive health care policy.
  - Iterative evaluation of implementation and effectiveness of PCC intervention strategies
  - Central coordination of PCC research initiatives according to predefined targets and expert meetings to renew or refine intervention strategies.
  - Knowledge brokers need to be coordinated centrally so they can translate experiences in implementation of PCC in different settings to new area's in which there is no programmatic approach to PCC.
- GP's and midwives need to upscale and improve their PCC activities by:
  - utilizing moments in every day practice to point out availability of PCC consultations
  - integrating recruitment for PCC with other preventive health services
  - referring for PCC or deliver PCC themselves. If they deliver PCC themselves they need to deliver PCC in a structured uniform way using established risk assessment tools and

blueprints for preconception risk factors agreed on by multidisciplinary working groups.

- The role of the public health care system needs to be further defined. Trends to deliver preventive health care in the Netherlands according to a 'demand driven' or 'high risk' approach is not applicable to recruitment for PCC.
- To increase effectiveness of programmatic PCC all stakeholders need to invest in mutual collaboration.
- Recruitment models for PCC need to include a multiple hit approach to ensure women are reached out to at several moments in their reproductive lives.
- PCC strategies need to be tailored locally. This can be done by involving the respective target group prior to implementation and by adapting best practices from other settings.

CONCLUSION

This thesis provides reflection upon the agenda setting for PCC, selection of interventions for PCC, the design of a programmatic approach for PCC and implementation of PCC by different stakeholders in PCC. Despite evidence about PCC risk factors, comprehensive PCC only occurs at a small scale. By implementation of programmatic PCC within the HP4All study, PCC has been implemented at a large scale as a multilevel strategy. Main challenge of delivering programmatic PCC is to achieve the required organizational changes needed amongst all stakeholders within communities. Awareness needs to increase, mind shifts are required, knowledge and expertise needs to increase and new collaborations need to develop. It appears that these prerequisites need to be further developed before a PCC program for the general population can be effective.

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SUMMARY / SAMENVATTING

ENGLISH SUMMARY

Current perinatal care is inadequately addressing risk factors in early pregnancy. By the time antenatal care commences (at best in the 8th week of gestation) the foetus has already been exposed to risk factors during crucial events in its development. These risk exposures are associated to perinatal mortality and morbidity. Over the past decade most focus has been set on perinatal mortality as indicator of perinatal health care quality. However, mortality is only the tip of the iceberg: being born with perinatal morbidity can give rise to disease and illness in childhood and adulthood. Preconception care (PCC) addresses risk factors before conception and therefore reduces chances of perinatal morbidity and mortality. It is the most primary form of prevention there is. Perinatal care should include PCC in order to promote perinatal health, which is the first step in having a health society.

Countries are facing challenges regarding how PCC can be delivered effectively with sufficient outreach. In the Netherlands, it has been advocated to deliver PCC in the form of individual consultations to the general public.

This thesis looks back upon events in the past decade and research regarding the organization of individual PCC within the Dutch primary care and public health system. This thesis is presented according to the following cycle in which health policy is ideally developed. Firstly, a health issue reaches the agenda and interventions are selected (Part I); an intervention approach is designed (Part II); lessons are drawn from implementation and evaluation in practice (Part III) and findings are back translated to policy and practice (Part IV).

Hence the title of this thesis: 'Preconception care - from policy to practice and back'.

Part I – Agenda setting and intervention selection

Preconception care was selected as an intervention during the policy process described in **Chapter 2**. Intervention selection is ideally performed in light of available evidence and with experts in the field (**Chapter 3 and 4**).

Chapter 2 provides a chronologic reconstruction of how the relatively unfavorable perinatal mortality and morbidity rates of the Netherlands compared to other European countries (EURO-PERISTAT reports) and the inequalities in perinatal health (**Chapter 5**) led to policy reform between 2004 and 2010. The perinatal health problem became a national health issue with a high priority. This was promoted by the quantification of perinatal mortality and morbidity, the nature of the topic and involvement of the media and the political field. Where the typical Dutch organization of perinatal care was undisputed prior to the debate, the debate led to the recognition that how perinatal care was organized needed to be changed. The debate engaged a broad range of actors beyond the curative field. Proposed measures reflected the multidisciplinary collaboration of actors. The importance of preventive approaches in which socioeconomic determinants of perinatal health was acknowledged and this emphasized the important role of municipalities. The scope of prenatal care was (re)defined as care including the preconception period until early childhood.
Involvement of municipalities was deemed important to address socioeconomic determinants of perinatal health. A contextual factor impeding the policy process was the tiered organization

of perinatal health care in the Netherlands. The different tiers have fundamentally different perspectives regarding the ideal organization of perinatal health care. The Healthy Pregnancy 4 All (HP4All) study is one of the products of this policy process. It is in accordance with the several key aspects of the newly formulated perinatal health policy identified in **Chapter 2**.

Aim of the Dutch national summit on PCC (2012) was to contribute to policy making and implementation by evaluating current evidence, gaps in knowledge and opinions of experts in the field. **Chapter 3** presents the results of this meeting. Highlights concern:

- *Definition:* The definition of PCC was broadened with regards to three aspects. Firstly, PCC is a program or a set of interventions rather than a single intervention. Secondly, non-medical risks are addressed besides medical risks. Thirdly, the definition now highlights that counselling and informed decision making are important goals of PCC.
- *Organizational approaches:* There was consensus to categorize PCC into collective measures, general individual PCC and specialist individual PCC. The role of different health care professionals within general and specialized preconception care needs to be defined.
- *Target groups:* It was acknowledged that a broader range of actors needed to become involved in advocating PCC to target groups.
- *Contents:* PCC was expanded to address more risk factors. Future research should point out how caregivers should prioritize in interventions when multiple risk factors are present.
- *Risk assessment instruments:* There was consensus to adopt a generic risk assessment instrument. The field stated the need to optimize and validate existing tools or to develop new tools.

Chapter 4 shows there is evidence for the effectiveness of preconception interventions addressing nutrition, alcohol, smoking and folic acid intake. Generalizability of these findings may be limited since interventions were mostly delivered as single measures and amongst selected populations. Evidence is deemed sufficient to provide lifestyle recommendations to the general public while effectiveness of interventions is evaluated iteratively.

Part II - Development of an intervention strategy

This section provides the design of the Healthy Pregnancy 4 All (HP4All) study.

Chapter 5 shows how we decided upon the areas for dissemination of the intervention study. We contemplated that municipalities with highest perinatal mortality and morbidity would benefit most from intervention. We performed a geographic analysis of perinatal mortality and morbidity after which 14 municipalities were selected. All approached municipalities agreed to participate in the HP4All study. The HP4All study was designed to consist of interventions that aimed to reduce risks in early pregnancy: a programmatic approach to preconception care and early standardized antenatal risk assessment during early pregnancy. The Preconception care sub-study and the Risk Assessment sub-study were set up to evaluate the effectiveness of both interventions.

Chapter 6 describes the rationale and design of the HP4ALL Preconception care sub-study. The intervention consisted of an individual PCC consultation delivered by general practitioners (GP's) and midwives in the community. The PCC consultation consisted of an initial consultation during which risk assessment was performed and a tailored management plan was made. A follow-up

consultation took place 3 months later. Additionally, a recruitment strategy was designed to target women to utilize the PCC services. Invitational letters were sent by municipal public health services and participating general practices and women were referred by Youth health care centers and peer health educators.

The effectiveness of the PCC sub-study is evaluated with a cohort study. Primary outcome regarding the effectiveness of consultations is behavioural change regarding preconception health behaviours (folic acid supplementation, cessation of smoking, alcohol consumption and/or drug use). Primary outcome regarding the effectiveness of the recruitment strategy is outreach expressed in the number of women recruited and characteristics of women approached. Sample size calculation resulted in a study size of 839 women. Participants were enrolled between February 2013 and December 2014.

Part III - Evaluation of Implementation

This part reflects on what can be learned from different stakeholders in preconception care: midwives and general practitioners (**Chapter 7**), women contemplating pregnancy (**Chapter 8**) and municipal public health partners including peer health educators (**Chapters 9**).

Chapter 7 provides the results of a cross-sectional survey to evaluate current activities, perceptions and prerequisites of GP's and midwives regarding individual PCC consultations.

- *Current activities:* This study confirms that systematic delivery of PCC consultations only occurs at a small scale. Activities GP's and midwives are mostly opportunistic: risk factors are pointed out and questions about preconception risks are answered upon confrontation in daily practice. Explicit promotion and delivery of an actual individual PCC consultation only occurs occasionally. The content of the delivered PCC is not uniform amongst caregivers.
- *Perceptions:* Respondents' perceptions about PCC consultations are generally positive. Midwives see themselves as the professionals who are primarily responsible for the delivery of PCC. GP's are ambivalent as to whether GP's or midwives are primarily responsible for PCC. Respondents are willing to increase their promotion of a comprehensive PCC consultation during various moments in routine care. Providers are willing to use risk assessment tools, which promote uniformity of consultations.
- *Prerequisites:* Respondents find more training about PCC, staff support, promotion of PCC and adequate reimbursement to be prerequisites for future delivery of PCC.

Chapter 8 presents findings of consumer research. This is the first step towards social marketed preconception care consultations. The philosophy of social marketing is that products are designed, so both the needs of women and the system are met. A qualitative study design was used to assess preferences across the four essential components (or the four P's) of the social marketing: 'Product, Place, Price and Promotion'. The most striking finding was the low knowledge of the purpose and benefits of the product (PCC). Perceived needs of women depend on their obstetric history and concerns about fertility and parenthood. PCC is not addressing these concerns. Low knowledge of the product emphasizes the importance of promotion. Women express that they want to make the informed decisions whether they utilize PCC services. They see the primary care setting as the most

suitable place to be informed about PCC. We identify several specific occasions for professionals to bring up PCC. However, women also prefer to be informed about PCC, regardless of their risk factors because they might have risk factors they don't know about themselves. This should support health care professionals to become more active in the promotion of systematic PCC consultations. Regarding place characteristics, women find the community based primary care system as the most suitable care echelon. Lack of reimbursement is a dilemma for women that see the benefits of PCC yet have financial means to attend PCC.

Chapter 9 provides an in-depth process evaluation of the peer health education strategy in HP4All. In HP4All we integrated peer education from the public health care domain into a strategy to promote uptake of PCC consultations. Strategy was that peer educators would refer participants of peer education sessions to preconception consultations centers in the community. This strategy was adopted in 7 municipalities.

The implementation criteria were met in 4 of the 7 municipalities. However, implementation at overall program level was insufficient because outreach was insufficient. Peer educators did reach underserved women. However the seldomly referred women. Qualitative data provided that this was due to lack of time to set up the program as intended, lack of adherence to the target population and lack of effective working relationships between peer educators / municipal health services and the centers delivering PCC consultations. The strategy needs to be refined to draw conclusions regarding the effectiveness of the strategy.

Part IV - Translation of findings back to policy and practice

In **Chapter 10** we reflect upon the main findings of this thesis, as well as the strength and limitations of the study. We conclude by providing recommendations regarding the organization of general PCC within the Dutch health care system.

NEDERLANDSE SAMENVATTING

De huidige perinatale zorg schiet tekort in het tijdig aanpakken van risicofactoren in de vroege fase van de zwangerschap. Tegen de tijd dat antenatale zorg start (in het meest gunstige geval rond de achtste week van de zwangerschap) heeft de foetus al tijdens kritische ontwikkelingsprocessen blootgestaan aan risicofactoren die geassocieerd zijn met perinatale mortaliteit en morbiditeit. Bijvoorbeeld roken of het gebruik van geneesmiddelen door de moeder. Lange tijd was er focus op perinatale mortaliteit als indicator voor de kwaliteit van perinatale zorg. Perinatale mortaliteit is echter slechts het 'topje van de ijsberg.' Geboren worden met perinatale morbiditeit is geassocieerd met een grotere kans op het ontwikkelen van ziekten in het latere leven. Omdat men met preconceptiezorg risicofactoren aanpakt vóór de conceptie, kunnen deze risicofactoren aangepakt worden als zij nog geen (of minimale) schade hebben kunnen berokkenen. Preconceptiezorg is daarom de meest primaire vorm van preventie die er is. Prenatale zorg dient de preconceptiefase te benutten voor gezondheidsbevordering voor moeder en kind. Dit ligt ten grondslag aan een gezonde maatschappij.

Verschillende landen staan voor de uitdaging hoe preconceptiezorg effectief en met voldoende bereik geleverd kan worden. In Nederland hebben we het adagium om algemene preconceptiezorg in de vorm van individuele consulten in de eerste lijn aan te bieden aan de algemene populatie.

Dit proefschrift blikt terug op de gebeurtenissen van het afgelopen decennium en op onderzoek met betrekking tot de organisatie van individuele preconceptiezorg in de eerste lijn en in het publieke gezondheidsbestel. Het proefschrift is ingedeeld volgens de chronologische stappen van gezondheidsbeleid. Eerst komt een gezondheidsprobleem op de agenda, worden er interventies geselecteerd (Deel I). Vervolgens wordt er een interventiebeleid ontwikkeld (Deel II), wordt implementatie van de interventie geëvalueerd (Deel III) en vervolgens worden bevindingen terugvertaald naar beleid en praktijk (Deel IV). Vandaar de titel van dit proefschrift: 'Preconceptiezorg – van beleid naar praktijk en terug.'

Deel I – Agendasetting en interventie selectie

Preconceptiezorg is geselecteerd als interventie tijdens het beleidsproces dat beschreven wordt in **Hoofdstuk 2**. Interventie selectie wordt idealiter uitgevoerd in het licht van beschikbaar bewijs voor de interventie en met experts uit het veld (Hoofdstuk 3 en 4).

De beleidsanalyse in **Hoofdstuk 2** geeft weer hoe de relatief ongunstige cijfers voor perinatale mortaliteit en morbiditeit hebben geleid tot een vernieuwd perinataal gezondheidsbeleid. Perinatale gezondheid kreeg hoge prioriteit toen bleek dat Nederland ongunstig scoorde op perinatale sterftecijfers ten opzichte van omliggende landen. Daarnaast werd in Nederland een grote ongelijkheid gezien in perinatale gezondheid. De kwantificering van het gezondheidsprobleem, de aard van het onderwerp en de betrokkenheid van de media en de politiek hebben bijgedragen aan de prioriteitstelling om maatregelen te nemen. Er ontstond bewustzijn dat er verandering nodig was in de manier waarop perinatale zorg georganiseerd werd. Maatregelen werden geformuleerd voor de hele perinatale zorgketen, die gedefinieerd werd als zorg vanaf de preconceptie fase tot zorg in de vroege kinderjaren. Voorgestelde maatregelen reflecteerden de inbreng van de

verschillende actoren, afkomstig van verschillende disciplines. Zo kwam de nadruk te liggen op preventieve maatregelen en het rekening houden met socio-economische determinanten van perinatale gezondheid. Hierbij werd een rol toegekend aan gemeenten. Het 'lijnen systeem' van de Nederlandse zorg en de verschillende perspectieven van verloskundigen en gynaecologen die met elkaar in strijd waren bemoeilijkten het beleidsproces.

De 'Healthy Pregnancy 4 All' studie is één van de initiatieven die zijn oorsprong vindt in het beschreven beleidsproces. Het programma komt op meerdere punten tegemoet aan speerpunten in het beleid dat tijdens deze periode geformuleerd is.

Hoofdstuk 3 beschrijft de resultaten van de Nederlandse expertmeeting over preconceptiezorg in 2012. Deze expertmeeting heeft geresulteerd in de volgende kernpunten:

- *De definitie:* De definitie van preconceptiezorg is verbreed. Het is gedefinieerd als een programma of een set van maatregelen in plaats van een interventie t.a.v. een enkele risicofactor. Verder omvat de definitie nu ook dat preconceptiezorg niet-medische risicofactoren adresseert en dat counseling en geïnformeerde besluitvorming doelstellingen zijn.
- *Organisatorische benaderingen:* Er was consensus om organisatorische benaderingen voor preconceptiezorg onder te verdelen in collectieve maatregelen, algemene individuele preconceptiezorg en specialistische individuele preconceptiezorg. Er dient afgestemd te worden wat de rol is van verschillende zorgverleners in algemene en specialistische preconceptiezorg.
- *Doelgroepen:* Er moeten meer disciplines betrokken raken bij het promoten van preconceptiezorg onder doelgroepen.
- *Inhoud:* De inhoud van preconceptiezorg is uitgebreid. Onderzoek moet uitwijzen hoe er geprioriteerd moet worden in interventies als er meerdere risicofactoren aanwezig zijn.
- *Risicoselectie instrumenten:* Er is consensus om één generiek risico instrument te gebruiken. Beschikbare tools moeten geoptimaliseerd en gevalideerd worden of er moeten nieuwe instrumenten ontwikkeld worden.

Hoofdstuk 4 toont de effectiviteit voor interventies in de preconceptiefase gericht op voeding, alcohol, roken en foliumzuurinname. Generaliseerbaarheid van deze bevindingen naar de algemene populatie kan beperkt zijn omdat de interventies geïmplementeerd zijn als losse interventies (in plaats van in een programma) en omdat veel studies binnen geselecteerde populaties zijn uitgevoerd. Toch is de bewijsvoering voldoende om de betreffende leefstijl-interventies te implementeren, bij voorkeur iteratief.

Deel II - Ontwikkeling van een interventie strategie

Dit deel geeft inzicht in de ontwikkeling van de 'Healthy Pregnancy 4 All (HP4All) studie.

Hoofdstuk 5 laat zien hoe we de gebieden voor de uitrol van het HP4All programma hebben geselecteerd. Er werd verondersteld dat de gemeenten met de hoogste perinatale mortaliteit en morbiditeit de meeste winst zouden behalen met de interventies. Na een geografische analyse van perinatale mortaliteit en morbiditeit werden 14 gemeenten geselecteerd. Alle benaderde gemeenten hebben ingestemd met deelname aan het HP4All programma. In lijn met het bewijs dat

embryonale gezondheid cruciaal is voor verloop en de uitkomst van de zwangerschap, omvat de HP4All studie twee interventies: 1. een programmatische aanpak voor individuele preconceptiezorg en 2. systematische risicoselectie in de zwangerschap. Effectiviteit van de interventies werd binnen tegelijk lopende zorgexperimenten geëvalueerd.

Hoofdstuk 6 gaat in op de opzet en de onderbouwing van het HP4All preconceptiezorg experiment. De interventie bestond uit een individueel preconceptiezorgconsult bij deelnemende huisartsen en verloskundigen. Het consult bestond uit een eerste bezoek waarin risicoscreening plaatsvond en een plan werd gemaakt om bestaande risicofactoren te bestrijden. Drie maanden later vond er een vervolgconsult plaats. Om het gebruik van de preconceptiezorgspreekuren te bevorderen werd een wervingsstrategie toegepast. Er werden uitnodigingsbrieven door gemeente en door deelnemende huisartsen verstuurd. Consultatiebureaus, Centra voor Jeugd en Gezin (CJG's) en speciaal opgeleide voorlichters preconceptiezorg verwezen vrouwen naar de spreekuren.

De effectiviteit van het programma wordt geëvalueerd door middel van een cohort studie. De primaire uitkomstmaat om de effectiviteit van de consulten te meten is gedragsverandering t.a.v. enkele preconceptionele leefstijl factoren (foliumzuur suppletie, stoppen met roken, alcohol en drugsgebruik). De effectiviteit van de wervingsstrategie wordt gemeten aan de hand van het bereik van het programma. Er werd berekend dat er 839 vrouwen nodig zouden zijn om de effectiviteit van preconceptiezorg te kunnen evalueren. Inclusie vond plaats tussen februari 2013 en december 2014.

Deel III - Evaluatie van implementatie

In dit deel wordt nagegaan wat er geleerd kan worden van de verschillende 'stakeholders' in de algemene preconceptiezorg. **Hoofdstuk 7** geeft inzicht over implementatie door verloskundigen en huisartsen, **Hoofdstuk 8** geeft inzicht in de visie van vrouwen over het preconceptiezorg consult en **Hoofdstuk 9** over de rol van de publieke gezondheidszorg en gezondheid voorlichters.

Hoofdstuk 7 geeft inzicht in de huidige activiteiten, percepties en randvoorwaarden van huisartsen en verloskundigen m.b.t. preconceptiezorgconsulten.

- *Actiteiten:* Dit onderzoek bevestigd dat preconceptiezorgconsulten slechts op kleine schaal aangeboden en uitgevoerd worden. Activiteiten van huisartsen en verloskundigen zijn voornamelijk ad hoc: ze wijzen vrouwen te vaak alleen op risicofactoren als ze ermee geconfronteerd worden tijdens de alledaagse zorg. Expliciet aanbod van een apart preconceptiezorgconsult gebeurt nagenoeg niet. Wanneer het wel plaatsvindt, blijkt de inhoud niet uniform.
- *Percepties:* Zorgverleners waren positief over preconceptiezorgconsulten. Verloskundigen zien zichzelf als de primair verantwoordelijke zorgverlener voor preconceptiezorg, terwijl huisartsen ambivalent zijn of ze zelf primair verantwoordelijk zijn of dat verloskundigen dit zijn. Respondenten waren bereid om gebruik te maken van diverse momenten in alledaagse zorg om vrouwen te wijzen op de mogelijkheid van een preconceptiezorgconsult. Verder waren zij bereid om gebruik te maken van instrumenten voor risicoscreening, hetgeen de inhoudelijke uniformiteit van consulten zou bevorderen.

- *Randvoorwaarden:* (Meer) training over preconceptiezorg, personele ondersteuning, strategieën om vrouwen naar preconceptiezorgconsulten toe te leiden en adequate vergoeding zijn randvoorwaarden voor het aanbieden van preconceptiezorg in de toekomst.

Tot slot wordt in **Hoofdstuk 8** het resultaat van het consumentenonderzoek gepresenteerd. Dit is de eerste stap richting preconceptiezorg volgens het 'social marketing' principe. De filosofie van deze strategie is dat een zorgproduct zo wordt ontworpen dat het tegemoet komt aan de doelen van zowel de doelgroep als het zorgsysteem. D.m.v. kwalitatief onderzoek zijn preferenties binnen de 4 domeinen (of de 4 P's) van social marketing onderzocht: 'Product, Plaats, Prijs en Promotie.' De meest opvallende bevinding t.a.v. het product was de lage kennis over het doel en de potentiele baten van het preconceptiezorgconsult. Of vrouwen noodzaak ervaarden voor een preconceptiezorg consult bleek vooral af te hangen van de verloskundige voorgeschiedenis van vrouwen en van hun vragen over vruchtbaarheid en ouderschap. De laatste elementen komen niet standaard aan de orde binnen preconceptiezorg consulten. Beperkte kennis over het product benadrukt het belang van promotie strategieën. Vrouwen willen graag geïnformeerde keuzes maken over het wel of niet gebruik maken van het preconceptiezorg consult. Ze zien de huisartsen en verloskundigen setting als de meest geschikte plaats om geïnformeerd te worden over een preconceptiezorg consult. Vrouwen vinden diverse aanleidingen in dagelijkse zorg van hun huisarts of verloskundige een goed moment om gewezen te worden op het preconceptiezorg consult. Bovendien vinden vrouwen het ook acceptabel om geïnformeerd te worden als ze geen evident risicoprofiel hebben, dit kan immers pas blijken na uitgebreide risicoscreening. Dit zou zorgverleners moeten ondersteunen om een actievere houding aan te nemen in het promoten van preconceptiezorg consulten. Vrouwen hebben een voorkeur voor preconceptiezorg in de eerste lijn, bij huisartsen en verloskundigen of in gezondheidscentra. Moeten betalen voor preconceptiezorg zadelt vrouwen met beperkte financiële middelen op met een dilemma t.a.v. bezoeken van het preconceptiezorgconsult.

Hoofdstuk 9 bevat de procesevaluatie van de voorlichting preconceptiezorg binnen HP4All. Waar het gebruikelijk is om een voorlichtingsstrategie te implementeren binnen de context van de publieke gezondheid, is met de HP4All strategie getracht om een brug te slaan naar zorg binnen de curatieve setting: de huisartsen en verloskundigen die preconceptiezorg aanbieden in het project. Doel van voorlichters in de HP4All strategie was dat speciaal opgeleide voorlichters deelnemers van groepsvoorlichtingen zouden verwijzen naar preconceptiezorgconsulten. Hiermee vervullen voorlichters een brugfunctie naar individuele eerstelijns preconceptiezorg. De strategie is geadopteerd in 7 gemeenten. Vier van de 7 gemeenten voldeden aan de implementatiecriteria. Op programma niveau was de implementatie onvoldoende omdat het bereik onvoldoende was. De moeilijk te bereiken groep werd bereikt, maar er werd niet verwezen naar preconceptiezorgconsulten. Kwalitatief onderzoek gaf inzicht in verklaringen. Voornaamste redenen waren tijdsgebrek, het niet vasthouden aan de afgesproken doelgroep en het gebrek aan effectieve samenwerking relaties tussen voorlichters, gemeenten en de praktijken die preconceptiezorg aanboden in het programma. De strategie moet verbeterd worden om conclusies te trekken over de effectiviteit van voorlichters als verwijzers naar individuele preconceptiezorg.

Deel IV - Terug naar beleid en praktijk

Tot slot reflecteren we in **Hoofdstuk 10** over de hoofdbevindingen en de methodologische sterkte- en zwaktepunten van dit proefschrift. We vertalen bevindingen terug naar aanbevelingen voor de organisatie van algemene preconceptiezorg in het Nederlandse zorgsysteem.

ADDENDUM

LIST OF ABBREVIATIONS

AUTHORS AND AFFILIATIONS

LIST OF PUBLICATIONS

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DANKWOORD

LIST OF ABBREVIATIONS

ABS	Absolute rate
CCKL	Coördinatie Commissie ter bevordering van de Kwaliteit beheersing
CDC	Centers for Disease Control and Prevention (CDC)
CDT%	Carbohydrate deficient transferrin
CI's	confidence intervals
cm	centimeter
CPZ	Commission for Perinatal Health (CPZ)
EtG	ethylgluconeride
GBA	Gemeentelijke Basis Administratie (GBA) or the municipal administrative records
GP	General Practitioner
HP4All	Healthy pregnancy 4 All
INEQ	Inequality rate
IQR	Interquartile range
kg	Kilogram
PeTH	phosphatidylethanol
PCC	Preconception care;
PRN	Perinatal Registry Netherlands;
R4U	Rotterdam reproductive risk reduction score card;
SD	Standard deviation
SES	Socio-economic status;
SGA	Small for gestational age;
STND	Standardized rate
YHC	Youth Health Care

AUTHORS AND AFFILIATIONS

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Gouke J. Bonsel, Chantal A. ten Kate, Semiha Denktaş, Lieke L.C.A. de Jong-Potjer, Sophie C.N. Plasschaert, Jashvant Poeran, Eric A.P. Steegers, Carissah J.C. Stewarts, Sevilay Temel, Danielle W. van Veen, Sabine F. van Voorst, Amber A. Vos, Adja A.J.M. Waelput

From the Erasmus University College, Department of Social Sciences, Rotterdam, the Netherlands:
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From the Boston University School of Medicine, Department of Family Medicine, Boston Massachusetts, United States of America:
Brian W. Jack

LIST OF PUBLICATIONS

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S.F. van Voorst‡, A.A. Vos‡, E.A.P. Steegers, S. Denktaş. Analysis of policy towards improvement of perinatal mortality in the Netherlands (2004–2011). *Social Science and Medicine*. 2016 May;157:156-64.
‡ shared first authorship

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Four Barriers in the Delivery and Uptake of Preconception Care: A Qualitative Study
H. Ismaili M'Hamdi, **S.F. van Voorst**, W. Pinxten, I.D. de Beaufort, M. Hilhorst, E.A.P. Steegers. *Maternal and Child Health Journal*. 2017 Jan;21(1):21-28.

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M.K. Sijpkens, **S.F. van Voorst**, L.C. de Jong- Potjer, S. Denktaş, A.R. Rosman, L.C.M. Bertens, A.P. Verhoeff, E.A.P. Steegers. Effectiveness of preconception care recruitment strategies (the Healthy Pregnancy 4 All study). *Manuscript in preparation.*

PHD PORTFOLIO

PhD candidate:	Sabine Francisca van Voorst
Institution:	Erasmus MC
Department:	Obstetrics and Prenatal Medicine
PhD Period:	September 2012 to March 2015
Promotors:	Prof.dr. E.A.P. Steegers, Prof.dr. S. Denktaş
Copromotor:	dr. L.C. de Jong - Potjer

1. PhD training	Year	ECTS
Courses		
• Introduction to Biostatistics for Clinicians (NIHES).	2012	0.7
• Regression analysis for Clinicians (NIHES).	2012	1.4
• SPSS course for research in care (Erasmus MC).	2012	0.5
• Scale Development (Karma Short Course).	2012	0.5
• Basiscursus Regelgeving en Organisatie voor Klinisch onderzoekers (BROK; Erasmus MC).	2013	1.0
• Principles of analysis in Epidemiology (NIHES).	2014	0.7
Conferences		
Presentations at International conferences		
• 2nd European Conference on Preconception Care and Health, Rotterdam, the Netherlands:	2012	
· Oral presentation: "A systematic Review on Preconceptional Risk factors: New Risk Factors to Address in Preconception Care."		1.0
· Flash presentation: "Consensus on a definition on Preconception Care in the Netherlands."		0.5
· Flash presentation: "Experimenting with Programmatic Preconception Care in 14 High Risk Municipalities in the Netherlands."		0.5
· Flash Presentation: "A Systematic Review on Preconceptional Risk factors: New Risk Factors to Address in Preconception Care."		0.5

• Satellite meeting, Developmental Origins of Health and Disease (DOHAD), Rotterdam, the Netherlands: · Poster presentation: "Experimenting with Programmatic Preconception Care in 14 High Risk Municipalities in the Netherlands."	2012	0.5
• 61st Annual meeting of the Society for Gynaecologic investigation, Florence, Italy: · Poster presentation: "General Preconception Care in Primary and Youth Health Care – Implementation in the Netherlands."	2014	0.5
• Ministerial Conference of Women's Health, Rome, Italy: · Invited speaker: "Preconception Care: A Life course approach."	2014	1.0
• 3rd European Conference on Preconception Care and Health, Uppsala, Sweden: · Oral presentation: "Consumers preferences as a point of departure for social marketed preconception care consultations."	2016	1.0
Presentations at national conferences, seminars or research meetings		
• HP4All local kick-off meetings.	2012	1.0
• HP4All progress meetings with the field.	2013 - 2014	1.0
• HP4All program manager meetings.	2012 - 2014	1.0
• Research meetings of the Department of Obstetrics and Prenatal Medicine: three presentations on the design and progress of the HP4All Preconception care sub-study.	2012 - 2013	1.5
• HP4All Symposium Preliminary findings of the Preconception care sub-study.	2014	1.0
Attended meetings/ Conferences		
• Attending weekly research meetings of the Department of Obstetrics and Prenatal Medicine and giving 3 presentations.	2011 - 2014	5.0
• Annual RCOG Wladimiroff Symposia.	2011 - 2014	0.5
• Ready for a Baby (Klaar voor een Kind) End Symposium.	2013	0.3
• Symposium Urban Perinatal Health (SCEN).	2011	0.3

PHD PORTFOLIO (CONTINUED)

2. Teaching	Year	ECTS
Lecturing		
• Guest lecture NIHES course: Urban Perinatal Health and Health Care. Lecture "Measuring Health Care Utilization – amongst minorities."	2012	1.0
• Guest lecture NIHES course: Maternal and Child Health. Lecture "Preconception Care."	2012	1.0
• Guest Lecture Erasmus Faculty of Medicine: Minor: circle of life. Lecture "Preconception Care."	2012	1.0
• Guest Lecture Erasmus University College (EUC): Introduction to the social sciences. Lecture: "Application of sociology in Health Care: Andersen's model for utilization of Health care services."	2014	1.0
• Annual Guest Lecture at the VAR (Rotterdam School of Midwifery). Lecture: "Preconception Care."	2012 - 2014	3.0
Trainings		
• Practical at HP4All's participating General Practices and Midwife practices. Practical: implementing tools for Preconception Care (ZwangerWijzer, PreconceptieWijzer).	2012 - 2013	1.0
• Practicals within the Peer Health Educators training.	2013	1.0
• Round table discussion about Preconception Care at the `Wereld café.´ VAR (Rotterdam School of Midwifery).	2015	1.0
• Practical about Preconception Care at the Erasmus Faculty of Medicine: Minor: Mystery of creation.	2015	0.5
Supervision activities		
• Supervising elective research programs: S. Plasschaert, C. Stewart.	2012 - 2014	4.0
• Supervising research: C. ten Kate.	2013 - 2014	1.0

Other		
• Obtaining approval by the Medical Ethics committee for the WMO associated multicenter study (Protocol title: Project Healthy Pregnancy 4 All, Aanpak babysterfte in Nederlandse gemeenten: ontwikkeling en implementatie van zorgexperimenten. Deel A: Zorgexperiment Preconceptiezorg MEC- 2012-425).	2012	1.0
• Obtaining approval by the Medical Ethics committee for the not-WMO associated study ("Women's preference for individual Preconception Care" (MEC-2013-586)	2013	1.0
• Answering questions of the City council about Municipal invitations for preconception care	2014	0.5
• Obtaining approval to receive data from the Municipal Administrative records of all 14 HP4All municipalities.	2012 - 2014	0.5
• Peer reviewing an article for a scientific journal	2014	0.5
• Collaboration with PREGEVA study (Dr. M. Franssen)	2013-2014	0.5

ABOUT THE AUTHOR

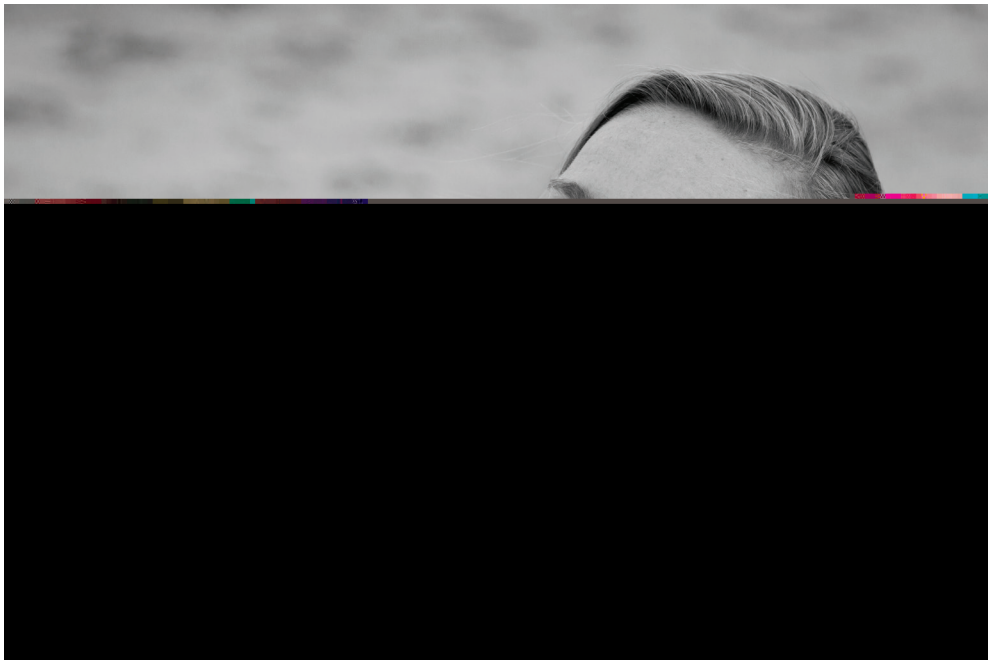
Sabine Francisca van Voorst was born as the first of a twin pregnancy in Rotterdam, the Netherlands (1984). As the daughter of a Civil Engineer and a French teacher, she spent the first years of her upbringing abroad in Burkina Faso, Indonesia, Curaçao and Suriname. At the age of 12 she repatriated to The Hague, where she graduated from the Aloysius College in 2002.

From 2002 – 2008 she went to Medical School at the University of Maastricht. In her final year, she combined a clinical internship with a research elective at the department of reproductive health of the Maxima Medical Center in Veldhoven and at the Cochrane Menstrual disorders and Subfertility group in Auckland, New Zealand. She graduated as a Medical Doctor in 2008.

After her study Sabine worked as a junior resident at the department of Obstetrics and Gynaecology of the Reinier de Graaf Gasthuis in Delft and in the Erasmus Medical Center in Rotterdam. Between 2011 and 2015 Sabine was a PhD Candidate within the Healthy Pregnancy 4 All study. In accordance to the hypothesis that the course of pregnancy and its outcome is influenced by events before and in early pregnancy, this study consisted of two pillars: preconception care and systematic risk assessment with medical and non-medical care-pathways. Sabine was dedicated to the design, implementation and evaluation of the preconception care sub-study. This study was the point of departure for her thesis.

In November 2015 Sabine started her residency in Obstetrics and Gynaecology.

Sabine is married to Ronald Koekkoek, they live in The Hague.



DANKWOORD

Over een paar dagen gaat mijn proefschrift dan echt naar de drukker. Een moment om terug te kijken op de afgelopen jaren.
Het is waar dat je vooraf niet kan bedenken wat je promotie je allemaal gaat brengen. Tijdens Healthy Pregnancy 4 All (HP4All) heb ik de de kans gekregen om de hele verloskundige zorgketen en de samenwerking met de publieke gezondheidszorg te verkennen. Die samenwerking met veel verschillende mensen in deze keten heeft geleid tot het resultaat dat voor jullie ligt. Zonder een groot aantal mensen was dit nooit zo goed gelukt en was het zeker niet zo leuk geweest.

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