Introduction

"Well begun is half done" - Aristotle & Mary Poppins

PRECONCEPTION CARE AND INTERCONCEPTION CARE

Preventive healthcare deserves more attention as the burden of healthcare costs, non-communicable (chronic) diseases and health inequalities increases.[1 2] The earliest form of primary prevention is preconception care (PCC), which can make a lifetime difference. PCC aims to prevent biomedical, behavioral, and psychosocial risks already before conception to promote health of the future child.[3 4] PCC after one pregnancy and before a potential next pregnancy is referred to as interconception care (ICC).[5] PCC and ICC can be considered part of a life course approach, improving the health of men and women of reproductive age and the health of future generations.[6] PCC and ICC also offer an opportunity to extend to obstetric care and to be integrated into routine healthcare visits for women and their children. It should lead to increased awareness on the association between maternal health, pregnancy outcomes and health in later life of both the woman and the child.

RATIONALE

In the periconception period, defined as the fourteen weeks before and ten weeks after conception, crucial developments of the gametes, embryo and placenta take place.[7] This development is of importance for the course of pregnancy and health outcomes. Embryonic development is associated with perinatal health outcomes as well as health later in life, such as birthweight and cardio-vascular health status in young children.[8 9] It is also known that this early periconceptional phase is already affected by risk factors. For instance, lifestyle behaviors such as smoking, alcohol consumption, and inadequate folic acid intake, are negatively associated with embryonic growth.[10-12] Therefore, prevention of risk factors should be aimed for as early as possible. Regular antenatal care starts too late to ovoid risk factors affecting early pregnancy.[13] PCC is needed to promote health in the periconception period. Based on associations of many risk factors with adverse perinatal outcomes, the content of PCC encompasses medical and non-medical domains. Thirteen domains for PCC activities have been described: health promotion, immunization, infectious diseases, medical conditions, psychiatric conditions, parental exposures, genetics and genomics, nutrition, environmental exposures, psychosocial stressors, medications, reproductive history.[14]

RELEVANCE

In the Netherlands, perinatal mortality has been high compared to other European countries.[15] In addition, in the Netherlands as well as many other countries, substantial inequalities in perinatal health exist.[16 17] These inequalities, in line with general health inequalities, negatively

affect people with a lower socio-economic status in particular.[16 18 19] The inequalities in perinatal outcomes are in a large part explainable by inequalities in both medical and non-medical risk factors, such as smoking, obstetric history and a low educational background.[20 21] In general, risk factors are widely prevalent in the preconception and early pregnancy period, providing opportunities for modification and prevention.[20 22-25] Lifestyle behavioral factors are known to be difficult to change and need a timely approach for it to be effective before pregnancy. Altogether, this emphasizes the need for PCC interventions to timely promote parental health and offer an opportunity for informed decision-making.

IMPLEMENTATION QUEST: POINT OF DEPARTURE FOR THIS THESIS

The need and potential benefits of PCC interventions are clear, yet implementation of PCC is lacking behind.[26] In the Netherlands, the Inspectorate of Public Health advised on periconceptional folic acid supplements for the prevention of neural tube defects in 1993 and this was translated in a mass media campaign two years later.[27 28] In 2007, an advisory report by the Dutch Health Council recommended integration of PCC into the Dutch obstetric care system.[29] Also around that time, guidelines and tools for professionals and the target group were developped.[30 31] However, actual implementation of individual PCC for the general public was not pursued due to political changes, and hence delivery of PCC remained uncommon.[32 33] Before politically advancing the implementation of PCC, more evidence was required on reaching high-risk women and on the effectiveness of PCC with regards to health outcomes.

Since reaching women before pregnancy is difficult, it is challenging to deliver PCC at a population level and different complementary approaches are likely to be necessary.[34 35] Important barriers to delivery of PCC include low awareness and perceived necessity about PCC of both healthcare providers as well as the target group.[36-39] The target group itself, recommends active outreach to address every couple with a desire to have a child as well as integration in routine care.[38 40] The latter is particularly relevant to ICC, since most women who have been pregnant are known to maternal and child healthcare providers. A valuable opportunity to embed ICC is within Preventive Child Healthcare (PCHC) centers, since almost all parents visit these clinics regularly with their young children for routinely scheduled appointments.[41] Such routine encounters provide a meaningful gateway to PCC and ICC, but are generally not optimally utilized.[5 33 41 42] Due to the scarce delivery of PCC and ICC the limited evidence of effective interventions to reduce risks before conception, the actual effectiveness of PCC and ICC remains debated.[4 14 43-46]

The described knowledge gaps and opportunities have resulted in experimenting with the implementation of PCC and ICC in the context of two nationwide programs. From 2011 until 2017,

the Dutch Ministry of Health, Welfare and Sport financed the successive programs HP4All-1 and HP4All-2 to improve perinatal and child health in disadvantaged neighborhoods.[17 47] Together, these programs aimed at broadening risk assessment and increasing health promotion from the preconception period through to pregnancy and the postpartum period, up to and including the interconception period. Within the programs, PCC and ICC interventions were developed, implemented and evaluated. These interventions involved stakeholders of municipal public healthcare and primary care, such as general practitioners, midwifes and PCHC professionals. The PCC and ICC interventions of the HP4ALL programs formed the point of departure for this thesis.

AIMS OF THE THESIS

The overall aim of this thesis is to evaluate and advance the implementation of PCC and ICC in primary care settings. This has resulted in the following objectives:

1. To evaluate the effects of recruitment strategies on uptake of PCC and ICC in primary care settings.
2. To study the effects of individual PCC and ICC consultations in primary care.
3. To assess the level of adoption and implementation of PCC and ICC by different stakeholders.
4. To explore considerations of women and healthcare professionals about involvement in PCC or ICC.
5. To examine and develop specific conditions related to the implementation of ICC;
    5.1. To describe the rationale for ICC in the context of geographical differences in the prevalence of adverse pregnancy outcomes and child poverty outcomes.
    5.2. To search for consensus on the concept of ICC.
    5.3. To investigate implementation outcomes of ICC in preventive child healthcare.

THESIS OUTLINE

This thesis is based on research performed within or parallel to the Healthy Pregnancy 4 All (HP4All) programs. The first program (HP4All-1) made no distinction between PCC and ICC; the second program (HP4All-2) focused specifically on ICC. This difference is reflected in the outline of this thesis, which consists of two parts.

Part I concerns different evaluations of the PCC intervention within HP4All-1, in search for opportunities to advance future implementation. In **chapter 2**, we evaluate outreach and PCC uptake following a four-pronged outreach strategy for PCC, which includes describing the

formation of a study cohort of women who visited the PCC services. Building upon this cohort, in **chapter 3** we report the effects of having a PCC consultation by determining the change in lifestyle behaviors and other indicators. **Chapter 4** provides a quantitative and qualitative process evaluation of the implementation of the HP4All-1 intervention at different levels (i.e. involvement of local stakeholders, the recruitment strategy and the PCC service delivery). In **chapter 5**, using semi-structured interviews, we report on exploring the perceptions about preparing for pregnancy, of women with a low to middle educational attainment including a subgroup from our PCC cohort, in search for possibilities to better adapt PCC to this vulnerable group.

Part II addresses conditions supporting the implementation of ICC within the HP4All2 program. In **chapter 6**, we illustrate the rationale for perinatal and postpartum preventive measures such as ICC by describing the Dutch prevalence of two adverse pregnancy outcomes and two child poverty outcomes, as well as geographical differences in the prevalence of these outcomes. In **Chapters 7,** we reflect on the concept of ICC (i.e. the term, definition, content, target group and outreach methods), based on a literature review and expert discussions. In **chapter 8**, we search for potential determinants of integrating ICC in PCHC using focus group discussions. The results of the implementation of ICC in PCHC are described in **chapter 9**, measured primarily as the proportion of eligible women who were informed about an ICC consultation (‘coverage’). Secondary study outcomes include implementation outcomes assessed by surveying women who consider to get pregnant and PCHC professionals.

REFERENCES

1. Marmot M, Allen J, Bell R, et al. WHO European review of social determinants of health and the health divide. Lancet 2012;380(9846):1011-29.
2. Stringhini S, Carmeli C, Jokela M, et al. Socioeconomic status and the 25 x 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1.7 million men and women. Lancet 2017;389(10075):1229-37.
3. Posner SF, Johnson K, Parker C, et al. The national summit on preconception care: a summary of concepts and recommendations. Matern Child Health J 2006;10(5 Suppl):S197-205.
4. Temel S, van Voorst SF, de Jong-Potjer LC, et al. The Dutch national summit on preconception care: a summary of definitions, evidence and recommendations. J Community Genet 2015;6(1):107-15.
5. Johnson KA, Gee RE. Interpregnancy care. Semin Perinatol 2015;39(4):310-5.
6. Misra DP, Grason H. Achieving safe motherhood: applying a life course and multiple determinants perinatal health framework in public health. Womens Health Issues 2006;16(4):159-75.
7. Steegers-Theunissen RP, Twigt J, Pestinger V, et al. The periconceptional period, reproduction and long-term health of offspring: the importance of one-carbon metabolism. Hum Reprod Update 2013;19(6):640-55.
8. van Uitert EM, Exalto N, Burton GJ, et al. Human embryonic growth trajectories and associations with fetal growth and birthweight. Hum Reprod 2013;28(7):1753-61.
9. Jaddoe VW, de Jonge LL, Hofman A, et al. First trimester fetal growth restriction and cardiovascular risk factors in school age children: population based cohort study. BMJ 2014;348:g14.
10. van Uitert EM, van der Elst-Otte N, Wilbers JJ, et al. Periconception maternal characteristics and embryonic growth trajectories: the Rotterdam Predict study. Hum Reprod 2013;28(12):3188-96.
11. Mook-Kanamori DO, Steegers EA, Eilers PH, et al. Risk factors and outcomes associated with first-trimester fetal growth restriction. JAMA 2010;303(6):527-34.
12. De-Regil LM, Pena-Rosas JP, Fernandez-Gaxiola AC, et al. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. Cochrane Database Syst Rev 2015(12):CD007950.
13. Atrash HK, Johnson K, Adams M, et al. Preconception care for improving perinatal outcomes: the time to act. Matern Child Health J 2006;10(5 Suppl):S3-11.
14. Jack BW, Atrash H, Coonrod DV, et al. The clinical content of preconception care: an overview and preparation of this supplement. Am J Obstet Gynecol 2008;199(6 Suppl 2):S266-79.
15. Mohangoo AD, Hukkelhoven CW, Achterberg PW, et al. [Decline in foetal and neonatal mortality in the Netherlands: comparison with other Euro-Peristat countries between 2004 and 2010] Afname van foetale en neonatale sterfte in Nederland: vergelijking met andere Euro-Peristat-landen in 2004 en 2010. Ned Tijdschr Geneeskd 2014;158:A6675.
16. Vos AA, Posthumus AG, Bonsel GJ, et al. Deprived neighborhoods and adverse perinatal outcome: a systematic review and meta-analysis. Acta Obstet Gynecol Scand 2014;93(8):727-40.
17. Denktas S, Poeran J, van Voorst SF, et al. Design and outline of the Healthy Pregnancy 4 All study. BMC Pregnancy Childbirth 2014;14:253.
18. Weightman AL, Morgan HE, Shepherd MA, et al. Social inequality and infant health in the UK: systematic review and meta-analyses. BMJ Open 2012;2(3).
19. Daoud N, O'Campo P, Minh A, et al. Patterns of social inequalities across pregnancy and birth outcomes: a comparison of individual and neighborhood socioeconomic measures. BMC Pregnancy Childbirth 2015;14:393.
20. Timmermans S, Bonsel GJ, Steegers-Theunissen RP, et al. Individual accumulation of heterogeneous risks explains perinatal inequalities within deprived neighbourhoods. European Journal of Epidemiology 2011;26(2):165-80.
21. Jansen PW, Tiemeier H, Looman CW, et al. Explaining educational inequalities in birthweight: the Generation R Study. Paediatr Perinat Epidemiol 2009;23(3):216-28.
22. Robbins CL, Zapata LB, Farr SL, et al. Core state preconception health indicators - pregnancy risk assessment monitoring system and behavioral risk factor surveillance system, 2009. Morb Mortal Wkly Rep Surveill Summ 2014;63(3):1-62.
23. Vink-van Os LC, Birnie E, van Vliet-Lachotzki EH, et al. Determining Pre-Conception Risk Profiles Using a National Online Self-Reported Risk Assessment: A Cross-Sectional Study. Public Health Genomics 2015;18(4):204-15.

24. Poels M, van Stel HF, Franx A, et al. Actively preparing for pregnancy is associated with healthier lifestyle of women during the preconception period. Midwifery 2017;50:228-34.
25. Stephenson J, Patel D, Barrett G, et al. How do women prepare for pregnancy? Preconception experiences of women attending antenatal services and views of health professionals. PLoS One 2014;9(7):e103085.
26. Shawe J, Delbaere I, Ekstrand M, et al. Preconception care policy, guidelines, recommendations and services across six European countries: Belgium (Flanders), Denmark, Italy, the Netherlands, Sweden and the United Kingdom. Eur J Contracept Reprod Health Care 2014:1-11.
27. de Walle HE, Cornel MC, de Jong-van den Berg LT. Three years after the dutch folic acid campaign: growing socioeconomic differences. Prev Med 2002;35(1):65-9.
28. Inspectorate of Public Health (The Netherlands). Prevention of neural tube defects. Rijswijk, 1993.
29. Health Council of the Netherlands. Preconception care: a good beginning. The Hague: Health Council of the Netherlands. Publication no. 2007/19E, 2007.
30. de Jong-Potjer LB, M. Bogchelman, M., Jaspar AHJVA, K.M. The Preconception care guideline by the Dutch Federation of GP's: Dutch College of General Practitioners (NHG); 2011 [Available from: https://guidelines.nhg.org/product/pre-conception-care.
31. Landkroon AP, de Weerd S, van Vliet-Lachotzki E, et al. Validation of an internet questionnaire for risk assessment in preconception care. Public Health Genomics 2010;13(2):89-94.
32. Vos AA, van Voorst SF, Steegers EA, et al. Analysis of policy towards improvement of perinatal mortality in the Netherlands (2004-2011). Soc Sci Med 2016;157:156-64.
33. van Voorst S, Plasschaert S, de Jong-Potjer L, et al. Current practice of preconception care by primary caregivers in the Netherlands. Eur J Contracept Reprod Health Care 2016;21(3):251-8.
34. Shannon GD, Alberg C, Nacul L, et al. Preconception Healthcare Delivery at a Population Level: Construction of Public Health Models of Preconception Care. Maternal and Child Health Journal 2013:1-20.
35. Lassi ZS, Dean SV, Mallick D, et al. Preconception care: delivery strategies and packages for care. Reprod Health 2014;11 Suppl 3:S7.
36. Poels M, Koster MP, Boeije HR, et al. Why Do Women Not Use Preconception Care? A Systematic Review On Barriers And Facilitators. Obstet Gynecol Surv 2016;71(10):603-12.
37. M'Hamdi H I, van Voorst SF, Pinxten W, et al. Barriers in the Uptake and Delivery of Preconception Care: Exploring the Views of Care Providers. Matern Child Health J 2017;21(1):21-28.
38. van Voorst SF, Ten Kate CA, de Jong-Potjer LC, et al. Developing social marketed individual preconception care consultations: Which consumer preferences should it meet? Health Expect 2017.
39. van der Zee B, de Beaufort ID, Steegers EA, et al. Perceptions of preconception counselling among women planning a pregnancy: a qualitative study. Family Practice 2013;30(3):341-6.
40. Poels M, Koster MPH, Franx A, et al. Parental perspectives on the awareness and delivery of preconception care. BMC Pregnancy Childbirth 2017;17(1):324.
41. de Smit DJ, Weinreich SS, Cornel MC. Effects of a simple educational intervention in well-baby clinics on women's knowledge about and intake of folic acid supplements in the periconceptional period: a controlled trial. Public Health Nutr 2015;18(6):1119-26.
42. Rosener SE, Barr WB, Frayne DJ, et al. Interconception Care for Mothers During Well-Child Visits With Family Physicians: An IMPLICIT Network Study. Ann Fam Med 2016;14(4):350-5.
43. Temel S, van Voorst SF, Jack BW, et al. Evidence-based preconceptional lifestyle interventions. Epidemiol Rev 2014;36(1):19-30.
44. Whitworth M, Dowswell T. Routine pre-pregnancy health promotion for improving pregnancy outcomes. Cochrane Database Syst Rev 2009(4).
45. Hussein N, Kai J, Qureshi N. The effects of preconception interventions on improving reproductive health and pregnancy outcomes in primary care: A systematic review. Eur J Gen Pract 2016;22(1):42-52.
46. Shannon GD, Alberg C, Nacul L, et al. Preconception healthcare and congenital disorders: systematic review of the effectiveness of preconception care programs in the prevention of congenital disorders. Matern Child Health J 2014;18(6):1354-79.
47. Waelput AJM, Sijpkens MK, Lagendijk J, et al. Geographical differences in perinatal health and child welfare in the Netherlands: rationale for the healthy pregnancy 4 all-2 program. BMC Pregnancy Childbirth 2017;17(1):254.