General discussion

The overall aim of this thesis was to evaluate and advance the implementation of PCC and ICC in primary care settings. The studies described in the thesis were conducted within or parallel to the Healthy Pregnancy 4 All (HP4All 1&2) programs. In community-based intervention studies, we have evaluated opportunities to advance the outreach and effects of PCC and ICC. In addition, in qualitative studies with women and healthcare professionals, we have explored factors influencing the implementation of PCC and ICC.

This last chapter reflects on the principal findings. It relates the results from the two parts of this thesis and its different chapters, structured around four domains associated with implementation (i.e. the innovation, the consumer, the provider and the organization or setting). Besides, methodological considerations and future perspectives are discussed.

PROMOTING THE OUTREACH AND EFFECT OF PCC AND ICC

Preconception health offers a genuine case for prevention

There is ample evidence on periconception risk factors associated with an adverse pregnancy course and adverse maternal and neonatal health outcomes.[1-3] Our studies have shown once again that both such risk factors as well as adverse pregnancy outcomes are highly prevalent (**chapter 2, 3, 6 and 9**). At the same time, geographical differences in the prevalence of premature and small for-gestational-age births indicate inequalities in adverse birth outcomes (**chapter 6**). Inequalities in behavioral risk factors were found in **chapter 3**. In line with other research, this suggests that women who are younger, have an ethnic minority background, or have a lower socio-economic status need more attention to prevent, for instance, inadequate folic acid supplementation and smoking.[4-7] Parous women need attention as well, since they may display more inadequate preconceptional behavior than nulliparous women and prior obstetrical complications can affect their future health and future pregnancies.[8] These findings demonstrate an important opportunity for prevention of risk factors before the start of pregnancy. PCC and ICC are thought to achieve this by optimizing preconception health; thereby regarding ICC not being substantially different from PCC (**chapter 7**). In a recent lancet series on preconception health, the authors also advocate the urge to ensure that women (or couples) are healthy before conception, for instance by identifying women contemplating pregnancy and simultaneous population-level initiatives reducing determinants of preconception risks, to “improve maternal and child health and reduce the growing burden of non-communicable diseases”.[9-11] In another lately published paper on Interpregnancy Care by the American Journal of Obstetrics and Gynecology, the authors state that all women of reproductive age who have been pregnant should receive interpregnancy care as a continuum from postpartum care to well-women care since it is an important opportunity for the prevention of many adverse health outcomes.[12]

PCC and ICC consultations can affect preconception health

Evidence that PCC and ICC interventions improve preconception health and pregnancy outcomes is scarce as illustrated in previous systematic reviews on PCC and the scoping review on ICC specifically, in **chapter 7**.[3 13 14] Our intervention study of PCC consultations with GPs and midwives contributes to the small number of previous studies that have suggested a positive change in folic acid supplementation and alcohol reduction after comprehensive PCC in primary care (**chapter 3**).[13] With the intervention, we aimed at areas with a higher prevalence of adverse pregnancy outcomes than the national average to include women who would benefit most. Although we assume that more attention may have been necessary for vulnerable women, behavior change and non-medical risk factors, it is hard to demonstrate the impact of the intervention on these specific components due to the small sample size. This points at the currently self-sustaining situation in which on the one hand proper implementation is needed to further study effectiveness, and on the other, evidence on effectiveness is required to support implementation. This impedes large-scale implementation of PCC and ICC. However, there is enough evidence on the possible harm of periconceptional risk factors that we should not wait to translate into practice the available knowledge on risk factors associated with adverse pregnancy or health outcomes.[15] It has societal and medical implications, as a way of disease prevention.[10] We should continue to increase the perceived importance of preconception health and care.

Promotion is necessary to increase outreach of PCC and ICC

The percentage of pregnant women reporting to have discussed at least one risk factor with a healthcare provider before pregnancy varies from 25% in a Dutch study to 51% in a British study.[5 16] The percentage of pregnant women who had a more comprehensive PCC consultation is likely to be much lower. Standardized delivery of PCC and ICC is uncommon in The Netherlands, as well as in other comparable western European countries.[17 18] An important barrier to the delivery and uptake of PCC is low awareness about PCC of both healthcare providers as well as the target group, which indicates the need for promotion of PCC.[19-21] Many promising suggestions had been made or studied, but earlier Dutch initiatives such as community-based research projects, web-based tools, and guidelines supporting the delivery of PCC had not resulted in routine practice of PCC at the time when the HP4All-1 program was started.[17 22-24]

In the HP4All programs, several of these ideas for PCC promotion have been combined and rolled out in multiple municipalities. We have shown that it is possible to promote delivery and uptake of PCC and ICC via different outreach strategies, but that it is challenging **(chapter 2, 4 and 9)**. It is challenging in terms of the execution (i.e. adoption of the strategy) and in terms of the effect. In absolute numbers, recruitment for PCC through large-scale mailings of invitation letters by municipalities and GPs resulted in the highest uptake of consultations. Yet, the effect was small relative to the number of pregnancies in these areas and diminished after three

months. More active recruitment by peer educators, GPs, midwifes, and PCHC professionals resulted scarcely in registered consultations. Still, this active recruitment has the advantage to be able to give further information and to reach vulnerable populations directly. As suggested by Velott et al., there is probably not a single "best" method for PCC promotion.[25]

Should we aim for different methods to promote preconception health?

To attain good population preconception health, requires either ensuring that the health of the total reproductive population is good, or ensuring that prospective parents prepare for pregnancy by aiming for good preconception health. In this thesis, the focus is on the latter by encouraging PCC and ICC consultations. However, the question is whether PCC or ICC consultations should be the single goal in the promotion of preconception health. The different outreach methods in **chapter 2 and 9** can have contributed to awareness about preparing for pregnancy in a much larger number of women than the number of PCC consultations may suggest. Unfortunately, this was outside the scope of our studies, but other Dutch studies have suggested that after local promotional campaigns more women are aware of the importance of folic acid and prepare for pregnancy.[26 27] Preparing for pregnancy by searching information and discussing single risk factors with a healthcare provider have been associated with improved preconception health behavior.[5 16]

Maybe the goal should be that prospective parents prepare for pregnancy, which can include a PCC or ICC consultation. This can also stimulate involvement of other parties that should offer a form of PCC, but not necessarily a comprehensive consultation, as suggested in the expert discussions reported on in **chapter 7**.

We can make a distinction between providing preconception information and preconception care. For instance, neurologists should address medication risks to ensure their patients prepare for pregnancy. In case the patient is actively considering becoming pregnant, the neurologist can refer to a comprehensive specialist PCC consultation. Although evidence is limited, there is a case for reproductive intention screening in routine general and specialist care.[28 29] Promoting comprehensive PCC consultations could then be part of a larger approach to promote preparing for pregnancy, since both can contribute to preconception health. This promotion has to serve the different needs of all couples and not unintentionally enlarge inequalities as found before in case of folic acid interventions.[30 31] Every woman should be informed about preventive options before pregnancy and be guided to informed choices.

CHALLENGES AND OPPORTUNITIES AT DIFFERENT LEVELS OF STAKEHOLDERS

To understand and improve implementation PCC and ICC, analysis at the level of the target group, the healthcare professionals, and organizations or settings is essential.[32 33]

Women

Our studies involved women of reproductive age (≥18 years) who were considering a future pregnancy (**chapter 2,3,5 and 9**). In **chapter 9**, we report on a study in which women were specifically recruited who were eligible for ICC and in **chapter 5**, we describe a study in which we recruited women with a low to intermediate education of which a subgroup had experience with PCC or ICC. Barrett et al. have described three different groups of women with varying levels of investment in pre-pregnancy healthcare, being the prepared group, the poor knowledge group and the absent pre-pregnancy period group.[34] We assume to have a representation of these different groups in this thesis, but we included probably few women from the so called absent pre-pregnancy period group. In our study populations, we studied attitude, knowledge, motivations, and constraints regarding preparing for pregnancy and PCC.

In general, women were positive about promotion of pregnancy preparation and PCC by healthcare providers (**chapter 5 and 9**). However, this did not necessarily lead to adequate preparation for pregnancy and rarely led to uptake of PCC. A recent systematic review has given an overview of barriers for the uptake of PCC; the most frequently identified barriers were not (fully) planning pregnancy, perceived absence of risks, lack of awareness and having pregnancy experience.[19] Facilitators were believing in benefits and availability of PCC.[19] The barriers identified in our studies show great overlap with the results of previous studies. Barriers included: 1) not wanting to plan pregnancy as it could lead to stress and could take away its 'naturalness', and 2) not being convinced of need to prepare because of perceived limited control over becoming pregnant and the health of the unborn (**chapter 5**). Furthermore, reasons not to make use of PCC included not knowing what to expect and not seeing the added value because of prior pregnancy experience (**chapter 9**). Women who received PCC also mentioned not knowing what to expect prior to the consultation and experiencing only modest added value (**chapter 3 and 5**). Many women mentioned that they would search for information themselves, for instance on Internet (**chapter 5 and 2**). Previous studies have shown that women are inclined to acquire preconception health information themselves, but that women still indicate interest in PCC by healthcare providers.[26 35] Reasons to prepare for pregnancy and (possibly) use PCC often relate to concerns about a healthy pregnancy and fertility (**chapter 2, 5 and 9**). Besides, women who used PCC suggested to include more examinations on general health and fertility in a PCC consultation, and to provide a more personalized approach responding to individual needs (**chapter 3**). Apart from these suggestions for improvement, women generally appreciated the

PCC consultation (**chapter 3**). It offered an opportunity to ask questions, get confirmation and be reassured (**chapter 5**). Patient experience with PCC has hardly been studied before, except studies that showed that general and specialist PCC did not induce anxiety.[36-38] Women had generally good knowledge of preconception health, yet knowledge gaps were also identified (**chapter 2 and 5**) and the meaning of 'PCC' was generally unknown. As suggested earlier in a systematic review, knowledge and awareness do not lead to healthy preconception behavior per se.[39] Different PCC approaches are probably needed for different individuals.[34] Overall, because of low awareness, promotion of preconception health and PCC is still necessary. Promoting preparing for pregnancy by raising preconception health at relevant encounters with the target group is a start.[40] Triggering knowledge gaps related to health concerns and fertility (e.g. the negative effects of smoking on the success of conception (**chapter 2 and 5**)) may motivate women for PCC and promote preconception health. In addition, illustrating ICC as opportunity to discuss prior pregnancy experiences, future pregnancies, and future health may promote uptake of ICC. These potential promoting factors were also identified in a previous study on consumer preferences for PCC.[35] Specific attention has to be given to aspects such as poor health literacy, perceived limited control and fear of medicalization to support all women in obtaining good preconception health. Lastly, including men's preconception health in PCC approaches, may promote preconception health at large.[40]

Healthcare providers

In this thesis we aimed at advancing PCC and ICC via GPs, midwives and PCHC providers.

Around the start of the HP4All-1 program, just one in four GPs had provided a PCC consultation in the past two months before they responded to a survey.[17] More GPs, about two thirds of them, had pointed out to patients a risk factor for in a future pregnancy. Relatively fewer midwives delivered a form of PCC.[17] In PCHC, ICC was still an unknown concept (**chapter 9**). The interventions had to change daily practice. Since healthcare providers in PCHC were unfamiliar with ICC, we started off by discussing possible facilitators and barriers for ICC. Resulting from these discussions, we expected that PCHC providers would acknowledge their unique positions in reaching women for ICC, but that the unfamiliarity with ICC would be a barrier (**chapter 8**). Therefore, we arranged local training sessions and supporting material (**chapter 9**). In HP4All1, midwives and GPs also received information and an explanation about delivering PCC consultations (**chapter 4**). Subsequent adoption of the interventions was fairly good, but varied as not all practices and providers decided to adhere to the intervention (**chapter 4 and chapter 9**). Some GP practices decided to refer to the local midwives for PCC. Low affiliation of GPs with PCC has been described before in another municipal project.[26] Roles and responsibility in PCC should be further outlined, as they appear not always clear both nationally as well as internationally.[5 18 20 41] As expected, most PCHC providers were positive about having a role in

ICC, but the majority preferred responsibility in giving advice about ICC consultations instead of delivering an individual ICC consultation.

However, the advice by PCHC providers resulted hardly in any ICC consultations. Also, the effects of the delivered consultations by midwives and GPs on behavior change should be improved (**chapter 3**). It would have been good to use observations of the consultations to study actual execution of the interventions. Some healthcare providers said that the low uptake made it difficult to become skilled in delivery of PCC. To promote uptake and normalize talking about ICC, we therefore advised PCHC to routinely inform women about ICC. In one PCHC center, they also routinely and proactively arranged an appointment for ICC in case women were interested after the regular PCHC visit, which might have helped both the PCHC provider and women in delivery and uptake of PCHC. Nevertheless, since it appears so difficult to increase uptake of individual PCC and ICC consultations, healthcare providers can optimize integration of PCC and ICC in their regular encounters with women. Studies that included few ICC items in routine preventive pediatric care show a promising role for PCHC providers.[42-45] In addition, midwives and gynecologists should optimally use the postpartum visit. This visit offers the possibility to reflect on the previous pregnancy and adapt ICC accordingly, but currently the postpartum visit is often a missed opportunity.[46] For GPs, many opportunities exist to integrate PCC and ICC when women of reproductive age visit them for a consultation. Especially, when these visits include consultations about chronic (or hereditary) diseases, drug prescriptions, contraceptive questions and fertility matters.

Organizations and settings

In the PCC and ICC interventions of this thesis, different healthcare organizations were involved. Local municipal project managers were recruited to facilitate local collaboration (**chapter 4**). Despite their involvement, it took effort to convince parties of their responsibility in promoting preconception health. Plenty studies and reports have advised that many parties should take responsibility in the implementation of PCC and ICC.[24] "Preconception interventions need to be supported by a social movement and political will, both of which require skilful engagement with powerful commercial interests."[11] This was also a common theme in our qualitative studies on ICC in which different representatives were involved (e.g. gynecologists, pediatricians, occupational physicians, policymakers, health insurance providers, members of national healthcare expertise centers and members of representative bodies) (**chapter 7 and 8**). One could argue that even the corporate sector may take responsibility in promoting preconception health, for instance of employees. Nevertheless, most parties currently actually take only moderate responsibility. It was promising that the national representative body of PCHC physicians and pediatricians showed their intention to promote PCC in their routine practice, however they have still not reached consensus on their plans.[47]

With the interventions and consensus on ICC described in this thesis, we have contributed to awareness about the importance of preconception health, preparing for pregnancy and PCC. However, context or setting factors proved to impede implementation. Firstly, this included limited resources (e.g. time and funding), for which we arranged some financial compensation during the HP4All programs (e.g. reimbursement for consultations). For PCC by midwives, reimbursement has been improved since 2017, however for PCHC reimbursement still depends on municipal negotiations. Secondly, the tendency towards a demand-driven approach in PCHC and general practice is not compatible with primary prevention such as PCC. Thirdly, segregated preventive care for women and children makes it difficult to integrate the two. Fourthly, culture norms make it unusual to discuss reproductive plans and this even applies to medical settings. Lastly, we lag behind in strategies to change behavior and reach the most vulnerable in society. The focus on areas with higher rates of adverse pregnancy outcomes and socio-economic deprivation is likely a good approach, but healthcare providers may need extra support. On a setting level, PCC implementation could be encouraged by normalizing preparing for pregnancy with political attention, campaigns, education and taking up PCC in quality measures. Current guidelines, the prospective 'Preconception Indication List' (mutual agreement by different health care disciplines about the content of and cooperation around PCC and ICC), and web-based tools such as 'Zwangerwijzer'[48 49] and 'Slimmer Zwanger'[50 51] are helpful, but need sufficient promotion. Although implementation outcomes at different levels of stakeholders are related to implementation success, we also realized the importance of contributions by individual persons. Some individual managers and healthcare providers really contributed to PCC and ICC and proved to be change leaders.

METHODOLOGICAL CONSIDERATIONS

Study designs

The studies in this thesis comprise a combination of different study populations, data sources, and study designs when evaluating various factors related to the implementation of PCC. This thesis included quantitative and qualitative studies, which involved data collected from women, healthcare providers and other stakeholders as well as registration-based data. Besides, different primary care settings for PCC and ICC were studied. As a result, a comprehensive overview of challenges and opportunities for the implementation of PCC and ICC is provided.

The fact that the intervention studies described in **chapter 2,3 and 9** were 'real-time' community-based studies can be seen as a strength, as it reflects 'real circumstances' instead of a controlled situation. This is useful for further refinement, applicability, and sustainability of the intervention, however it also has limitations. Firstly, since the GPs, midwives, and PCHC providers were neither familiar with the proposed intervention (PCC and ICC), nor with being

involved in research, it was challenging to execute the intervention and study as intended. It required balancing between adapting to the study setting and not changing the intervention too much.[52] In addition, it resulted in difficulty to obtain data; healthcare providers had to register information that we subsequently had to obtain, and they had to include participants to the studies. This led to logistic challenges and especially obtaining written informed-consent form participants proved to be complex. In HP4All-1, the problem was receiving informed consent forms by mail after study counseling by telephone by the research team (chapter 2 and 3). In HP4-All2, counseling and retrieving informed consent forms was done locally by the healthcare providers, yet this took place on a small scale. As a result, study populations were smaller than intended and entailed probably a selected group of women, which was a second limitation of our cohort studies. Women with a high socio-economic status seemed to be participating more often. Lastly, our cohort studies had a follow-up period limited to six months and had no comparative aspect. Altogether, this made it hard to disentangle the actual effect of the PCC and ICC interventions. Many studies in this thesis merely an exploratory character, which was the case for the described qualitative analyses as well. Besides, the qualitative studies may have included participants who were more positive about PCC than non-responders.

Implementation approach

We have applied an implementation research approach in this thesis. This includes applying and describing different stages described in implementation research. For instance we planned our interventions by means of using the framework of healthcare utilization of Andersen (**chapter 2**), analyzing possible determinants of implementation (**chapter 8**) and aligning with local stakeholders.[53] We have used multiple implementation research methods as described by Peters et al.[54] Accordingly, we studied various types of implementation outcomes, to some extent service outcomes (i.e. effectiveness), and client outcomes (i.e. experience or satisfaction).[33 54] We could have given more attention to observing the delivery of care and to other patients outcomes, since PCC comprises such comprehensive content. We explored multiple stakeholders' perspectives as suggested in the literature on implementation research.[33 53] Unfortunately, we were not able to study long-term outcomes such as sustainability, long-term health outcomes, equity and cost-effectiveness, which could yield valuable insights for the implementation of PCC.[53]

Specific conditions

We studied specific PCC and ICC situations, which included first of all primary care settings of GPs, midwives and PCHC. Secondly, we aimed at reaching more vulnerable populations for adverse pregnancy outcomes within a general population approach. Thirdly, we focused on individual PCC and ICC consultations and promotion thereof. Other approaches such as integration of PCC and ICC in routine primary, as well as specialist care could also be worthwhile. Our studies were embedded in the HP4All programs, and therefore project-based. This meant that

logistic, financial and motivational support was guaranteed, but only temporarily. Nonetheless, the interventions and results described in this thesis can be of value to other situations as well.

FUTURE PERSPECTIVES

In summary, this thesis shows that it is necessary and possible to include promotion of PCC and ICC in municipal, GP, and PCHC services. It also shows the potential of individual consultations at GPs and midwifery practices. At the same time, it demonstrates that the outreach and effect of PCC and ICC should be further enhanced. More should be done to inform prospective parents about preventive options before pregnancy and offer possibilities to make informed choices. Preparing for pregnancy (or conception), including PCC and ICC, needs continuous active and passive promotion to optimize preconception health. The limited adoption of PCC and ICC by healthcare professionals indicates room for improvement. While implementing PCC and ICC, special attention is warranted for vulnerable populations, difficult lifestyle behavior changes such as smoking, and socio-economically related risk factors. The importance of social determinants of health in the delivery of reproductive healthcare has also recently been underlined by American College of Obstetricians and Gynecologists.[55]

The observations in this thesis and reflection thereupon lead to the following recommendations for the implementation of PCC and ICC:

- Individual comprehensive PCC consultations with GPs and midwives should become more common. Simultaneously integrating PCC in different settings is necessary to promote preparing for pregnancy and PCC consultations. Integrate PCC in…
  - o … collective prevention strategies, routine primary care and specialist care.
  - o … a life course approach with multiple hits, i.e. ‘every woman every time’.
  - o … an active approach instead of ‘demand driven’ approach in providing care
  - o … particular in contraceptive care, fertility care, chronic care and psychosocial.
  - o … related health education programs, websites and mobile applications.
  - o … postpartum care for mother and child.

- Prerequisites for effective implementation of PCC and ICC in terms of delivery, uptake and improvements of health outcomes include the following:
  - o Involvement of (local) stakeholders (couples trying to achieve pregnancy, care providers, organizations and policymakers).
  - o Continuous education for all stakeholders on the importance of preparing for pregnancy in relation to fertility, embryonic development in first weeks of pregnancy and future health outcomes. This should be integrated in all forms of regular education and training curricula.

- Personalized PCC, responsive to individual needs such as health concerns, fertility concerns, and non-medical concerns. This needs further research, including research on different forms of PCC (e.g. individual consultations, integration in routine care, e-health, peer education) patient experience, behavior change and involvement of the partner.
- Increasing the role of the public healthcare system in response to health inequalities related to socio-economic inequalities, which may require specific support for vulnerable populations and changing context factors that keep these inequalities in place (i.e. promoting a healthy environment).
- Further integration of care by the curative domain and public health domain, from the preconception period, through pregnancy, into the interconception period. This requires further integration of maternal (or parental) care and pediatric care. It should be supported by more collaboration, less inefficient paper work, and sufficient reimbursement. Steps are taken on further integrated obstetric care (between the different tiers within obstetric care), reimbursement of PCC for midwives, and the formulation of the Preconception Indication List (PIL), but more efforts are needed.
- Available measures on preconception health and PCC. This requires better registration of preconception and prenatal risk factors for adverse pregnancy outcomes, as well as routine registration of PCC performance. Prioritization of certain measures is likely needed to integrate these measures in the existing Dutch Perinatal Registry called Perined. A suggestion of nine measures has been made in the USA: 1) pregnancy intention, 2) access to care, 3) preconception multivitamin with folic acid use, 4) tobacco avoidance, 5) absence of uncontrolled depression, 6) healthy weight, 7) absence of sexually transmitted infections, 8) optimal glycemic control in women with pregestational diabetes, and 9) teratogenic medication avoidance.[56] Ideally, registration would start preconceptionally and be linked to future pregnancies to evaluate and advance implementation of PCC and ultimately preconception health.

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