



**Karolinska  
Institutet**

**Institutionen för Kvinnors och Barns hälsa**

# **Fruktsamhet och Barnafödande** **-upplevelser, tankar och attityder bland kvinnor** **som inte fött barn**

**AKADEMISK AVHANDLING**

som för avläggande av medicine doktorsexamen vid Karolinska  
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## ABSTRACT

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*Aim:* The overall aim of this thesis is to describe experiences of fertility, interpret thoughts on childbearing, and compare attitudes to fertility and childbearing with background characteristics, among women not yet mothers.

*Methods:* In study I a phenomenological method was used to describe women's experiences of fertility. In study II a lifeworldhermeneutic approach was used to interpret women's thoughts on childbearing. In study III explorative factor analysis with principal component analysis was used to develop an instrument and in study IV principal component analysis was used and Student's t-test and ANOVA was performed between components and women's background characteristics. Data were collected from interviews with ten (I) and nine (II) women not yet mothers, and by using questionnaires (III, IV). A sample of 138 (III) and 424 (IV) women not yet mothers participated.

*Findings:* Fertility was experienced as paradoxical, as follows: fertility as a power that has to be suppressed, experiencing fertility in the present time and as a future finite possibility, and having one's own fertile responsibility governed by society (I). Childbearing includes dimensions of both immanence and transcendence. Immanence, as childbearing is seen as stagnant to women's freedom in present life. Transcendence, as childbearing is thought of as a project for future life, a part of female identity, and a conscious standpoint for which the woman wants to be prepared and for which she wants to create the best conditions (II). The instrument showed acceptable sample adequacy, factorability, and reliability. Three components were revealed, each one representing a specific underlying dimension of the construct (III). The results in study IV showed acceptable sample adequacy, factorability and reliability. The three components were *Importance for future*, *Hindrance at present* and *Female identity*. The youngest women (20-23y), of single status, students and women living in large cities were more likely to score high with the component *Hindrance at present*. Women having a partner were more likely to score high on *Importance for future* and *Female identity* (IV).

*Conclusions:* Fertility and childbearing are important to young adult women's future lives. Fertility is a possibility, and childbearing a future project initiated in present time, relevant to female identity. Attitudes to fertility and childbearing showed that it had importance for the women's future although it could be a hindrance at present. Fertility, childbearing and mothering need to be confirmed in young women's lives.

**Keywords:** Childbearing, fertility, phenomenology, hermeneutics, interviews, lifeworld, women's health, female identity, factor analysis, instrument development.

## Abstract

During the past decades our knowledge of innate immunology has increased drastically. This has improved our understanding about how innate immune cells can distinguish self from non-self, commensal bacteria from pathogens, and how it affects later adaptive immune responses. This knowledge can lead to new approaches for treatment of diseases and autoimmunity, and the development of new vaccines.

Vaccines are among the greatest inventions in medical history. However traditional vaccine approaches, such as live attenuated or inactivated viruses, have failed as vaccine candidates to address certain diseases including HIV/AIDS. Non-living non-replicating DNA vaccines represent an alternative approach, capable of inducing broad cell-mediated and humoral responses, while being safe and fast to produce. Still, despite its efficacy in animal models, DNA vaccines have not yet succeed to induce effective immune responses in human. To enhance the immunogenicity, a combination of more optimized vectors, delivery methods and adjuvants will be required. Skin electroporation (EP) is a promising method known to elicit robust humoral and CD8<sup>+</sup> T cell responses. However, the data on CD4<sup>+</sup> T cell responses has been limited. In **paper I** we compare immunization by skin EP with intramuscular injection, and find that EP increases both the magnitude and the polyfunctionality of the CD4<sup>+</sup> T cell responses to the HIV antigen Gag.

In **paper II** we show that plasmid encoding a secreted flagellin (pFliC) adjuvant promotes both humoral and MHC Class I-dependent cellular immunity when delivered through different routes representing dermal, systemic, and mucosal tissues. Additionally, it enhances mucosal humoral and MHC Class II-dependent cellular immunity when delivered mucosally. With *in vitro* studies we could show that secreted pFliC has the ability to activate macrophages through Toll-like receptor 5 (TLR5) but also cytoplasmic Nod-like receptor C4 (NLRC4), leading to inflammasome dependent cell death (pyroptosis).

In **paper III** we continue to study NLRC4 activation upon recognition of flagellin. We have established a system that allows for inducible expression of a NLRC4 agonist in a macrophage cell line, without additional stimuli. Using this system we have shown that NLRC4 induced caspase-1-dependent pyroptosis is independent of LPS priming, reactive oxygen species, or classical mitochondrial involvement. Nevertheless, pyroptotic macrophages release the alarmin high mobility group box 1 (HMGB1). Importantly, the functional isoform of HMGB1 is affected by the priming event and unprimed pyroptotic cells release a chemotactic form of HMGB1. However, priming during pyroptosis causes oxidation of the protein thereby changing it to a TLR4-agonist.

Combined, these studies will contribute to the understanding of the regulation of inflammasome activity, and how to deliver the next generation of DNA vaccines in combination with adjuvants.